

Literature on CytoSorb®-Therapy and Related Topics

Rating:

- very helpful and worth reading
- helpful and worth reading
- helpful and worth reading to a limited extent

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1 New Publications

1. Clinical Data

1.1 Studies

1.1.2 Cardiac

NEW; Impact of Intraoperative Haemoadsorption on Outcomes of Patients undergoing Aortic Surgery: A Single-Centre, Prospective, Observational Study

Mehta Y, Singh A, Singh M, Bhan A, Trehan N.

Interdisc CardioVasc & Thor Surg 2024; 38(4):ivae050

1.1.5 Other indications

NEW; CytoSorb® in burn patients with septic shock and acute kidney injury on continuous kidney replacement therapy was associated with improved clinical outcome and survival

Mariano F, Greco D, Depetris N, Mella A, Sciarrillo A, Stella M, Berardino M, Rizzo D, Gambino R, Biancone L.

Burns 2024; epub

1.3 Case Reports

1.3.4 Myoglobin

NEW; Severe rhabdomyolysis after exertional heat stroke treated with a hemoadsorber CytoSorb: lesson for the clinical nephrologist

Mikacic M, Begovic TI, Jerkovic I, Batinic MM, Kovacic V.

J Nephrol 2024; epub

3. Background & Reviews

NEW; Systematic review with expert consensus on use of extracorporeal hemoadsorption in septic shock: An Indian perspective

Mehta Y, Ansari AS, Mandal AK, Chatterjee D, Sharma GS, Sathe P, Umraniya PV, Paul R, Gupta S, Singh V, Singh YP.

World J Crit Care Med 2024; 13(1):89026

1. Clinical data

1.1 Studies

1.1.1 Septic Shock

The effect of cytokine adsorption on leukocyte and platelet activation after extracorporeal cardiopulmonary resuscitation

Zahn T, Schanze N, Staudacher D, Wengenmayer T, Maier S, Benk C, Gauchel N, Durschmied D, Supady A.
Thromb Haemost 2024; epub

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Summary

In this sub-study of the original CYTER study, the blood from 13 patients who received CytoSorb® for three days after extracorporeal cardiopulmonary resuscitation (ECPR) following cardiac arrest was compared to 11 controls. The aim was to better understand the cellular effects of cytokine adsorption by comparing the activation status of neutrophils, monocytes, and platelets as well as the formation of platelet-leukocyte complexes. At 48 hours after initiation of ECPR, flow cytometry analyses did not reveal significant differences in neutrophil (CD11b, CD66b, L-selectin, and PSGL-1) and monocyte (CD11b, L-selectin, and PSGL-1) surface molecule expression or in circulating platelet-monocyte complexes. In general, CD11b and CD66b expression on circulating neutrophils was significantly increased at 48 hours in patients who died until day 30. The authors conclude that there was no relevant effect of cytokine adsorption on neutrophil and monocyte activation during the first 48 hours after initiation of ECPR, but there was an observed relationship between activation of neutrophils and mortality which might highlight their potential role in the pathophysiology of post cardiac arrest syndrome.

<https://www.ncbi.nlm.nih.gov/pubmed/38081312>

Impact of CytoSorb and CKRT on hemodynamics in pediatric patients with septic shock: the PedCyto study

Bottari G, Guzzo I, Cappoli A, Labbadia R, Perdichizzi S, Creteur CSJ, Cecchetti C, Taccone FS.
Front in Pediatrics 2023; 11:1259384

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Summary

This single arm pilot study looked at the use of CytoSorb® in 17 consecutive children (>10kg) with septic shock and compared them to 13 historical controls who also received continuous kidney replacement therapy (CKRP) in the setting of septic shock but no CytoSorb®. CytoSorb® was inserted into the CKRP circuit and changed every 24 hrs for up to 96 hrs. The primary outcome of the study was a reduction in vasopressor or inotrope dose of > 50% from baseline by the end of CytoSorb® therapy and secondary outcomes included hemodynamic and biological changes, changes in severity scores, and 28-day mortality. Results showed that there were significant decreases in the Vasoactive Inotropic Score (VIS) and the Pediatric Logistic Organ Dysfunction 2 (PELOD-2) score at 72 and 96 hours from the start of the CytoSorb® therapy compared to baseline; the reductions were larger in the hemoadsorption group than in the historical control group. Additionally significant improvement in left ventricular ejection fraction (LVEF) % was observed in those patients with a severe to moderate dysfunction. Mortality at 28-days was lower, although not significantly, in the hemoadsorption group compared to the controls [5/17 [29%] vs. 8/13 [61%]. No serious adverse events related to the device were reported. In conclusion, the use of hemoadsorption with CytoSorb therapy was associated with a significant reduction in vasopressor requirements over time, compared to baseline values and to a control group. Potential benefits on survival were also observed. Multicenter studies are warranted to confirm these initial promising findings.

<https://www.ncbi.nlm.nih.gov/pubmed/37780052>

A matched case-control study on the effectiveness of extracorporeal cytokine adsorption in critically ill patients

Jerman A, Gubensek J, Berden J, Persic V.
Sci Rep 2023; 13(1):13464

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Summary

This retrospective study compared interleukin-6 (IL-6) levels in intensive care patients treated with or without cytokine adsorber (CytoSorb®). Patients between 2017 and 2021 who had at least two IL-6 measurements were included. They were divided into an adsorber group (52 pts) and a standard of care (SOC) group (94 pts). Use of CytoSorb® had to be for at least 3 hours, however, the time interval between ICU admission and the start of adsorber and SOC treatment, as

well as the number of adsorbers used or time on adsorbers respectively, were not reported. Matching was performed and the groups were compared regarding IL-6, lactate, C-reactive protein -CRP, procalcitonin, vasopressor requirement, and mortality rate. After matching, there were 21 patients in each group. Patients had similar age (CytoSorb® 53 v SOC 61), use of extracorporeal membrane oxygenation (ECMO, 24% v 24%) and renal replacement therapy (RRT, 100% v 100%) and baseline noradrenaline requirements (0.04 v 0.03 mg/kg/h), which were relatively low. Additionally, serum lactate (6.8 v 5.4 mmol/l), pH (7.27 v 7.21, CRP (182 v 167 mg/L), and IL-6 levels (2,441 v 2,552 ng/L) were comparable. There were no significant differences in the 20 hour time course of IL-6, lactate, CRP, procalcitonin and noradrenaline requirement between groups. Two-day and ICU mortality and estimated survival were also comparable. In this matched case-control study the authors report no difference in IL-6, inflammatory parameters, noradrenaline requirement or mortality observed between patients treated with adsorber or standard of care over this short time period.

<https://www.ncbi.nlm.nih.gov/pubmed/37596304>

CytoSorb hemoperfusion markedly attenuates circulating cytokine concentrations during systemic inflammation in humans in vivo

Jansen A, Waalders NJB, van Lier DPT, Kox M, Pickkers P.

Critical Care 2023; 27(1):117

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Summary

In this experimental study with an endotoxemia model, a highly standardized and reproducible human in vivo model of systemic inflammation, twenty-four healthy male volunteers were injected with bacterial lipopolysaccharide (LPS, bolus injection followed by infusion for three hours on day 0, and day 7) to induce an inflammatory response. During the first challenge (day 0), 12 patients were also put in CytoSorb® hemoadsorption for 6 hours and twelve not (controls). Plasma cytokine concentrations and clearance rates were determined. Results showed that LPS administration led to a profound increase in plasma cytokine concentrations during both LPS challenge days. Compared to the control group, use of CytoSorb® resulted in significantly lower plasma levels of tumor necrosis factor (TNF, - 58%, $p < 0.0001$), interleukin (IL)-6 (- 71%, $p = 0.003$), IL-8 (- 48%, $p = 0.02$) and IL-10 (- 26%, $p = 0.03$) during the first LPS challenge. No differences in cytokine responses were observed during the second LPS challenge on day 7 when CytoSorb® was not used. The absence of any device-related adverse events suggests that the safety profile of CytoSorb® therapy is favorable. The authors conclude that CytoSorb® hemoperfusion effectively attenuates circulating cytokine concentrations during systemic inflammation in humans in vivo, whereas it does not affect long-term immune function. Continuous treatment regimens and timely renewal of the CytoSorb® cartridge might further increase chances of demonstrating a clinical effect. CytoSorb® therapy may be of benefit in conditions characterized by excessive cytokine release.

<https://www.ncbi.nlm.nih.gov/pubmed/36945034>

Dosing of Extracorporeal Cytokine Removal In Septic Shock (DECRIS): protocol of a prospective, randomised, adaptive, multicentre clinical trial

Kanjo A, Molnar Z, Zadori N, Gede N, Eross B, Szako L, Kiss T, Marton Z, Malbrain M, Szuldrzynski K, Szrama J, Kusza K, Kogelmann K, Hegyi P.

BMJ Open 2021; 11(8):e050464

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Summary

This is the published protocol of the DECRIS study that aims to compare the efficacy of standard medical therapy with continuous extracorporeal cytokine removal with CytoSorb® therapy in patients with early refractory septic shock. In this prospective, randomised, controlled, open-label, international, multicentre, phase III study, 135 patients fulfilling the inclusion criteria will be randomly assigned to receive standard medical therapy (group A) or-in addition to standard treatment-CytoSorb® therapy. CytoSorb® treatment will be continuous and last for at least 24 hours. The CytoSorb® adsorber device will be changed every 12 (group B) or 24 hours (group C). The primary outcomes are shock reversal and time to shock reversal. Ethics approval has already been obtained from the Scientific and Research Ethics Committee of the Hungarian Medical Research Council (OGYEI/65049/2020). ClinicalTrials.gov registration number: NCT04742764.

<https://www.ncbi.nlm.nih.gov/pubmed/34446497>

Cytokine adsorption in severe, refractory septic shock

Wendel Garcia PD, Hilty MP, Held U, Kleinert E-M, Maggiorini M.

Intensive Care Medicine 2021; 47(11):1334-1336

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Summary

This letter to the editor describes a single centre observational study where use of CytoSorb® in 48 patients is compared to 48 historical matched control patients. Patients in the CytoSorb® group received 72 hours of treatment (3 x 24 hrs) initiated within 24 h from shock onset. All patients were critically ill (lactate 5.8 mmol/l and sequential organ failure assessment SOFA score of 14), however, before matching CytoSorb® patients had higher vasopressor requirements, more elevated interleukin - IL 6 and serum lactate levels (supplementary data). Within the 72-h intervention period, circulating IL-6 levels ($p=0.254$) and vasopressor requirements ($p=0.555$) decreased irrespective of cytokine adsorption use. Intensive care mortality was more pronounced in patients treated with cytokine adsorption than in the control group.

<https://www.ncbi.nlm.nih.gov/pubmed/34471938>

First Evaluation of a New Dynamic Scoring System Intended to Support Prescription of Adjuvant CytoSorb Hemoadsorption Therapy in Patients with Septic Shock

Kogelmann K, Hubner T, Schwameis F, Druner M, Scheller M, Jarczak D.

J Clin Med 2021; 10(13);2939

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Summary

In this multicentre retrospective analysis, 502 patients who received standard therapy for septic shock were analyzed, 198 also received adjunctive CytoSorb® therapy. To assess patients with early septic shock the authors created a dynamic scoring system (DSS) which included lactate level (and change over 6hrs), norepinephrine amount (and change over 6 hrs), need for 2nd catecholamine, use of hydrocortisone, and fluid bolus. Score parameters were documented at the time of diagnosis (T0) and 6 hrs later (T6). Survival on day 7 and days 56 as well as intensive care unit (ICU) and hospital mortality were then analyzed in regard to the score as well as the delay of hemoadsorption therapy. Septic shock was typically represented by 5 points, while >6 points indicated a situation refractory to standard therapy with the worst outcome in patients shown by >8 points. In the overall patient population, the primary endpoint analysis showed that higher DSS scores were associated with an increase in day 56 mortality (<6 vs. >8; $p = 0.004$). Also a significant 56-day, ICU and hospital survival advantage in CytoSorb® patients was seen when therapy was started early, despite the patients having had higher lactate levels and norepinephrine needs. A multivariate logistic regression model revealed that the use of the CytoSorb® device reduced the odds of mortality at day 56 by 44.8%. With regard to the DSS Score, for each one unit increase in score, the odds of mortality at day 56 increased by 23.7% ($p < 0.001$). Similarly, for each additional hour of CytoSorb® therapy delay, the odds of mortality at day 56 increased by 1.5% ($p = 0.034$). The authors conclude that this easy-to-apply scoring system, which requires only classical clinical hemodynamic information and one additional laboratory value (lactate clearance), might present an option to better detect patients benefitting from the initiation of hemoadsorption therapy in septic shock, but prospective validation in this regard is required first.

<https://www.ncbi.nlm.nih.gov/pubmed/34209001>

Can the cytokine adsorber CytoSorb® help to mitigate cytokine storm and reduce mortality in critically ill patients? A propensity score matching analysis

Scharf C, Schroeder I, Paal M, Winkels M, Irlbeck M, Zoller M, Liebchen U.

Ann Intensive Care 2021; 11(1):115

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Summary

In this retrospective propensity score matching analysis, 19 matched patient pairs were analyzed from an original 38 CytoSorb® treated patients and 105 non-CytoSorb® treatment patients. Patients with an interleukin-6 (IL-6) > 10,000 pg/ml were included who were treated from between October 2014 and May 2020. As noted by the authors, patients had a wide range of causes for their cytokine storm including septic shock, acute respiratory distress syndrome (ARDS), polytrauma, abdominal emergency, and solid organ transplant. To be included patients in the CytoSorb® (CS therapy) group had to have received CytoSorb® for at least 90 mins and only the first treatment cycle was included in the analysis, which meant comparing 0-12h before starting CS therapy with the status 12-24 hrs after starting CS therapy. Results showed that there was a significant reduction in IL-6 in patients with ($p < 0.001$) and without CS treatment ($p = 0.005$) and the median relative reduction with and without CS was 89% and 80% respectively. Furthermore, there was no significant difference in the relative change in C-reactive protein, lactate, or norepinephrine demand in either group and the in-hospital mortality was similar between groups (73.7%). This small, heterogenous study showed no difference in

IL-6 reduction, hemodynamic stabilization, or mortality in patients with CytoSorb® treatment compared to a matched patient population.

<https://www.ncbi.nlm.nih.gov/pubmed/34292421>

High-dose CytoSorb hemoadsorption is associated with improved survival in patients with septic shock: A retrospective cohort study

Schultz P, Schwier E, Eickmeyer C, Henzler D, Köhler T.

Journal of Critical Care 2021; 64:184-192

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Summary

In this retrospective cohort study, data from 70 patients with septic shock and/or non-infectious systemic hyperinflammation (SIRS), who were treated with CytoSorb® incorporated into their renal replacement therapy were analyzed. The 28-day mortality was compared to predicted mortality. On average, CytoSorb® hemoadsorption was used for 85.6 hrs (number of adsorbers per patient 3.2) and started within 24 hrs after diagnosis. The APACHE II score was 30.2±6.3 with a predicted mortality of 73.3%, while the observed mortality was significantly lower (50%, p<0.05). Interleukin 6 decreased significantly (2144 – 445 pg/ml) after 72 hrs. For all patients, lactate decreased from 2.29 – 1.35 mmol/l after 72 hrs, and PaO₂/FiO₂ index increased from 212 – 269. The authors also studied the amount of blood purified (= duration of CytoSorb® treatment * blood flow / body weight) and found that the higher the amount purified the better survival (8.5±4.4 vs. 6.1±3.6 l/kgBW, p=0.017). The authors identified three clusters of patient body weights (<6l/kgBW, 6-13l/kgBW and ≥13l/kgBW) with a linear dose response relation between blood purification volume and survival that was best in the highest volume cluster (83.3%; p=0.045). The application of CytoSorb® appears to be effective and without associated side effects in various conditions of septic shock and SIRS. In the investigated cohort of severely ill patients the observed mortality rate was reduced if the blood purification volumes had exceeded 6 l/kg. The results suggest that hemoadsorption might improve survival in these severely ill patients provided that the applied dose is high enough.

<https://pubmed.ncbi.nlm.nih.gov/33962219/>

Improved Survival beyond 28 Days up to 1 Year after CytoSorb Treatment for Refractory Septic Shock: A Propensity-Weighted Retrospective Survival Analysis

Brouwer WP, Duran S, Ince C.

Blood Purif 2021; 50(4-5):539-545

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Summary

This publication is the long-term follow-up retrospective analysis of patients with septic shock who were treated with continuous renal replacement therapy (CRRT) + CytoSorb® (n = 67) or CRRT alone (n = 49) (original publication *Brouwer et al., Crit Care* 2019; 317 in which patients were analyzed for all cause 28-day mortality). In this 2nd study the median follow-up for the **total** cohort was 30 days after ICU admission, and **333 days** for those who survived beyond 28 days (n = 59). The same statistical analysis was used in both studies. As with the first study factors associated with time to event were analyzed both weighted by stabilized inverse probability of treatment weights (sIPTW), as well as unweighted stratified by therapy received. Results showed that survival beyond 28 days was sustained up to 1 year after ICU admission for both treatment regimens: 80% vs. 87% for CytoSorb® vs. CRRT, respectively. Using the statistical analysis approach of sIPTW, CytoSorb® treatment showed a significantly higher survival rate compared to CRRT. Independent factors associated with long-term outcome in CytoSorb®-treated patients were baseline lactate levels, age in the presence of comorbidity, and presence of abdominal sepsis. A lactate level above 6.0 mmol/L at the start of CytoSorb® therapy had a positive predictive value of 79% for mortality. This is the first ever CytoSorb® longitudinal study. It shows that survival achieved with CytoSorb® and CRRT for patients with septic shock beyond 28 days from ICU admission may be improved with CytoSorb® treatment. Lactate levels above 6.0 mmol/L at the start of CytoSorb® therapy are predictive of worse outcome with high specificity and positive predictive value.

<https://pubmed.ncbi.nlm.nih.gov/33352555/>

Multicentred prospective investigator initiated study to evaluate the clinical outcomes with extracorporeal cytokine adsorption device (CytoSorb) in patients with sepsis and septic shock

Paul, R, Sathe P, Kumar S, Prasad S, Aleem Ma, Sakhalvalkar P.

World Journal of Critical Care Medicine 2021; 10(1):22-34

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Summary

This prospective, multicentre, observational study included 45 patients with septic shock (diagnosed <48 hrs prior to enrolment). Before and at the end of CytoSorb® treatment a number of data were recorded and compared. A minimum of two adsorbers per patient were used in either hemodialysis mode (12 hours), or continuous renal replacement therapy mode (24 hrs). Post CytoSorb® therapy, 26 patients survived. In the survivor group there was a (non-significant) tendency to require less vasopressors (norepinephrine 51.4%, epinephrine 69.4%, vasopressin 13.9% decrease). In the non-survivor group the use of vasopressors either remained unchanged or increased. In the survivor group lymphocytes, serum creatinine and lactate levels decreased significantly, and interleukin (IL) 1 and 6 levels decreased by 52.3% (non-significant). In the survivors the APACHE II and SOFA scores both significantly reduced by the end of treatment. Survivors spent 4.44 days in ICU and non survivors 8.5 days. There were no adverse events noted including no significant changes to albumin and platelets. There was a 75% survival rate in patients given treatment within 24 hrs of admission. Overall, the authors observed improved clinical outcome in terms of reduced mortality as compared to predicted, improved hemodynamics as indicated by MAP, and reduced use of vasopressors and their doses. They conclude that CytoSorb® might be an effective adjuvant therapy in stabilizing septic shock patients, particularly if it is started within less than 24 hours after the onset of sepsis.

<https://pubmed.ncbi.nlm.nih.gov/33505870/>

Hemoadsorption with CytoSorb in Septic Shock Reduces Catecholamine Requirements and In-Hospital Mortality: A Single-Center Retrospective 'Genetic' Matched Analysis

Rugg C, Klose R, Hornung R, Innerhofer N, Bachler M, Schmid S, Fries D, Ströhle M.

Biomedicines 2020; 8(12):539

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Summary

In this retrospective single-center study, septic shock patients receiving CytoSorb® in addition to renal replacement therapy (n = 42) were analyzed and compared to closely matched control patients (n = 42). A generalized propensity-score and Mahalanobis distance matching method ('genetic' matching) was applied. Baseline comparability was high although the CytoSorb® group had higher Sequential Organ Failure Assessment (SOFA) scores (13 vs. 12) scores, and requirements for norepinephrine (0.54 vs. 0.25 ug/kg/min). CytoSorb® was started on average 21 hours after ICU admission, with most patients (38/42) receiving one treatment (24 hrs). While remaining fairly constant in the controls, the catecholamines levels were approximately halved to 0.26 ug/kg/min within 24 h after initiation of CytoSorb® therapy. In-hospital- as well as 28-day - mortality was significantly lower in the CytoSorb® group (35.7% vs. 61.9%, p=0.015 and 21.4% vs. 47.6%, p=0.029, respectively). Risk factors for mortality within the CytoSorb® group were high lactate levels (7.5 mmol/L) and low thrombocyte counts prior to initiation suggesting that this might indicate an absence of CytoSorb® benefit. This study shows that the addition of CytoSorb® to standard care in septic shock patients requiring renal replacement therapy approximately halved catecholamine requirements within 24 hrs. In-hospital as well as 28-day mortality were significantly reduced when compared to a generalized propensity-score and Mahalanobis distance matched group.

<https://pubmed.ncbi.nlm.nih.gov/33255912/>

Combined Use of CytoSorb® and ECMO in patients with severe pneumogenic sepsis

Akil A, Ziegeler S, Reichelt J, Rehers S, Abdalla O, Semik M, Fischer S.

The Thoracic and Cardiovascular Surgeon 2021; 69(3):246-251

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Summary

In this prospective case series, 13 patients with pneumogenic sepsis on high flow veno-venous extracorporeal respiratory support (vv-ECMO) and CytoSorb® were compared to retrospective data from 7 patients treated with ECMO alone. All patients in the CytoSorb® group survived to 30 days (57% mortality in the ECMO only group). The use of CytoSorb® resulted in the rapid and significant reduction in inflammatory markers (procalcitonin and C Reactive Protein). Patients in the CytoSorb® group could also be weaned off high dose catecholamine therapy within 48 hrs which was not the case in the ECMO only group. The authors conclude that the use of CytoSorb® in combination with ECMO is an effective therapy to prevent the escalation of sepsis, with rapid weaning off high dose catecholamines.

<https://www.ncbi.nlm.nih.gov/pubmed/32252114>

Cytokine Adsorption in Severe Acute Respiratory Failure Requiring Veno-Venous Extracorporeal Membrane Oxygenation

Rieder M, Duerschmied D, Zahn T, Lang C, Benk C, Lothar A, Biever P, Bode C, Wengenmayer T, Staudacher D, Supady A.

ASAIO J 2021; 67(3):332-338

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Summary

Veno-venous extracorporeal membrane oxygenation (V-V ECMO) is a last resort treatment option for patients with acute respiratory failure (acute respiratory distress syndrome [ARDS]). This is a report of a single-center registry data from nine all-comers with severe ARDS predominately from infectious cause, treated with V-V ECMO and cytokine adsorption using the CytoSorb® adsorber, compared with a control group of nine propensity score matched patients who had undergone V-V ECMO support without cytokine adsorption. Even though scores (SOFA - Severity of Organ Failure Assessment, RESERVE – Predicting Death for Severe ARDS on V-V ECMO) both predicted a higher mortality in the cytokine adsorption group, mortality was reduced in the CytoSorb® plus V-V-ECMO group compared with V-V ECMO alone. In total, 5 patients in the CytoSorb® plus V-V-ECMO group survived (55.6%), compared with 2 (22.2%) from the V-V-ECMO alone group. The need for fluid resuscitation and vasopressor support as well as lactate levels dropped significantly in the cytokine adsorption group within 72 hours, whereas vasopressor need and lactate levels did not decrease significantly in the control group. Therefore, the authors conclude that cytokine adsorption might be beneficial in patients with severe ARDS requiring V-V ECMO support by contributing to hemodynamic stabilization and, in turn impacting on survival.

<https://www.ncbi.nlm.nih.gov/pubmed/33181544>

Adsorption therapy in critically ill with septic shock and acute kidney injury: a retrospective and prospective cohort study

Schittek GA, Zoidl P, Eichinger M, Orlob S, Simonis H, Rief M, Metnitz P, Fellinger T, Soukup J.

Annals of Intensive Care 2020; 10(1):154

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Summary

The case series looked at whether hemoadsorption with CytoSorb® could influence intensive care unit (ICU) and hospital length of stay (LOS) and mortality as well as therapeutic support in patients with severe septic shock and sepsis associated acute kidney injury (SA-AKI) using a retrospective control group and prospective intervention group. All patients were treated in accordance with the local sepsis treatment protocol, however, to be included in the study, still had to have increasing catecholamine dependency (above 20 µg/min norepinephrine), elevated interleukin (IL) 6 levels >500 pg/ml, and required continuous veno-venous hemodiafiltration (CVVHDF) due to AKI (KDIGO stage 3). In the historical control group 33 patients were finally identified out of 672 patients with septic shock treated between 1/2012 and 12/2013. From 1/2015 to 5/2018 2,102 patients were treated with septic shock out of which 43 patients fulfilled the inclusion criteria for the CytoSorb® group. Severity of illness, as depicted by APACHE II, was higher in patients treated with hemoadsorption (39 versus 35), as was catecholamine dependency (norepinephrine 64 µg/min vs. 44 µg/min) and procalcitonin (28 v 7 ng/l). Approximately one cartridge per patient was utilised as the median (IQR 1, 2) for 35.5 h (17, 47). In univariate analysis of all patients, the authors found that LOS, ventilatory support, duration of CVVHDF and duration of catecholamine administration were significantly lower for patients in the hemoadsorption group (p < 0.01), however these differences did not remain significant in multivariate analysis.

<https://pubmed.ncbi.nlm.nih.gov/33206229/>

Hemoadsorption with CytoSorb® shows a decreased observed versus expected 28-day all-cause mortality in ICU patients with septic shock: a propensity-score-weighted retrospective study

Brouwer WP, Duran S, Kuijper M, Ince C.

Crit Care 2019; 23(1):317

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Summary

In this investigator-initiated retrospective study, patients with septic shock were treated with continuous renal replacement therapy (CRRT) + CytoSorb® (n = 67) or CRRT alone (n = 49). Patients were weighted by stabilized inverse probability of treatment weights (SIPTW), a statistical method applied to overcome differences in baseline patient characteristics and to make these independent from treatment assignment, with the target to mimic a randomized controlled trial. The primary endpoint was the 28-day all-cause mortality compared for CytoSorb® versus CRRT alone. Secondary endpoints included the comparison between the observed 28-day

mortality rate in the CytoSorb® treatment group versus the predicted mortality according to the SOFA score, and variables that predict mortality in the CytoSorb® group. This represents the largest cohort of septic shock patients treated with CytoSorb® therapy to date in which mortality was assessed as a primary outcome. At the start of therapy, CytoSorb®-treated patients had higher lactate levels ($p < 0.001$), lower mean arterial pressure ($p = 0.007$) and higher levels of noradrenaline ($p < 0.001$) compared to the CRRT group. For CytoSorb®, the mean predicted mortality rate based on a SOFA of 13.8 ($n = 67$) was 75%, while the actual 28-day mortality rate was 48% (mean difference – 27%, $p < 0.001$). By sIPTW analysis, patients treated with CytoSorb® had a significantly lower 28-day mortality rate compared to CRRT alone (53% vs. 72%, respectively, $p = 0.038$). Independent predictors of 28-day mortality in the CytoSorb® group were the presence of pneumosepsis, higher levels of lactate at the start of CytoSorb® and older age. In this study, measurements of antibiotic levels were not available. Nonetheless, there were no observations or indications of excessive need for antibiotics or persistence of infections in the CytoSorb® group. In summary, this study has demonstrated in the largest cohort of septic shock patients investigated to date, that CytoSorb® treatment was associated with a statistically significant improvement of 28-day survival, both on the basis of observed versus predicted mortality rates, as well as compared to a control group with CRRT alone.

<https://www.ncbi.nlm.nih.gov/pubmed/31533846>

Extracorporeal cytokine adsorption in septic shock: A proof of concept randomized, controlled pilot study

Hawchar F, László I, Öveges N, Trásy D, Ondrik Z, Molnar Z.

Journal of Critical Care 2019; 49:172-178

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Summary

The aim of this proof of concept, prospective, randomized pilot trial was to investigate the effects of extracorporeal cytokine removal with CytoSorb® applied as a standalone treatment in 20 patients with early (<24hrs) septic shock. Inclusion criteria also included: on mechanical ventilation; norepinephrine >10 µg/min; procalcitonin (PCT) >3 ng/mL; and without the need for renal replacement therapy (RRT). Patients were randomized into CytoSorb® ($n=10$) for 24 hours or Control groups ($n=10$). Clinical and laboratory data were recorded at baseline, 12, 24 and 48 hrs. Overall SOFA scores did not differ between the groups, however, in the CytoSorb®-group norepinephrine requirements and PCT concentrations decreased significantly ($p=0.016$ and $p=0.004$ respectively). Big-endothelin-1 concentrations were also significantly lower in the CytoSorb® group ($p = 0.003$). All patients in the CytoSorb® group survived to 48 hrs (2 patients in the control arm died before the 48 hr period). The authors note that the level of norepinephrine dose for the CytoSorb® group was almost twice that of the controls at study entry. There were no CytoSorb® therapy-related adverse events. This is the first trial to investigate the effects of early extracorporeal cytokine adsorption treatment in septic shock patients, used without RRT. CytoSorb® was found to be safe with significant effects on norepinephrine requirements, PCT and Big-endothelin-1 concentrations when compared to controls.

<https://www.ncbi.nlm.nih.gov/pubmed/30448517>

The effect of a novel extracorporeal cytokine hemoadsorption device on IL-6 elimination in septic patients: A randomized controlled trial

Schaedler D, Pausch C, Heise D, Meier-Hellmann A, Brederlau J, Weiler N, Marx G, Putensen C, Spies C, Jorres A, Quintel M, Engel C, Kellum JA, Kuhlmann MK.

PLoS One 2017; 12(10):e0187015

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Summary

This first clinical study ever conducted with CytoSorb® (2008 – 2011) was a randomized, controlled, open-label, multicenter trial that reported on the use of CytoSorb® for 6 hours daily for 7 days in 97 mechanically ventilated patients with severe sepsis or septic shock and acute respiratory distress syndrome (ALI / ARDS). The study was not able to detect differences in systemic plasma IL-6 levels between the two groups ($n = 75$; $p = 0.15$) although significant IL-6 elimination, averaging between 5 and 18% per blood pass throughout the entire treatment period was recorded. There was also no statistically significant difference in the secondary outcomes multiple organ dysfunction score, ventilation time and time course of oxygenation. The proportion of patients receiving renal replacement therapy at the time of enrollment was higher in the treatment group (31.9%) compared to the control group (16.3%). After adjustment for patient morbidity and baseline imbalances, no association of hemoperfusion with mortality was found ($p = 0.19$).

<https://www.ncbi.nlm.nih.gov/pubmed/29084247>

Extracorporeal Cytokine Elimination as Rescue Therapy in Refractory Septic Shock - a Prospective Single-Center Study

Friesecke S, Stecher SS, Gross S, Felix SB, Nierhaus A.

Artif Organs 2017; 20(3):252-259

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Summary

Mortality from refractory septic shock may reach 90-100% despite optimum therapy. In this study cytokine adsorption using CytoSorb® in addition to regular therapy was studied prospectively in 20 patients with refractory shock (defined as increasing vasopressor dose required to maintain mean arterial blood pressure above 65 mmHg or increasing lactate levels despite protocol-guided shock therapy for six hours). CytoSorb® treatment was started after 7.8 ± 3.7 hours of shock therapy. Following the initiation of CytoSorb®, noradrenaline dose could be significantly reduced after 6 ($p=0.03$) and 12 hours ($p=0.001$). Lactate clearance improved significantly. Shock reversal was achieved in 13 (65%) patients; 28-day survival was 45% (predicted mortality from the SOFA score was >80%). The use of CytoSorb® adsorption therapy resulted in shock reversal in two thirds of these particularly difficult to treat patients.

<https://www.ncbi.nlm.nih.gov/pubmed/28589286>

1.1.2 Cardiac

NEW; Impact of Intraoperative Haemoadsorption on Outcomes of Patients undergoing Aortic Surgery: A Single-Centre, Prospective, Observational Study

Mehta Y, Singh A, Singh M, Bhan A, Trehan N.

Interdisc CardioVasc & Thor Surg 2024; 38(4):ivae050

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Summary

The prospective observational study included all comers using 'quasi-randomization', i.e. strictly alternating inclusion on a 1:1 basis into either treatment including intraoperative haemoadsorption (HA) with CytoSorb or standard treatment. Sixty patients undergoing elective aortic surgery were included. Types of surgery included ascending aortic aneurysm including aortic root surgery (Bentall procedure, redo Bentall, Bentall and mitral valve replacement, and Bentall and coronary artery bypass grafting). In the treatment group, one adsorber was used for the duration of the cardiopulmonary bypass (CPB), being 135 mins. Primary outcomes were impact of CytoSorb on hemodynamic stability and need for vasopressors (vasoactive inotropic score: VIS), and sequential organ failure assessment (SOFA)-score. Secondary parameters included the impact of CytoSorb on the course of hyperinflammation using interleukin (IL)-6 and procalcitonin (PCT), duration of mechanical ventilation, and lengths of intensive care unit (ICU)- and hospital-stay. Results showed that noradrenaline (norepinephrine) requirements were significantly reduced in the CytoSorb group postoperatively compared to controls ($0.03\mu\text{g}/\text{kg}/\text{min}$ vs. $0.08\mu\text{g}/\text{kg}/\text{min}$, $p=0.004$ at 2h, and $0.02\mu\text{g}/\text{kg}/\text{min}$ vs. $0.04\mu\text{g}/\text{kg}/\text{min}$, $p=0.004$ at 24h). This translated into a significantly lower VIS score. SOFA-score was less in the CytoSorb group at all time points and reached statistical significance 2h postoperatively. Intraoperative CytoSorb use significantly reduced IL-6 levels ($383.85\text{pg}/\text{mL}$ vs. $638.35\text{pg}/\text{mL}$, $p<0.05$) which then remained lower at all time points. PCT levels were similar in the two groups at T1 (post induction), but the levels were significantly less at T2 (2 hours after CPB in the CytoSorb group, $5.62\text{ng}/\text{mL}$ vs. $11.93\text{ng}/\text{mL}$, $p=0.005$). Finally, the duration of ventilation (13.63 hours vs. 20.03), ICU (39.3 hrs vs. 50.93 hrs)- and hospital-stays (8.57 days vs. 10.83 days) were all significantly shorter in the CytoSorb group compared to controls. In conclusion, in this prospective, observational study, use of CytoSorb as an adjunctive therapy in patients undergoing aortic surgery was associated with significantly improved hemodynamics, reduced inflammatory response, shorter time on mechanical ventilation and shorter ICU and hospital stays.

<https://www.ncbi.nlm.nih.gov/pubmed/38514401>

Effect of haemoadsorption during cardiac surgery for S. aureus endocarditis - a REMOVE trial post-hoc analysis

Caldonazo T, Van den Eynde J, Doenst T, Kirov H, Franz M, Hagel S, Lehmann T, Diab M.

Eur J Cardiothorac Surg 2024; 65(3):ezae093

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Summary

This is a post-hoc analysis of the REMOVE trial* that randomized 288 patients with infective endocarditis (IE) who underwent cardiac surgery with hemoadsorption using CytoSorb or control. The primary outcome was the change in Sequential Organ Failure Assessment (SOFA), defined as the difference between the mean total postoperative and baseline SOFA scores within 24 hours of surgery. Among the total of 282 patients included in the original REMOVE trial, 73 (25.9%) had *S. aureus* IE (38 patients in the hemoadsorption group and 35 patients in the control group). The overall SOFA score did not differ between the groups and neither did 30-day mortality. There were also no differences observed with regard to any of the other secondary outcomes. The authors conclude that based on this post-hoc analysis from the original REMOVE trial, the intraoperative use of hemoadsorption in patients with *S. aureus* IE was not associated with a reduction in postoperative organ dysfunction, 30-day mortality or other major clinical end-points.

*Diab et al., *Circ* 2022; 145(13):959-968

<https://www.ncbi.nlm.nih.gov/pubmed/38460546>

Use of intraoperative haemoadsorption in patients undergoing heart transplantation: A proof-of-concept randomized trial

Nemeth E, Soltesz A, Kovacs E, Szakal-Toth Z, Tamaska E, Katona H, Racz K, Csikos G, Berzsenyi V, Fabry S, Ulakcsai Z, Tamas C, Nagy B, Varga M, Merkely B.

ESC Heart Failure 2024;11(2):772-782

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Summary

In this randomized control trial the effect of intra-operative CytoSorb® use compared to standard care was studied in 55 orthotopic heart transplantation (OHT) patients (30 CytoSorb® and 25 standard care). Results showed that the CytoSorb® group had significantly lower vasoactive-inotropic scores (VIS, $p=0.046$), a 6.4 fold decrease in the odds of developing vasoplegic syndrome ($p=0.028$), lower procalcitonin (PCT) levels, shorter duration of mechanical ventilation (MV) hours ($p=0.025$), and intensive care unit stay (ICU, $p=0.022$). Patients in the CytoSorb® group also had lower rates of acute kidney injury ($p=0.004$), renal replacement therapy ($p=0.037$) and more stable hepatic bilirubin excretion. The authors also measured the intraoperative changes in the immunosuppressant, mycophenolic acid (MPA), used to prevent organ transplant rejection and found that concentrations were comparable to the control group at all pre-defined time points. There was also no increase in the frequency of early cardiac allograft rejection in the CytoSorb® group. In summary, in this the largest RCT to date in OHT patients, intraoperative use of CytoSorb® was associated with better hemodynamic stability, less vasoplegia, mitigated PCT response, lower rates of AKI and need for RRT, and shorter durations of MV and ICU stay. There were no device related complications and no evidence of MPA adsorption.

<https://www.ncbi.nlm.nih.gov/pubmed/38111338>

Extracorporeal Blood Purification with CytoSorb in 359 Critically Ill Patients

Pieri M, Bonizzoni MA, Belletti A, Calabró MG, Fominskiy E, Nardelli P, Ortalda A, Scandroglio AM.

Blood Purification 2023; 52(9-10):759-767

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Summary

This case series included 359 consecutive high risk intensive care patients who were treated with CytoSorb®. The main admission diagnosis was refractory cardiac arrest (34%), profound cardiogenic shock (28%), post cardiotomy shock (23%), respiratory failure (10%) and other (5%). Most patients (77%) were on intra-aortic balloon pump, impella or extracorporeal membrane oxygenation (ECMO), and 99% were on mechanical ventilation. CytoSorb® treatment was started according to clinical judgement by the attending physician where there was a severe inflammatory state with systemic clinical compromise and hemodynamic derangement. The adsorber was changed every 24 hrs and duration dictated by clinical need (average three in survivors and 2 in non survivors). All patients were described as responders to CytoSorb® treatment. The authors found a 30-day mortality of 49%, an ICU mortality of 57%, and a hospital mortality of 62%, all significantly lower than the 71% predicted by the Simplified Acute Physiology Score (SAPS) II score, and the 68% predicted by sequential organ failure assessment (SOFA) score calculated at the day of CytoSorb® start (day 0) suggesting a mortality benefit with the use of CytoSorb®. Parameters of shock and organ failure, and in particular the vasoactive inotropic score reduced during CytoSorb® treatment. In a relevant portion of the non-survivors multiple organ donation was possible (14% overall). CytoSorb® is described as safe and feasible to use in the acute care setting, with no adverse events recorded. The authors state that CytoSorb® treatment should be not exclusively evaluated in terms of cytokine and interleukin reduction, but also with a clinical perspective in terms of shock control, as shown by the reduction of inotropes and laboratory parameter improvement in these patients. The authors

conclude that CytoSorb® treatment was effective in reducing laboratory parameters of shock and vasoactive inotropic score with possible survival implications in a large population of critically ill patients.

<https://www.ncbi.nlm.nih.gov/pubmed/37669640>

The addition of Cytosorb in patients on VA-ECMO improves urinary output and ICU survival

Lovric D, Pasalic M, Krizanac S, Kovacic K, Skoric B, Jurin H, Milicic D, Premuzic V.

Ther Apher Dial 2024; 28(1):103-111

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Summary

The aim of this study was to analyze the efficiency of CytoSorb® in patients presenting with cardiogenic shock and treated with venoarterial extracorporeal membrane oxygenation (VA-ECMO). Sixteen patients were included and stratified according to the use of CytoSorb® in the first 24 h (9 CytoSorb® versus 7 controls) and results compared for different clinical outcomes. There were no differences in the group prior to use of CytoSorb®. Results showed that significantly lower vasopressor doses were required among patients treated with CytoSorb® at the initiation and before weaning from ECMO. Furthermore, these patients showed significantly higher urine output before weaning and lower lactate levels during the extracorporeal support. Finally, the mortality rate was lower among the CytoSorb® therapy group (22.2% vs 57.1%). While a decrease in vasopressor doses has already been shown to be associated with CytoSorb® use, this is the first study showing an increase in urinary output and a trend towards better survival among patients on VA ECMO treated with CytoSorb®.

<https://www.ncbi.nlm.nih.gov/pubmed/37697687>

Impact of CytoSorb® on interleukin-6 in cardiac surgery

Geisler D, Arleth N, Grabenwöger J, Arnold Z, Aschacher T, Winkler B, Mach M, Grabenwöger M.

Frontiers in Cardiovascular Medicine 2023; 10: 1166093

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Summary

The aim of this single centre study was to investigate the effect of CytoSorb® on interleukin (IL)-6 levels in patients undergoing complex cardiac surgery in comparison to a control group chosen within the same period. A total of 56 patients (28 CytoSorb®, 28 controls) undergoing acute and elective cardiac surgery were retrospectively analyzed with CytoSorb® being employed non-randomly at the surgeon's discretion. The primary endpoint was the difference in IL-6 levels between the groups and secondary endpoint was periprocedural mortality. The CytoSorb® group was however, as noted by the authors, generally sicker, with e.g. twelve CytoSorb® patients scheduled as re-do surgery, compared to 0 in the control group. There were also significantly more ascending aorta replacements and aortic arch replacements (partial / full) in the CytoSorb® group compared to controls. This resulted in significantly longer surgery and cardiopulmonary bypass times. Results showed no significant effects on IL-6 levels between the two groups. IL-6 peaked on the first postoperative day (HA: 775.3 ± 838.4 vs. control: 855.5 ± 1,052.9 pg/ml, p = 0.856). In total, three patients died in the HA group, none in the control (p = 0.996). In patients with an increased EuroSCORE II of 7 or more there was a reduced IL-6 response compared to patients with an EuroSCORE II below 7 (178.3 ± 63.1 pg/ml vs. 908.6 ± 972.6 pg/ml, p-value = 0.00306). The authors conclude that there were no significant reductions in IL-6 levels or periprocedural mortality through intraoperative HA with CytoSorb® in patients undergoing cardiac surgery. However, this study was able to show a reduced immunologic response in patients with a high EuroSCORE II. The routine application of CytoSorb® in cardiac surgery to reduce inflammatory mediators has to be scrutinized in future prospective randomized studies.

<https://www.ncbi.nlm.nih.gov/pubmed/37711559>

Impact of a VA-ECMO in Combination with an Extracorporeal Cytokine Hemadsorption System in Critically Ill Patients with Cardiogenic Shock-Design and Rationale of the ECMOsorb Trial

Haertel F, Lehmann T, Heller T, Fritzenwanger M, Pfeifer R, Kretzschmar D, Otto S, Bogoviku J, Westphal J, Bruening C, Gecks T, Kaluza M, Moebius-Winkler S, Schulze PC.

J Clin Med 2023; 12(15):4893

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Summary

This is a published protocol of a single center, blinded randomized control trial looking at the use of CytoSorb® with veno-arterial extracorporeal membrane oxygenation (VA-ECMO) or VA-ECMO alone in patient with cardiogenic shock refractory to conventional resuscitation (with or without prior cardiopulmonary resuscitation). The authors hypothesise that CytoSorb® will reduce cytokine levels leading to faster weaning from inotropic and mechanical circulatory support,

and ultimately to improved recovery. Fifty-four patients will be randomized in a 1:1 fashion to the intervention or control group over a 36-month period. The primary endpoint of the study (called ECMO_{sorb}) is the improvement of the Inotropic Score (IS) 72 h after initiation of the adsorber. Prognostic indicators, including mortality rates, hemodynamic parameters, laboratory findings, echocardiographic assessments, quality of life measurements, and clinical parameters are all secondary outcome measures. A safety evaluation will encompass endpoints such as air embolisms, allergic reactions, peripheral ischemic complications, vascular complications, bleeding incidents, and the incidence of stroke. ClinicalTrials ID NCT05027529

<https://www.ncbi.nlm.nih.gov/pubmed/37568295>

Intraoperative ticagrelor removal via hemoadsorption during on-pump coronary artery bypass grafting

Hassan K, Geidel S, Zamvar V, Tanaka K, Knezevic-Woods Z, Wendt D, Deliargyris EN, Storey RF, Schmoeckel M. *JTCVS Open* 2023; 15:190-196

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Summary

This three centre study prospectively included 11 patients on ticagrelor undergoing urgent coronary artery bypass graft (CABG) surgery. CytoSorb® hemoadsorption was incorporated in the cardiopulmonary bypass (CPB) circuit and remained there for the duration of the pump run. Blood samples were collected pre and post CPB so that mean ticagrelor levels could be measured. The time interval between surgery and last ticagrelor dose was ≤48 hrs and the mean intraoperative hemoadsorption duration was 97 minutes with a mean flow rate through the device of 422 mL/min. Mean ticagrelor levels pre-CPB were 103±63.8 ng/mL compared to mean post CPB levels of 34.0±17.5 ng/mL (significant reduction of 67.1%, p< 0.001). There were no re-operations performed for bleeding and no BARC-4 bleeding events occurred. Median chest tube drainage over 24 hours was 520mL (375mL-930mL). Intraoperative integration of CytoSorb® into the CPB circuit was simple and safe without any device related adverse events reported. This is the first *in vivo* report showing that the intraoperative use of CytoSorb® can efficiently remove ticagrelor and significantly reduce circulating drug levels. As the authors state, whether this active removal can reduce serious postoperative bleeding in patients undergoing urgent cardiac surgery is currently being evaluated in the double blinded randomized Safe and Timely Antithrombotic Removal – Ticagrelor (STAR-T) trial.

<https://www.ncbi.nlm.nih.gov/pubmed/37808047>

Effect of intraoperative haemoadsorption therapy on cardiac surgery for active infective endocarditis with confirmed *Staphylococcus aureus* bacteraemia

Haidari Z, Leiler S, Mamdooh H, Fittkau M, Boss K, Tyczynski B, Thielmann M, Bagaev E, El Gabry M, Wendt D, Kribben A, Bertsch T, Ruhparwar A, Fischlein T, Kalisnik JM.

Interdisciplinary CardioVascular and Thoracic Surgery 2023; 36(1):ivad010

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Summary

This retrospective study of prospectively collected data included consecutive patients operated on for confirmed staphylococcus aureus infective endocarditis (SA-IE) at two centres in Germany. Patients whose intraoperative treatment included the use of hemoadsorption (HA) with CytoSorb® (75 pts) were compared to a control group (55 pts). The authors hypothesis was that using CytoSorb® in this setting was for the removal of *S. aureus* endotoxin by the adsorber, which might be the cause of postoperative vasoplegia and poor outcomes. There were no differences in the baseline characteristics. The mean EuroSCORE II for both groups was 11.9% and 12.0%, indicating a high-risk surgical population. Cardiopulmonary bypass time was 133 mins in the HA group and 142 mins in the control group. Results showed improved postoperative hemodynamic stabilization with a significantly decreased vasoactive-inotropic score (VIS) in the HA group at all time points from 6 – 72 hrs post operatively. Importantly, sepsis-related mortality (8.0% vs. 22.8%, p=0.02) as well as 30-day (17.3% vs. 32.7%, p=0.03) and 90-day overall mortality (21.3% vs. 40%, p=0.03) were also significantly lower in the HA group. New, postoperative renal failure requiring hemodialysis developed in 38 patients, 16 in the HA group and 22 in the control group (P = 0.03). In conclusion the intraoperative use of hemoadsorption with CytoSorb® during cardiac surgery for SA-IE was associated with significantly lower postoperative vasopressor and inotropic requirements and resulted in lower sepsis-related and overall 30- and 90-day mortality in this high-risk population.

<https://pubmed.ncbi.nlm.nih.gov/36802263/>

Intraoperative Hemoadsorption (Cytosorb™) during open thoracoabdominal aortic repair: A pilot randomized controlled trial

Doukas P, Hellfritsch G, Wendt D, Magliani M, Barbati ME, Jalaie H, Jacobs MJ, Gombert A.
J Clin Med 2023; 12:546

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Summary

The aim of this pilot randomized control trial was to assess the feasibility and effect of perioperative hemoadsorption during open thoracoabdominal aortic aneurysm (TAAA) repair, which still carries a significant risk for postoperative complications and has a high mortality rate, especially in emergency cases. Ten pts were randomized to the intervention arm with CytoSorb® inserted into the cardiopulmonary bypass (CPB), and 17 patients to the control (standard treatment) arm, (including 3 non-randomized pts included during the roll-in phase). Baseline and perioperative characteristics were similar, with no device related adverse events reported. The mean CPB time was around 150 mins for both groups. Patients in the intervention arm who received intraoperative hemoadsorption had a shorter ventilation time (non-significant, median 88 hrs versus 510 hrs, $p = 0.08$) and required significantly less prolonged mechanical ventilation (MV), defined as greater than 21 days of MV for at least 6 h per day (1 vs. 9, $p = 0.03$). Moreover, the incidence of acute respiratory distress syndrome was significantly less in the intervention arm ($p = 0.02$, 0% versus 41% in the controls). Although non-significant, there was less incidence of re-thoracotomies (40% versus 52.3%), dialysis (50% versus 70%), and sepsis (30% versus 41%) in the intervention arm compared to the controls. In conclusion, this is the first pilot study showing that the intraoperative use of hemoadsorption in open TAAA -repair patients may be feasible and safe, although larger trials are needed to evaluate whether intraoperative hemoadsorption is associated with improved clinical outcomes.

<https://www.ncbi.nlm.nih.gov/pubmed/36675474>

Cytokine hemoadsorption with CytoSorb in post-cardiac arrest syndrome, a pilot randomized controlled trial

Monard C, Bianchi N, Poli E, Altarelli M, Debonneville A, Oddo M, Liaudet L, Schneider A.
Crit Care 2023; 27(1):36

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Summary

This pilot randomized control trial investigated the feasibility, safety and efficacy of hemoadsorption (HA) with CytoSorb® in cardiac arrest (CA) survivors at risk of post-cardiac arrest syndrome. Inclusion criteria for patients included those on norepinephrine (> 0.2 microg/kg/min), and/or with a serum lactate > 6 mmol/l, and/or a time-to-return of spontaneous circulation (ROSC) > 25 min. Those requiring ECMO or renal replacement therapy were excluded. Eligible patients were randomly allocated to either receive standard of care (SOC) or SOC plus HA. Hemoadsorption was performed as stand-alone therapy for 24 h, using CytoSorb® and heparin-protamine anticoagulation. 21 patients were enrolled, of whom 16 (76%) had out-of-hospital CA. Median time-to ROSC was 30 minutes. Ten were assigned to the HA group and 11 to the SOC group. The proportion of patients with out-of-hospital CA and shockable rhythm was higher in the intervention group compared with the control group. Hemoadsorption was initiated in all patients allocated to the HA group within a median delay of 25 (20, 27) h after CA or within 18 (11, 23) h of ICU admission respectively and conducted for a median duration of 21 hrs. The intervention was well tolerated except for a trend for a higher rate of aPTT elevation and mild (100-150 G/L) thrombocytopenia at day 1, but this did not lead to an increased need for transfusions. Interleukin (IL)-6 plasma levels at randomization were low (< 100 pg/mL) in 10 (48%) patients and elevated (> 1000 pg/mL) in 6 (29%). The median relative reduction in IL-6 at 48 h was 75% in the HA group versus 5% in the SOC group ($p = 0.06$). Among patients with very high IL-6 level at randomization ($> 10,000$ pg/mL, $n=5$), 2/2 patients in the HA group decreased their level to < 1000 pg/mL within 48 h versus only 1/3 in the control group. The authors show that in CA survivors at risk of PCAS, HA with CytoSorb® is feasible, safe and associated with a nonsignificant reduction in cytokine plasma levels although future trials are needed to further define the role of HA after CA.

<https://www.ncbi.nlm.nih.gov/pubmed/36691082>

Hemoadsorption in Complex Cardiac Surgery – A Single Center Experience

Manohar M, Jawali V, Neginahal S, Sudarshan GT, Muniraj G, Chakravarthy M.
J Clin Med 2022; 11:7005

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Summary

In this retrospective study, patients undergoing complex cardiac surgery with the use of CytoSorb® intraoperatively (23 pts), were compared to a group of control patients (29 pts). Criteria for the use of

CytoSorb® were patients with a cardiopulmonary bypass (CPB) time longer than 120 min and if the procedure was labelled as “complex” by the operating team, or it was a redo procedure. So almost all patients required combined procedures comprising of multiple valve surgery, coronary artery bypass grafting (CABG), and various procedures involving the aorta. There were some differences between the groups; CytoSorb® group was older (57 v 64 yrs) and the use of intra-aortic balloon pumps was only present in the CytoSorb® group (22%), while there were more redo procedures in the control group (45% v 22%) as well as longer cross clamp times (154 v 121.5 mins). The primary outcome was the change in vasopressor-inotropic score (VIS), pre- to post-operatively. The mean VIS score increase was significantly lower in the CytoSorb® group indicating better hemodynamic stability (3.5 v 5.5). In-hospital mortality was also lower in the CytoSorb® group (2 pts/9.1 % vs 6 pts/20.7 %). There were no device related adverse events seen. The authors conclude that the study provides real world data and excellent insight into CytoSorb®’s potential to improve clinical outcomes. Signals from this study point toward better hemodynamic stability with the use of CytoSorb® in complex cardiac surgery, and a trend towards lower mortality.

<https://pubmed.ncbi.nlm.nih.gov/36498579/>

Hemadsorption in patients requiring V-A ECMO support: comparison of Cytosorb vs Jafron HA330

Lesbekov T, Nurmykhametova Z, Kaliyev R, Kuanyshbek A, Faizov L, Bekishev B, Jabayeva N, Samalavicius R, Pya Y.

Artif Organs 2023; 47(4):721-730

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Summary

In this retrospective study, patients on veno arterial extracorporeal membrane oxygenation (vaECMO), 10 patients also on CytoSorb® were compared to 10 patients on vaECMO and Jafron HA330. In a further 10 vaECMO supported patients, no cytokine adsorption was used so served as a control group. Initiation of vaECMO was due to post cardiotomy refractory shock with ECMO implantation in the operating room in 90% of cases. Either CytoSorb® or HA330 was started at the discretion of the treating doctor for (suspected) severe hyperinflammation. Three consecutive procedures of cytokine hemoadsorption were applied for each patient. Evaluation of the levels of inflammatory markers (interleukin IL-1, 6, 8; C-Reactive Protein - CRP, leukocyte, lactate, procalcitonin - PCT, N-terminal pro B-type natriuretic peptide - NT-proBNP and tumor necrosis factor - TNF-alpha) were performed. Results showed that the patient groups were similar, although the hemoadsorption groups were sicker (higher APACHE II and EuroSCORE II scores). Consequently, here were statistically significant longer cardiopulmonary bypass (CPB) times, aortic cross clamp times and intensive care unit (ICU) stay in the cytokine adsorption groups than in the control group, but with no differences between devices. The mortality rate was higher in the control group than the cytokine adsorption groups (60 % vs 20%, p 0.02). All patients had elevated inflammatory markers in both the perioperative and immediate postoperative period. After 72 hours of intensive care, blood inflammation markers had a tendency to decline. The authors conclude that hemadsorption in patients requiring vaECMO support has a good therapeutic effect and that this effect is permanent for the whole period of extracorporeal cytokine hemadsorption application for both the CytoSorb® and HA330 devices.

<https://www.ncbi.nlm.nih.gov/pubmed/36398369>

Influence of Venoarterial Extracorporeal Membrane Oxygenation Integrated Hemoadsorption on the Early Reversal of Multiorgan and Microcirculatory Dysfunction and Outcome of Refractory Cardiogenic Shock

Soltész A, Molnár ZA, Szakal-Toth Z, Tamaska E, Katona H, Fabry S, Csikos G, Berzsenyi V, Tamas C, Edes IF, Gal J, Merkely B, Nemeth E.

Journal of Clinical Medicine 2022; 11(21):6517

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Summary

The purpose of this retrospective study was to evaluate the impact of venoarterial extracorporeal membrane oxygenation (VA-ECMO) integrated hemoadsorption using CytoSorb® on the reversal of multiorgan and microcirculatory dysfunction, and early mortality in refractory cardiogenic shock patients. From a total of 150 patients, it was possible to propensity score match 29 pairs of patients (119 control patients v 31 CytoSorb® pts). Subjects received either VA-ECMO supplemented with hemoadsorption or standard VA-ECMO management. There was a lower mean sequential organ failure assessment (SOFA) score (p = 0.04), lactate concentration (p = 0.015), P(v-a)CO₂ gap (p < 0.001), vasoactive inotropic score (p = 0.007), and reduced delta C-reactive protein level (p = 0.005) in the hemoadsorption compared to control groups after 72 hrs of CytoSorb® therapy use. In-hospital mortality was similar to predictions in the control group (62.1%) but was much lower than the predicted value in the hemoadsorption group (44.8%). There were less ECMO-associated bleeding complications in the hemoadsorption group compared to controls

($p = 0.049$). Overall, 90-day survival was better in the hemoadsorption group than in controls without statistical significance. The authors conclude that VA–ECMO integrated hemoadsorption treatment was associated with accelerated recovery of multiorgan and microcirculatory dysfunction, mitigated inflammatory response, less bleeding complications, and lower risk for early mortality in comparison with propensity matched control patients.

<https://www.ncbi.nlm.nih.gov/pubmed/36362744>

Removal of Apixaban During Emergency Cardiac Surgery Using Hemoadsorption With a Porous Polymer Bead Sorbent

Hassan K, Thielmann M, Easo J, Kamler M, Wendt D, Haidari Z, Deliargyris E, El Gabry M, Ruhparwar A, Geidel S, Schmoeckel M.

J Clin Med 2022; 11(19):5889

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Summary

In this three site, case controlled series, 12 consecutive control patients undergoing cardiac surgery whilst on concurrent therapy with the Factor Xa inhibitor, apixaban - prescribed for atrial fibrillation, were compared to the next 13 consecutive similar patients who were operated on with the CytoSorb® device integrated into the cardiopulmonary bypass (CPB) circuit (HA-group). Baseline characteristics were comparable between both groups. However, preoperative mean daily dose of apixaban was higher in the HA-group (8.5 ± 2.4 vs. 5.6 ± 2.2 mg, $p=0.005$), whilst time since last apixaban dose was longer in the controls (1.3 ± 0.9 vs. 0.6 ± 1.2 days, $p<0.001$). CPB time was not significantly different, with slightly longer times in the HA group (119.7 ± 30.5 vs. 109.1 ± 28.1 min, $p = 0.37$). No BARC-4 (Bleeding Academic Research Consortium) bleeding events and no repeat-thoracotomies occurred in the HA-group compared with 3 and 1, respectively, in the control group. Postoperative 24-hour chest tube drainage (CTD) volume was significantly lower in the HA-group (510 ± 152 mL vs. 893 ± 579 mL, $p=0.03$) and there was no need for 1-deamino-8-d-arginine-vasopressin (DDAVP [desmopressin]) administration to achieve hemostasis compared to controls, who received an average of 10 ± 13.6 mg ($p=0.01$). The total operation time (skin-to-skin) was shorter in the HA group without reaching statistical significance (279.8 ± 56.0 vs. 305.2 ± 76.9 min, $p = 0.35$). In conclusion, in this multicentre case controlled study in patients on apixaban undergoing emergent cardiac surgery, the intraoperative use of CytoSorb® was both feasible and safe. Compared to patients operated on without hemoadsorption, BARC-4 bleeding complications did not occur and 24 hour CTD was significantly lower as was the need for DDAVP administration. In brief: This is the first study to show that intra-operative hemoadsorption has the potential to improve outcomes in patients on apixaban undergoing non-deferrable on-pump cardiac surgery by mitigating the risk of perioperative bleeding complications.

<https://pubmed.ncbi.nlm.nih.gov/36233756/>

Preliminary Experience of Extracorporeal Cytokine Hemoadsorption during Left Ventricular Assist Device Implantation in Cardiogenic Shock Patients

Pausch J, Mersmann J, Bhadra OD, Barten MJ, Alassar YA, Schulte-Uentro L, Reichensperner H, Bernhardt AM. *Thorac Cardiovasc Surg* 2022; epub

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Summary

Out of 25 high-risk patients in cardiogenic shock (Interagency Registry for Mechanically Assisted Circulatory Support/INTERMACS class 1 and 2) who underwent continuous-flow left ventricular assist device (LVAD) implantation, 9 patients also had CytoSorb® integrated into the cardiopulmonary bypass at the discretion of the attending surgeon based on clinical criteria, and the results compared to the other 16 patients (controls). Preoperative patient characteristics, postoperative lactate clearance, vasopressor administration and mean arterial pressure, perioperative complication, and 30-day mortality rates were retrospectively analyzed. Apart from an increased rate of reoperations and significantly increased preoperative serum lactate levels within the CytoSorb® group, baseline characteristics including the severity of ventricular dysfunction and consecutive signs of end-organ failure were similar in both groups. Procedural characteristics including intraoperative volume management and postoperative vasopressor administration were similar in both groups. There was no difference regarding postoperative lactate clearance, although postoperative mean arterial pressure was significantly higher in the control group (71.3 vs. 57.4 mm Hg; $p < 0.01$). Furthermore, the 30-day mortality rate was significantly higher in the CytoSorb® group (33.3 vs. 0.0%; $p = 0.01$) with all deceased CytoSorb® group patients having been categorized as INTERMACS class 1. In conclusion, in this study, the use of extracorporeal

cytokine hemoadsorption during high-risk LVAD implantation was not associated with a decrease of postoperative vasopressor support, improved hemodynamics, or an accelerated lactate clearance.

<https://www.ncbi.nlm.nih.gov/pubmed/36216331>

Intraoperative hemoadsorption in high-risk patients with infective endocarditis

Haidari Z, Demircioglu E, Boss K, Tyczynski B, Thielmann M, Schmack B, Kribben A, Weymann A, El Gabry M, Ruhparwar A, Wendt D.

PLoS One 2022; 17(7):e0266820

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Summary

In this study, the clinical effects of intraoperative hemoadsorption in high-risk patients with infective endocarditis were evaluated. Patients with intraoperative hemoadsorption (CytoSorb®) were compared to patients without hemoadsorption (controls). The endpoints were the incidence of postoperative sepsis, sepsis-associated death and in-hospital mortality. Additionally, postoperative vasopressor need, systemic vascular resistance index and Sequential Organ Failure Assessment (SOFA) scores were compared. After propensity score matching, 70 high-risk patients were included. Rates of postoperative sepsis were similar (14 patients in the hemoadsorption group and in 16 patients in the control group, $p = 0.629$). However, four patients died due to postoperative sepsis in the hemoadsorption group, while 11 postoperative septic patients died in the control group, $p = 0.041$. In-hospital mortality was 34% in the hemoadsorption group versus 43% in the control group, $p = 0.461$. On ICU-admission and the first postoperative day, the cumulative vasopressor need (norepinephrine and epinephrine) was 0.17 versus 0.25 $\mu\text{g}/\text{kgBW}/\text{min}$, $p = 0.123$ and 0.06 versus 0.11 $\mu\text{g}/\text{kgBW}/\text{min}$, $p = 0.037$, and the systemic vascular resistance index was 1448 versus 941 $\text{dyn}\cdot\text{s}\cdot\text{cm}^{-5}$, $p = 0.013$ and 1156 versus 858 $\text{dyn}\cdot\text{s}\cdot\text{cm}^{-5}$, $p = 0.110$ in the hemoadsorption versus control group, respectively. Postoperative course of SOFA score normalized significantly ($p = 0.01$) faster in the hemoadsorption group. Respiratory failure requiring reintubation occurred in 20 pts (six in the hemoadsorption group and 14 in the control group, $p=0.034$). In summary, sepsis-associated death was significantly lower in patients with intraoperative hemoadsorption therapy, which was reinforced by favorable hemodynamic parameters and reintubation rates. Furthermore, the SOFA score showed significantly faster normalization during the postoperative course in the hemoadsorption group. The authors conclude that intraoperative hemoadsorption seems to attenuate the severity of postoperative sepsis and reduce sepsis-associated mortality in high-risk patients undergoing surgical therapy for infective endocarditis.

<https://www.ncbi.nlm.nih.gov/pubmed/35900987>

Single-Centre Retrospective Evaluation of Intraoperative Hemoadsorption in Left-Sided Acute Infective Endocarditis Cytokine adsorption in patients with post-cardiac arrest syndrome after extracorporeal cardiopulmonary resuscitation (CYTER) – A single- centre, open-label, randomised, controlled trial

Supady A, Zahn T, Kuhl M, Maier S, Benk C, Kaier K, Bottiger BW, Bode C, Lothar A, Staudacher DL, Wengenmayer T, Duerschmied D.

Resuscitation 2022; 173:169-178

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Summary

The aim of this small, single centre randomized controlled trial was to investigate the effect of cytokine adsorption in patients receiving extracorporeal cardiopulmonary resuscitation (ECPR) after cardiac arrest. Patients were assigned to veno-arterial extracorporeal membrane oxygenation (VA ECMO) support with or without CytoSorb® (1:1) replaced every 24 hours and removed after 72 hours. The primary endpoint was serum interleukin (IL)-6 concentration at 72 hours and secondary endpoints included 30-day survival, vasopressor support and biomarkers of end-organ injury. Of 50 patients enrolled in the trial, 41 patients were included in the primary analysis (22 CytoSorb® v 19 controls). Several prognosis-relevant parameters such as IL-6, blood lactate and arterial pH were worse at baseline in the CytoSorb® group compared with the control group. Furthermore, a greater proportion of patients in the CytoSorb® group had experienced OHCA (out of hospital cardiac arrest) compared with the control group (59% vs 42%). Median IL-6 levels (IQR) decreased from 408 (93.4-906.5) to 324 (134.3-4617.3) pg/mL and increased from 133 (56.2-528.5) to 241 (132.8-718.0) pg/mL in the cytokine adsorption and control group, respectively. Ten patients (45 %) died before 72 hours of VA ECMO in the CytoSorb® group, in comparison to five patients (26 %) dying before 72 hours of VA ECMO treatment in the control group. Three (14%) patients treated with cytokine adsorption and 8 (42%) patients treated without cytokine adsorption survived to day 30. Vasopressor support and other biomarkers of injury were similar between groups. No complications related to the use of the cytokine adsorbers were detected, and no additional early changes of the adsorbers were necessary. The authors conclude that cytokine adsorption in

patients receiving ECPR did not reduce serum IL-6 and had no significant effect on survival, vasopressor support, or biomarkers of injury.

<https://www.ncbi.nlm.nih.gov/pubmed/35143902>

Single-Centre Retrospective Evaluation of Intraoperative Hemoadsorption in Left-Sided Acute Infective Endocarditis

Kalisnik JM, Leiler S, Mamdooh H, Zibert J, Bertsch T, Vogt FA, Bagaev E, Fittkau M, Fischlein T.
Journal of Clinical Medicine 2022; 11(14);3954

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Summary

The objective of this study was to assess the efficacy of intraoperative hemoadsorption with CytoSorb® in active left-sided native (135 pts)- and prosthetic (67 pts) infective endocarditis (IE). Active IE was defined as an ongoing infection under antibiotic therapy. Patients with intraoperative hemoadsorption were compared to patients without hemoadsorption (control) over a 6 year period. Ninety-nine patients received intraoperative hemoadsorption inserted into the cardiopulmonary bypass circuit and 103 patients did not. Ninety-nine propensity-matched pairs were selected for final analyses. Postoperative sepsis and sepsis-related mortality was reduced in the hemoadsorption group (22.2% vs. 39.4%, $p = 0.014$ and 8.1% vs. 22.2%, $p = 0.01$, respectively). In-hospital mortality tended to be lower in the hemoadsorption group (14.1% vs. 26.3%, $p = 0.052$). Key predictors for sepsis associated mortality and in-hospital mortality were preoperative inotropic support, lactate-levels 24 h after surgery, C-reactive protein levels on postoperative day 1, chest tube output, cumulative inotropes and white blood cell counts on postoperative day 2, and new onset of dialysis. Multivariate regression analysis revealed, for the first time, that intraoperative hemoadsorption with CytoSorb® as a preventative measure was significantly associated with lower sepsis-associated, as well as in-hospital mortality. The authors conclude that intraoperative hemoadsorption holds promise to reduce sepsis and sepsis-associated mortality after cardiac surgery for active left-sided native and prosthetic valve infective endocarditis. Use of CytoSorb® intraoperatively was reported to be safe and easy to use without any adjustments needed for the intraoperative anticoagulant (heparin) regime.

<https://www.ncbi.nlm.nih.gov/pubmed/35887719>

Whole blood adsorber during CPB and need for vasoactive treatment after valve surgery in acute endocarditis – a randomized controlled study

Holmén A, Corderfeldt A, Lannemyr L, Dellgren G, Hansson EC.
Journal of Cardiothoracic and Vascular Anesthesia 2022; 36(8ptB):3015-3020

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Summary

In this single-center randomized controlled trial patients with infective endocarditis (IE) requiring urgent surgery were randomized to receive either intraoperative CytoSorb® therapy whilst on cardiopulmonary bypass circuit (10 pts) or standard care (9 pts). Results showed that the accumulated dose of norepinephrine (NE) was at least doubled in the control group postoperatively at all time points after surgery, however, this did not reach statistical significance. At 6 hours postoperatively, the median accumulated amount of NE in the intervention group was 28 µg vs 82 µg in the control group, at 24 hours 36 µg vs 114 µg, and after 48 hours it was 36 µg vs 261 µg. Duration of NE dose was also numerically longer in the control group (median 48 hrs vs 6 hrs in the intervention group) and mixed model analysis showed a trend for lower NE dose over time in the intervention group ($p=0.076$). There were numerical but not statistically significant differences in chest tube output at 12 hours (305 mL vs 500 mL) and 24 hours (380 mL vs 810 mL) as well as a significantly lower need for red blood cell transfusions in the CytoSorb® group (285 mL vs 1940 mL, $p=0.03$). The amounts of transfused plasma and platelets were also greater in the control group. There was a non-significant trend towards a shorter time on the ventilator and in the intensive care unit (ICU) in the CytoSorb® group as well as a trend towards better renal outcome in the intervention group compared to the control group at 48 hours after surgery. CytoSorb® therapy was feasible, and no device related adverse events were recorded. The primary endpoint for the study (amount of NE used 24 hrs and 48 hrs postoperatively) did not reach statistical significance, but the results showed a strong trend towards beneficial outcomes with the use of CytoSorb®, with better hemodynamic stability in the intensive care unit, and lesser amounts of transfused blood products postoperatively.

<https://pubmed.ncbi.nlm.nih.gov/35341666/>

Cytokine hemoadsorption during cardiac surgery versus standard surgical care for infective endocarditis (REMOVE): results from a multicenter, randomized, controlled trial

Diab M, Lehmann T, Bothe W, Akhyari P, Platzer S, Wendt D, Deppe AC, Strauch J, Hagel S, Günther A, Faerber G,

Sponholz C, Franz M, Scherag A, Velichkov I, Silaschi M, Fassl J, Hofmann B, Lehmann S, Schramm R, Fritz S, Szabo G, Wahlers T, Matschke K, Lichtenberg A, Pletz MW, Gummert JF, Beyersdorf F, Hagl C, Borger MA, Bauer M, Brunkhorst FM, Doenst T on behalf of the REMOVE Trial Investigators.

Circulation 2022; 145(13):959-968

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Summary

In this multi-center, non-blinded randomized control trial, 282 infective endocarditis patients with an indication for surgery were randomly assigned to either intraoperative hemoadsorption with CytoSorb® (138 pts) or standard treatment (144 pts). Results showed that there was no difference in the primary outcome (change in Sequential Organ Failure Assessment score (SOFA) from baseline, calculated for up to nine days postoperatively), mortality or duration of mechanical ventilation, use of vasopressors or renal replacement therapy. Plasma levels of four inflammatory mediators (interleukin (IL)-6, IL-1 β , IL-18, and CT-proET-1) were significantly lower in the CytoSorb® group at various time points. The authors conclude that routine use of CytoSorb® during cardiac surgery for infective endocarditis is not justified. As they note, the relatively short time on hemoadsorption may be a limitation, although this is a contentious issue. The distribution of adverse events between groups was equal.

<https://www.ncbi.nlm.nih.gov/pubmed/35213213>

Hemoadsorption of Rivaroxaban and Ticagrelor during Acute Type A Aortic Dissection Operations

Hassan K, Brüning T, Caspary M, Wohlmuth P, Pioch H, Schmoeckel M, Geidel S.

Annals of Thoracic and Cardiovascular Surgery 2022; 28(3):186-192

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Summary

In this retrospective cohort study 21 consecutive patients who had been admitted with acute type A aortic dissection requiring emergency surgery were investigated. Patients were pre-treated with either rivaroxaban (n = 9) or ticagrelor (n = 12). In ten of 21 cases a hemoadsorber (CytoSorb®) was installed into the heart–lung machine (HLM) and compared to the results of eleven patients who were operated on before CytoSorb® had been introduced into the department. Mean cardiopulmonary bypass (CPB) time without adsorption was 203 \pm 65 min and 207 \pm 45 min for the adsorption group. The adsorber was installed in the HLM system using a roller pump at 500ml/min. Results showed that the operation time was significantly shorter in the adsorber group (286 \pm 40 min vs. 348 \pm 79 min; p = 0.045). The postoperative 24-hour drainage volume was significantly lower after adsorption (p < 0.001; 482 \pm 122 ml vs. 907 \pm 427 ml) and no rethoracotomies had to be performed (compared to two [18.9%] among patients without CytoSorb® use). Also, patients without hemoadsorption required significantly more platelet transfusions (p = 0.049). Thirty-day mortality was 19% for all patients (3 from the non-adsorber group and 1 from the CytoSorb® group died). Intensive Care Unit stay tended to be shorter in the CytoSorb® group (10.2 \pm 7.6 vs. 8.0 \pm 6.9 days, non-significant). In summary, this is the first case series on patients with acute type A aortic dissection pre-treated with rivaroxaban or ticagrelor, who received intraoperative CytoSorb® during cardiopulmonary bypass. The method was found to be safe and effective for preventing bleeding and for improving outcome in this high-risk patient group.

<https://www.ncbi.nlm.nih.gov/pubmed/35046210>

Effect of Cytokine Adsorption on Survival and Circulatory Stabilization in Patients Receiving Extracorporeal Cardiopulmonary Resuscitation

Supady A, Zahn T, Rieder M, Benk C, Lothar A, Bode C, Wengenmayer T, Staudacher D, Kellum J, Duerschmied D.

ASAIO J 2022; 68(1):64-72

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Summary

In this study 23 patients who received extracorporeal cardiopulmonary resuscitation (ECPR) plus CytoSorb® hemoadsorption due to cardiac arrest, were compared to a propensity-matched cohort of 23 ECPR patients without cytokine adsorption. Survival, lactate clearance, vasopressor need, and fluid demand in both groups were compared. Cytokine adsorption was started after a mean of 14 hours after ECPR and the CytoSorb® cartridge was renewed after 24 hours, with treatment being continued for at least 72 hours. Survival to discharge from intensive care unit (ICU) was similar in both groups at around 20%. A decrease of serum-lactate, need for vasopressors, and fluid demand during the first 72 hours after ECPR was observed and there were no significant between-group differences. Impella 2.5 or CP percutaneous ventricular assist devices for left-ventricular unloading were used more often in the cytokine adsorption group. For platelet count and

international normalized ration (INR) values there were no significant differences discovered between cytokine adsorption and control groups. Duration of veno-arterial (V-A) Extracorporeal Membrane Oxygenation (ECMO) therapy was significantly longer in the cytokine adsorption group than in the control group (5.4 ± 5.1 vs. 2.6 ± 2.1 days, $p=0.02$) due to longer survival. Due to small case numbers and the retrospective design of the study, the authors state that the results should be interpreted cautiously and neither disprove nor confirm a clinically relevant treatment effect of cytokine adsorption.

<https://www.ncbi.nlm.nih.gov/pubmed/33883508>

Effect of Cytokine Adsorption on Survival and Circulatory Stabilization in Patients Receiving Extracorporeal Cardiopulmonary Resuscitation

Supady A, Zahn T, Rieder M, Benk C, Lother A, Bode C, Wengenmayer T, Staudacher D, Kellum JA, Duerschmied D.

ASAIO J 2022; 68(1):64-72

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Summary

In this study 23 patients who received extracorporeal cardiopulmonary resuscitation (ECPR) plus CytoSorb® hemoadsorption due to cardiac arrest, were compared to a propensity-matched cohort of 23 ECPR patients without cytokine adsorption. Survival, lactate clearance, vasopressor need, and fluid demand in both groups were compared. Cytokine adsorption was started after a mean of 14 hours after ECPR and the CytoSorb® cartridge was renewed after 24 hours, with treatment being continued for at least 72 hours. Survival to discharge from intensive care unit (ICU) was similar in both groups at around 20%. A decrease of serum-lactate, need for vasopressors, and fluid demand during the first 72 hours after ECPR was observed and there were no significant between-group differences. Impella 2.5 or CP percutaneous ventricular assist devices for left-ventricular unloading were used more often in the cytokine adsorption group. For platelet count and international normalized ration (INR) values there were no significant differences discovered between cytokine adsorption and control groups. Duration of veno-arterial (V-A) Extracorporeal Membrane Oxygenation (ECMO) therapy was significantly longer in the cytokine adsorption group than in the control group (5.4 ± 5.1 vs. 2.6 ± 2.1 days, $p=0.02$) due to longer survival. Due to small case numbers and the retrospective design of the study, the authors state that the results should be interpreted cautiously and neither disprove nor confirm a clinically relevant treatment effect of cytokine adsorption.

<https://www.ncbi.nlm.nih.gov/pubmed/33883508>

Rationale and Design of the Safe and Timely Antithrombotic Removal - Ticagrelor (STAR-T) Trial: A Prospective, Multi-center, Double-blind, Randomized Controlled Trial Evaluating Reductions in Postoperative Bleeding with Intraoperative Removal of Ticagrelor by the DrugSorb-ATR Device in Patients Undergoing Cardiothoracic Surgery within 48hrs from Last Ticagrelor Dose

Gibson CM, Mack MJ, Lee VT, Schneider DJ, Sellke FW, Ohman EM, Thourani VH, Doros G, Kroger H, Cutlip DE, Deliargyris EN.

Am Heart J 2021; 245:19-28

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Summary

This is the published protocol of a multicentre, double-blind randomized controlled trial called the 'Safe and Timely Antithrombotic Removal - Ticagrelor (STAR-T) trial'. The goal is to evaluate the effectiveness and safety of the DrugSorb-ATR hemoadsorption device for the intraoperative removal of ticagrelor to reduce postoperative bleeding in patients undergoing cardiothoracic surgery on cardiopulmonary bypass (CPB) within 48 hours of their last ticagrelor dose. Subjects will be randomized 1:1 to receive either the DrugSorb-ATR device or an identical sham device during CPB. The DrugSorb-ATR system comprises of a hemoperfusion cartridge filled biocompatible polymer beads, a pre-packaged tubing set for CPB integration and a flow detector to ensure device flow in the targeted range. The study will enrol up to 120 subjects from 20 U.S centers, and the primary outcome is the composite of fatal perioperative bleeding, moderate/severe/massive bleeding according to the Universal Definition of Perioperative Bleeding in Cardiac Surgery (UDPB) and 24hr chest tube drainage. The components of the composite are hierarchically ranked according to clinical significance and the primary analysis will utilize the Win Ratio method. Percentage change in ticagrelor levels before and after CPB (drug removal) will be the key secondary endpoint. Subjects will be followed through 30 days after the index operation. Additional safety endpoints include (among others) 30-day cardiac and all-cause mortality, as well as postoperative stroke and myocardial infarction (MI) during the index hospitalization. The results from STAR-T will potentially support FDA clearance of the device.

<https://www.ncbi.nlm.nih.gov/pubmed/34736855>

Initial experience with CytoSorb therapy in patients receiving left ventricular assist devices

Zhigalov K, Van den Eynde J, Zubarevich A, Chrosch T, Goerdt L, Arjomandi Rad A, Vardanyan R, Sa MPBO, Luedike P, Pizanis N, Koch A, Schmack B, Kamler, M, Ruhparwar A, Weymann A.

Artif Organs 2022; 46(1):95-105

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Summary

In this single centre study, the use of CytoSorb® intra-operatively in patients during left ventricular assist device (LVAD) implantation was compared to those who did not receive CytoSorb®. Over a 10 year period, 207 consecutive patients underwent LVAD implantation, of whom 72 received CytoSorb® therapy and 135 did not. Overall survival, major adverse events, and laboratory parameters were compared between 112 propensity score matched patients (CytoSorb®: 72 patients; non-CytoSorb®: 40 patients). Cardiopulmonary bypass time (and so use time of CytoSorb®) was around 70 minutes. Results showed that while white blood cells, C-Reactive Protein and interleukin- IL 6 significantly increased with all patients following LVAD implantation, the use of CytoSorb® did not influence this response (IL-6 67.7 ± 48.85 pre CS vs 82.9 ± 64.7 post CS). In-hospital mortality and overall survival during follow-up were similar between groups, however, patients treated with CytoSorb® were more likely to develop respiratory failure, and subsequently had higher need of mechanical ventilation for longer than 6 days post-implant, and requirement for a tracheostomy during hospitalization was more frequent. No other significant differences were observed with regard to major adverse events during follow-up. In conclusion, the need for larger scale randomized control trials to evaluate the potential role of CytoSorb® in improving outcomes of LVAD recipients therefore remains.

<https://www.ncbi.nlm.nih.gov/pubmed/34694644>

The effect of perioperative hemadsorption in patients operated for acute infective endocarditis - A randomized, controlled study

Asch S, Kaufmann T, Walter M, Leistner M, Danner BC, Perl T, Kutschka I, Niehaus H.

Artif Organs 2021; 45(22):1328-1337

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Summary

This small randomized controlled trial investigated the effects of perioperative hemoadsorption (HA) therapy with CytoSorb® on inflammatory parameters and hemodynamic status in 20 patients with infective endocarditis (IE). Ten patients were randomly assigned to HA therapy and 10 to the control group. HA therapy was initiated intraoperatively and continued for 24 hours, postoperatively. Adsorbers were exchanged every 8 hrs (total 4 adsorbers per patient). Cytokine levels (interleukin -IL-6, IL-1b, TNF-alpha), leucocytes, C-reactive protein (CRP) and procalcitonin (PCT) as well as catecholamine support and volume requirement were compared between both groups. Operative procedures included aortic (n=7), mitral (n=6) and multiple valve surgery (n=7). Median estimated perioperative mortality according to the EuroSCORE II was 8.5 vs. 3.6 (p=ns), however, all patients survived to discharge and there were no significant differences concerning median cytokine levels between both groups. CRP and PCT baseline levels were significantly higher in the HA group (59.5 vs. 26.3 mg/dl, p=0.029 and 0.17 vs. 0.05 microg/l, p=0.015) which equalized after surgery. Patients in the HA group required significantly higher doses of vasopressors at 12 hours postoperatively with a continuous decrease in both groups thereafter, as well as significantly more overall volume replacement. The incidence of postoperative adverse events was similar in both groups. The authors conclude that the use of HA therapy did not result in a reduction of inflammatory parameters nor in an improvement in hemodynamic parameters however, they note, that the relatively low severity of disease may be a possible explanation for the lack of a therapeutic effect. They suggest that a more expedient approach for future studies may be an observational approach rather than a randomized one. They also suggest a more targeted use of HA therapy with appropriate selection criteria is required.

<https://www.ncbi.nlm.nih.gov/pubmed/34152632>

Hemoadsorption during Cardiopulmonary Bypass in Patients with Endocarditis Undergoing Valve Surgery: A Retrospective Single-Center Study

Santer D, Miazza J, Koechlin L, Gahl B, Rrahmani B, Hollinger A, Eckstein FS, Siegemund M, Reuthebuch OT.

J Clin Med 2021; 10(4):564

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Summary

The aim of this retrospective single centre study was to evaluate the outcomes of infectious endocarditis patients undergoing valve surgery with CytoSorb® during cardiopulmonary bypass. Over a ten-year period from

2009 until 2019, 241 patients underwent valve surgery due to endocarditis and those who received CytoSorb® during surgery (n = 41, 17%) were compared to those without (n = 200), using inverse probability of treatment weighting in order to achieve balanced distributions of baseline characteristics. Even with this statistical approach, standardized difference with respect to the intake of platelet inhibitors did not drop below 0.2, indicating residual confounding. The results showed that in-hospital mortality, major adverse cardiac and cerebrovascular events and postoperative renal failure were similar in both groups. However, demand for norepinephrine, milrinone, red blood cell concentrates, and platelets were higher in the CytoSorb® group. In addition, there was also a higher incidence of reoperation for bleeding and a prolonged length of in-hospital stay observed in the CytoSorb® group. The authors conclude that there were no benefits of CytoSorb®-therapy observed in these patients with infective endocarditis undergoing valve surgery.

<https://pubmed.ncbi.nlm.nih.gov/33546164/>

Modulating the Inflammatory Response With Hemadsorption (CytoSorb) in Patients Undergoing Major Aortic Surgery

Mehta Y, Singh A, Singh A, Gupta A, Bhan A.

J Cardiothorac Vasc Anesth 2021 ;35(2):673-675

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Summary

In this retrospective pilot study, 8 patients undergoing elective major aortic surgery with CytoSorb® installed in the cardiopulmonary bypass (CPB) circuit were compared to 8 patients who received standard care. Despite the relatively short time on CPB (166 mins for the control group and 174 mins for the CytoSorb® group), patients who received CytoSorb® had significant reductions in interleukin-6 (IL-6) and procalcitonin levels. CytoSorb® use also preserved the mean arterial pressure better, with less norepinephrine requirements, and resulted in a better PaO₂/FIO₂ (PF) ratio and shorter durations of mechanical ventilation, intensive care unit stay, and hospital stay. The results may add important information to those who are planning to design prospective, randomized trials in this patient population.

<https://www.ncbi.nlm.nih.gov/pubmed/32620492>

Haemoadsorption – effective in reducing circulating fragments of the endothelial glycocalyx during cardiopulmonary bypass in patients undergoing on-pump cardiac surgery?

Hohn A, Baumann A, Pietroschinsky E, Franklin J, Illerhaus A, Buchwak D, Hinkelbein J, Zahn PK, Annecke T.

Min Anest 2021; 87(1):35-42

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Summary

Damage-associated molecular patterns (DAMPs) have been shown to enhance the inflammatory process and induce further the ischemia/reperfusion injury and endothelial glycoalyx degradation. This article included 15 patients undergoing on-pump cardiac surgery where the CytoSorb® adsorber was integrated into the cardiopulmonary bypass circuit. Pre- and post adsorber levels of DAMPs heparan sulphate (HEP), syndecan-1 (SYN) and hyaluronan (HYA) and the atrial natriuretic peptide (ANP) were measured at 10 (T1), 30 (T2), and 60 (T3) minutes after aortic cross-clamping and the end of CPB. Use of CytoSorb® significantly reduced concentrations of HEP, however concentrations of HYA, SYN and ANP could not be reduced.

<https://www.ncbi.nlm.nih.gov/pubmed/32643361>

Influence of hemoadsorption during cardiopulmonary bypass on blood vesicle count and function

Wisgrill L, Lamm C, Hell L, Thaler J, Berger A, Weiss R, Weber V, Rinoesl H, Hiesmayr MJ, Spittler A, Bernardi MH.

J Transl Med 2020; 18(1):202

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Summary

Microvesicles (MV) have recently been found to be responsible for part of the cellular communication network during inflammation. In this 2nd subgroup analysis of a previously published paper (Bernardi et al., Crit Care 2016; 1:96) the effect of circulating MVs during cardiopulmonary bypass (CPB) was assessed in a total of 18 patients with (n = 9) and without (n = 9) CytoSorb® inserted into the CPB. Levels of apoptotic bodies (AB – a vesicle that contains parts of a dying cell) was also assessed. MV and AB counting was conducted via flow cytometry and procoagulatory potential was measured by tissue factor-dependent MV assays. Both study groups exhibited comparable counts and post-operative kinetics in MV and AB subsets. Tissue factor-dependent pro-coagulatory potential was not detectable in the plasma at

any timepoint. Post-operative course and laboratory parameters showed no correlation with MV or AB counts in these patients undergoing CPB surgery. This study confirms that adding additional artificial surfaces into the CPB-circuit with the CytoSorb® device had no effect on the systemic immune cell activation in the circulation further confirming the safety of the device.

<https://www.ncbi.nlm.nih.gov/pubmed/32414386>

Assessing efficacy of CytoSorb haemoadsorber for prevention of organ dysfunction in cardiac surgery patients with infective endocarditis: REMOVE-protocol for randomised controlled trial

Diab M, Platzer S, Guenther A, Sponholz C, Scherag A, Lehmann T, Velichkov I, Hagel S, Bauer M, Brunkhorst FM, Doenst T.

BMJ Open 2020; 10(3):e031912

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Summary

This protocol describes the design of the REMOVE study (*Revealing mechanisms and investigating efficacy of hemoadsorption for prevention of vasodilatory shock in cardiac surgery patients with infective endocarditis*), an interventional randomised controlled multicenter trial for assessing efficacy of CytoSorb® in patients undergoing cardiac surgery for infective endocarditis. The change in mean total Sequential Organ Failure Assessment (SOFA) score between pre- and post-operative care is the primary endpoint with data on 30-day mortality, changes in cytokines levels, duration of mechanical ventilation, length of intensive care unit and hospital stay, and postoperative stroke as the secondary endpoints. An interim analysis will be conducted after including 25 participating patients per study arm (focusing on feasibility of recruitment as well as differences in cytokines and cell-free DNA levels). The protocol was approved by the institutional review board and ethics committee of the University of Jena, Germany, as well as by the corresponding ethics committee of each participating study centre. ClinicalTrials.gov registry (NCT03266302).

<https://www.ncbi.nlm.nih.gov/pubmed/32234739>

Extracorporeal Hemadsorption versus Glucocorticoids during Cardiopulmonary Bypass: A Prospective, Randomized, Controlled Trial

Taleska Stupica G, Sostaric M, Bozhinovska M, Rupert L, Bosnic Z, Jerin A, Ihan A, Klokocovnik T, Podbregar M. *Cardiovascular Therapeutics* 2020; 7834173

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Summary

In this randomized control trial, intraoperative hemadsorption (CytoSorb®) or methylprednisolone was compared to usual care in sixty complex cardiac surgery patients on cardiopulmonary bypass (CPB). Allocation was into three groups: Methylprednisolone (n 20), CytoSorb® (n 20), and Control group (usual care, n 20). Proinflammatory (TNF- α , interleukin (IL)-1 β , IL-6, and IL-8) and anti-inflammatory (IL-10) cytokines with complement C5a, CD64, and CD163 expression by immune cells were analyzed for the first five postoperative days, in addition to hemodynamic and clinical outcome parameters. The methylprednisolone group, compared to CytoSorb® and control groups had significantly lower levels of TNF- α (until the end of surgery, $p < 0.001$), IL-6 (until 48 h after surgery, $p < 0.001$), and IL-8 (until 24 h after surgery, $p < 0.016$). CD64 expression on monocytes was the highest in the CytoSorb® group and lasted until the 5th postoperative day ($p < 0.016$). IL-10 concentration (until the end of surgery) and CD163 expression on monocytes (until 48 h after surgery) were the highest in the Methylprednisolone group ($p < 0.016$, for all measurements between three groups). There were no differences between groups in the cardiac index or clinical outcome parameters. Methylprednisolone was reported to more effectively ameliorate inflammatory responses after CPB surgery compared to CytoSorb® or usual care however, this did not translate into better short-term outcomes. Use of CytoSorb® had a beneficial effect intraoperatively, with patients from the CytoSorb® group having the lowest need for norepinephrine, and patients in the Methylprednisolone group having the highest; however, this was seen only during surgery and did not reach statistical significance. CytoSorb® use compared with usual care caused higher prolonged expression of CD64 on monocytes and higher expression of CD163 on granulocytes, which however lasted only until the end of surgery. Hemadsorption with CytoSorb® was safe and well tolerated. The authors note that the effects of hemadsorption with CytoSorb® might have been more pronounced if the duration of CPB was longer (median bypass time was around 140 mins), or if only high-risk patients had been included (i.e., aortic arch surgery with hypothermic arrest and selective perfusion of brain, endocarditis surgery, and higher EuroSCORE II).

<https://www.ncbi.nlm.nih.gov/pubmed/32292492>

Cytokine Removal in Critically Ill Patients Requiring Surgical Therapy for Infective Endocarditis (RECREATE): An Investigator-initiated Prospective Randomized Controlled Clinical Trial Comparing Two Established Clinical Protocols

Gisler F, Spinetti T, Erdoes G, Luedi MM, Pfortmueller CA, Messmer AS, Jenni H, Englberger L, Schefold JC.
Medicine (Baltimore) 2020; 99(15):e19580

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Summary

Infective endocarditis (IE) can induce significant changes in the immune response with patients developing persistent functional immunological phenotypes characterized by a profound anti-inflammation and/ or functional "anergy" particularly in patients with unresolved infectious foci (previously referred to as "injury-associated immunosuppression" (IAI)). IAI can be assessed by monocytic human leukocyte antigen-DR (mHLA-DR) expression, a global functional marker of immune competence. Persistence of IAI is associated with prolonged intensive care unit length of stay, increased secondary infection rates, and death. Immunomodulation to reverse IAI has been shown to be beneficial in early immunostimulatory (randomized controlled) clinical trials. This protocol (RECREATE) is a prospective 1:1 randomized controlled clinical study to compare the course of mHLA-DR in patients scheduled for cardiac surgery for IE. Fifty-four patients will be randomized to receive either best standard of care plus CytoSorb® adsorption during surgery while on cardiopulmonary bypass (protocol A) versus best standard of care alone, that is, surgery without CytoSorb® (cytokine) adsorption (protocol B). The primary endpoint is a change in quantitative expression of mHLA-DR from baseline (preoperation visit 1) to day 1 post-OP (visit 4). This protocol was registered in ClinicalTrials.gov NCT03892174.

<https://www.ncbi.nlm.nih.gov/pubmed/32282706>

Intraoperative hemoadsorption in patients with native mitral valve infective endocarditis

Haidari Z, Wendt D, Thielmann M, Mackowiak M, Neuhäuser M, Jakob H, Ruhparwar A, El Gabry M.
The Annals of Thoracic Surg 2020; 110(3):890-896

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Summary

This retrospective non-randomized study included 58 consecutive patients with infective endocarditis of the native mitral valve who were undergoing surgery between January 2014 and July 2018. Thirty patients who received intraoperative CytoSorb® therapy were compared to 28 patients who didn't. The two groups of patients were comparable in their baseline characteristics prior to surgery. Results showed that postoperative sepsis occurred in only 5 patients in the CytoSorb® (hemoadsorption) group and in 11 patients in the control group (p=0.05). There were no sepsis-associated deaths in the CytoSorb® group, whereas five septic patients died in the control group (p=0.02). Thirty-day-mortality was 10% in the hemoadsorption group versus 18% in the control group (statistically non-significant). Patients in the CytoSorb® group also showed greater hemodynamic stability (less need for norepinephrine and epinephrine). The authors conclude that the data suggest that intraoperative hemoadsorption with CytoSorb® may improve surgical outcome in patients with mitral valve endocarditis.

<https://www.ncbi.nlm.nih.gov/pubmed/32059855>

Early use of hemoadsorption in patients after out-of hospital cardiac arrest - a matched pair analysis

Akin M, Garcheva V, Sieweke JT, Flierl U, Daum HC, Bauersachs J, Schafer A.
PLoS One 2020; 15(11):e0241709

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Summary

This study aimed to assess the effect of cytokine adsorption on mortality in patients following out-of-hospital cardiac arrest by comparing a patient cohort with hemoadsorption after resuscitation for out-of-hospital cardiac arrest (24 pts) matched in a 1:2 fashion to a control cohort without adsorption (48 pts). Patients were matched according to age, gender, time to return of spontaneous circulation, initial left-ventricular ejection fraction, extracorporeal membrane-oxygenation or left-ventricular unloading by Impella, need for renal replacement therapy, admission lactate, pH, glomerular filtration rate. The CytoSorb® group had a higher (non-significant) requirement for vasopressors prior to the start of CytoSorb®, suggesting they were sicker. In the hemoadsorption group, use of CytoSorb® was within 4 hours of admission to ICU and was attempted for three days. There were no adverse events caused by the use of CytoSorb®. While there was no significant difference in baseline parameters, 30-day mortality was higher in patients treated with hemoadsorption than in the matched control group (83% vs 65%, Log rank p = 0.011). The authors point out the small number of patients examined and that the CytoSorb® patients may have been sicker, which may have contributed to the increased

mortality. They conclude that hemoadsorption should be investigated more closely in randomized controlled trials of suitable size.

<https://www.ncbi.nlm.nih.gov/pubmed/33141843>

Plasma Levels of Myocardial MicroRNA-133a Increase by Intraoperative Cytokine Hemoadsorption in the Complex Cardiovascular Operation

Wagner R, Soucek P, Ondrasek J, Fila P, Sterba J, Spacilova H, Michalcikova A, Freiburger T, Nemecek P.
J Clin Med Res 2019; 11(12):789-797

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Summary

This study evaluated if intraoperative cytokine reduction by CytoSorb® modulates the systemic inflammatory response syndrome (SIRS) and affects myocardial injury as measured by some relatively new markers for myocardial injury (miRNA-126, 223 and miRNA-1, 133a), respectively. Twenty-eight patients were assigned to CytoSorb® (n = 15) or a control (n = 13) group. CytoSorb® was integrated into the extracorporeal circuit. miRNA-133a plasma levels were increased postoperatively in both groups but were higher in the CytoSorb® group at 3 hrs (P = 0.037) and 18 h (P = 0.017) after reperfusion. miRNA-1 and miRNA-223 plasma levels were significantly increased postoperatively, but did not differ between groups. The vascular miRNA-126 was not affected. Intraoperative CytoSorb® use in these patients increased the plasma levels of miRNA-133a, suggesting higher myocardial injury. There was no difference in inflammatory mediators such as C-reactive protein, leukocytes, platelets and fibrinogen levels, and a marked reduction in procalcitonin in the CytoSorb® group that did not however reach statistical significance. There were no differences in clinical outcomes between groups (including need for vasoconstrictors and inotropes, time to extubation, time in intensive care and to hospital discharge).

<https://www.ncbi.nlm.nih.gov/pubmed/31803323>

Hemoadsorption to Reduce Plasma Free Hemoglobin during Cardiac Surgery: Results of REFRESH I Pilot Study

Gleason TG, Argenziano M, Bavaria JE, Kane LC, Coselli JS, Engelman RM, Tanaka KA, Awad A, Sekela ME, Zwischenberger JB.

Semin Thorac Cardiovasc Surg 2019; 31(4):783-793

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Summary

This prospective, multi-center REFRESH I (REduction in FREe Hemoglobin) randomized controlled trial (RCT) evaluated the safety and feasibility of CytoSorb® hemoadsorption therapy to reduce plasma free hemoglobin (pfHb) and activated complements (C3a and C5a) during prolonged (expected duration > 3hrs) cardiopulmonary bypass (CPB). Initially 46 patients underwent surgery (23 in each group), and 38 patients went on to have their pfHb and activated complements evaluated (18 in the CytoSorb® efficacy group, 20 in control group). In the CytoSorb® group, two parallel 300 ml cartridges were set up in a side circuit during CPB and the control group received standard care. CytoSorb® was ran for, on average, 2.5 hours. Results showed that the type and number of serious adverse events (44 vs 43 CONTROL) were similar, as was 30-day mortality. A transient reduction in platelets during CPB was observed in both groups, especially the treatment group, but returned to pre-treatment levels after CPB without bleeding. Peak pfHb was positively correlated with the length of time on CPB (p=0.01) but the high variability of pfHb, due to the broad surgical procedure mix, prevented detection of changes in pfHb in the CytoSorb® population. However, the valve replacement surgery subgroup (8 CytoSorb® vs 10 control) had the highest peak pfHb levels and use of CytoSorb® resulted in significant pfHb reductions vs the control group (p 0.05) in CPB ≥3h. In the 18 CytoSorb® patients who had their activated complements measured, C3a and C5a were significantly reduced by treatment throughout surgery. The authors conclude that intraoperative hemoadsorption with CytoSorb® was safe and feasible in this 8 centre, randomized, controlled pilot study during complex cardiac surgery and resulted in significant reductions in pfHb during valve replacement surgery and reductions in C3a and C5a in the overall CytoSorb® group.

<https://www.ncbi.nlm.nih.gov/pubmed/31085219>

Cytokine clearance with CytoSorb during cardiac surgery: A pilot randomized controlled trial

Poli EC, Alberio L, Bauer-Doerries A, Marcucci C, Roumy A, Kirsch M, De Stefano E, Liaudet L, Schneider AG.

Crit Care 2019; 23(1):108

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Summary

In this single center, pilot, randomized controlled trial, 30 patients undergoing elective cardiac surgery and deemed at risk of complications were included and randomly allocated to either standard of care (n=15) or CytoSorb® (n=15) during cardiopulmonary bypass (CPB). The primary outcome was the difference between the two groups in various cytokines levels measured at various time points. In a subgroup of patients (10 in the CytoSorb® group, 11 in control group), cross-adsorber as well as serial measurements of coagulation factors activity were also measured. CytoSorb® use during CPB was not associated with any increased incidence of adverse events, nor did the procedure result in any significant alterations in conventional hematological parameters or coagulation factors levels. However, in this patient population with predominantly low inflammatory response the use of CytoSorb® was not associated with a significant impact on pro- or anti-inflammatory cytokine levels, nor with a change in relevant clinical outcomes. However, the procedure appeared safe and feasible.

<https://www.ncbi.nlm.nih.gov/pubmed/30944029>

Haemadsorption improves intraoperative haemodynamics and metabolic changes during aortic surgery with hypothermic circulatory arrest

Saller T, Hagl C, Woitsch S, Li Y, Niedermayer S, Born F, Luehr M, Kammerer T, Pichlmaier M, Scheiermann P, Peters S.

Eur J Cardiothorac Surg 2019; 56(4):731-737

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Summary

In this single center study 336 patients who had undergone aortic surgery involving hypothermic circulatory arrest (HCA) were retrospectively analyzed. 168 patients with CytoSorb® hemoadsorption (HA) were matched to 168 patients receiving standard therapy without HA (control) by propensity score matching and then compared. When used, CytoSorb® was inserted into cardiopulmonary bypass circuit and continuously perfused at a rate of 500 ml/min. During aortic surgery, HA significantly reduced the requirement for vasopressors, including norepinephrine and vasopressin, and patients had a more stable acid-base balance and lower lactate levels throughout the procedure. CytoSorb® use also significantly decreased the need for transfusion of packed red blood cells, fresh frozen plasma and fibrinogen. In the HA group, a slight increase of the requirement of prothrombin complex concentrate was observed. There were not enough data on pro-inflammatory cytokine markers and hence, statistical tests could not be performed. The differences in 30 day mortality (HA: 7 patients, 4.8%; Control: 13 patients, 8.8%) and the length of hospital stay were not statistically significant. The authors conclude that the use of CytoSorb® in the setting of acute pathologies such as acute aortic surgery benefits the patients intraoperative course by improving hemodynamic stability as well as acid-base balance and reducing the need for transfusions.

<https://www.ncbi.nlm.nih.gov/pubmed/30891592>

Cytosorb adsorption during emergency cardiac operations in patients at high risk of bleeding

Hassan K, Kannmacher J, Wohlmuth P, Budde U, Schmoeckel M, Geidel S.

Annals of Thoracic Surgery 2019; 108(1);45-51

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Summary

This study included 55 consecutive patients undergoing emergency open-heart operations who were at high risk of bleeding due to prior treatment with coagulation-active substances (Ticagrelor – 43 pts, or Rivaroxaban - 12 pts). In 39 of 55 cases, CytoSorb® adsorption was installed into the heart-lung-machine (CA-group). Bleeding complications during and after surgery were analyzed in detail and compared to 16 patients without adsorption (WA-group), 11 of whom were on ticagrelor and 5 on rivaroxaban. In the CA-group no re-thoracotomies had to be performed. Drainage volumes over 24-hours were only 350 mls after Ticagrelor administration and 390 mls after Rivaroxaban therapy. In the majority of patients, transfusions of blood products were not needed. Compared to this, in the WA-group, multiple bleeding complications occurred and were associated with a longer total operation time, higher drainage volumes, more red blood cell and platelet transfusions, a higher re-thoracotomy rate, a prolonged retention in the intensive care unit and a longer hospital stay (all differences statistically significant between groups). The authors attribute these favorable results directly to the effect of CytoSorb® adsorbing Ticagrelor or Rivaroxaban during the surgery which, they note, is the only way currently available in this patient population to increase patient safety, and reduce bleeding complications. They also believe that the use of CytoSorb® helps to reduce the costs of such operations as its use was associated with an operation time reduced by almost one hour and the decreased use of blood components. Furthermore, there

could be cost savings made by faster discharge of patients from the ICU. They note the safe intraoperative use of CytoSorb® and recommend its use in patients with Ticagrelor or Rivaroxaban who require emergency cardiac surgery.

<https://www.ncbi.nlm.nih.gov/pubmed/30684482>

Hemadsorption during cardiopulmonary bypass reduces interleukin 8 and tumor necrosis factor α serum levels in cardiac surgery: a randomized controlled trial

Garau I, März A, Sehner S, Reuter DA, Reichenspurner H, Zöllner C, Kubitz JC.

Minerva Anesthesiol 2019; 85(7):715-723

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Summary

In this prospective, randomized single centre study, serum cytokine levels of interleukin 8 (IL-8), interleukin 6 (IL-6) and tumor-necrosis-factor α (TNF α) were assessed in elective on-pump (cardiopulmonary bypass – CPB) cardiac surgery patients with CytoSorb® hemoadsorption (study-group - SG, n=20) and without (control-group - CG, n=20). Cytokine levels were assessed prior to and at the end of CPB (mean duration of bypass 141 mins in SG and 139 mins in CG), and 6 and 24 hours after the end of CPB, together with a hemodynamic assessment. The CytoSorb® SG had significantly lower IL-8 serum levels at the end of CPB (p=0.008) and TNF α levels were also below those in the CG at both the end of and 6h after CPB (p=0.034). After 24 hours, TNF α levels were at baseline in both groups. No significant differences were found for IL-6. There was a significant impact of CytoSorb® treatment on the hemodynamic situation as evidenced by a higher cardiac index in the SG after weaning from CPB. This prospective randomized study shows a significant reduction in the pro-inflammatory cytokines IL-8 and TNF α as well as an improvement of the cardiac index, when CytoSorb® is used in on-pump cardiac surgery whilst also demonstrating safety in its application.

<https://www.ncbi.nlm.nih.gov/pubmed/30481999>

Hemoadsorption does not Affect Hemolysis During Cardiopulmonary Bypass

Bernardi MH, Rinoesl H, Ristl R, Weber U, Wiedemann D, Hiesmayr MJ.

ASAIO J 2019; 65(7):738-743

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Summary

Cardiopulmonary bypass (CPB) induces hemolysis, which manifests as plasma free hemoglobin (pfHb), which increases the risk of post-operative complications including decreased blood flow and organ damage. Haptoglobin scavenges hemoglobin but has limited capacity. This is a post hoc analysis from the previously published study (Bernardi MH et al. Effect of hemoadsorption during cardiopulmonary bypass surgery - a blinded, randomized, controlled pilot study using a novel adsorbent. *Crit Care* 2016; 20(1): 96) and investigated whether the use of CytoSorb® affected hemolysis during CPB. A total of 35 patients undergoing elective CPB surgery with expected CPB duration of more than 120 min were included in the analysis where CytoSorb® was used (17 in the intervention group and 18 in the control group). Postoperative pfHb levels were not significantly different between the groups, however, there were statistically significant differences between the treatment and control groups in the median levels of haptoglobin (58.4 vs. 17.9 mg/dL, respectively; P < 0.01) and lactate dehydrogenase (353.0 vs. 432.0 U/L, respectively; P < 0.05) on postoperative day 1. Although the study did not find a statistically significant effect on hemolysis in patients treated with hemoadsorption, statistically significant lower haptoglobin levels and higher secondary hemolysis markers on postoperative day 1 in patients not treated with the device may be an indication of some moderate positive effect of CytoSorb®.

<https://www.ncbi.nlm.nih.gov/pubmed/30325849>

Impact of intraoperative cytokine adsorption on outcome of patients undergoing orthotopic heart transplantation – an observational study

Nemeth E, Kovacs E, Racz K, Soltesz A, Szigeti S, Kiss N, Csikos G, Koritsanszky KB, Berzsenyi V, Trembickij G, Fabry S, Prohaszka Z, Merkely B, Gal J.

Clinical Transplantation 2018; 32(4):e13211

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Summary

The aim of this study was to assess the influence of intraoperative cytokine adsorption using CytoSorb® on the perioperative vasoplegia, inflammatory response and outcome during orthotopic heart transplantation (OHT). Patients were separated into the cytokine adsorption (CA) treated group or historic controls. In the 16 matched

pairs, the median noradrenaline requirement was significantly less in the CA-treated patients than in the controls on the first and second postoperative days ($P=0.039$ and $P=0.047$). The inflammatory responses (assessed by PCT and CRP) were similar in the two groups. There was a trend towards shorter length of mechanical ventilation and intensive care unit (ICU) stay in the CA-treated group compared to the controls. No difference in adverse events was observed, however, the frequency of renal replacement therapy was significantly less in the CA-treated than in controls ($P=0.031$). In summary, intraoperative CytoSorb® during OHT proved to be safe and was associated with reduced vasopressor demand and less frequent renal replacement therapy with a favorable tendency in length of mechanical ventilation and ICU stay.

<https://www.ncbi.nlm.nih.gov/pubmed/29377282>

Use of cytokine filters in cardiopulmonary bypass machines (Einsatz eines Zytokinfilters in die Herz-Lungen-Maschine)

Deppe AC, Weber C, Choi YH, Wahlers T.

Z Herz- Thorax-Gefäßschir 2016; 30(4):254-259

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Abstract and article in German, abstract only in English

Summary

Cardiac surgery using a cardiopulmonary bypass (CPB) machine induces a systemic inflammatory reaction due to activation of multiple inflammatory cascades which may result in systemic inflammatory response syndrome (SIRS). Activation of various inflammatory mediators, such as interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-alpha) can lead to postoperative complications, organ dysfunction, morbidity and mortality. The effect of adsorption of cytokines using CytoSorb® with a CPB machine is evaluated in this prospective, observational pilot study to determine the clinical impact on the serum levels of IL-6, IL-8 and TNF-alpha. This pilot study includes 300 patients planned for elective surgical myocardial revascularization, split into 3 groups; 100 patients with on-pump myocardial revascularization with CytoSorb®; on-pump myocardial revascularization without CytoSorb® and off- pump myocardial revascularization. Primary outcome measures are IL-6, IL-8, TNF- alpha, complement C3/C4, leucocyte counts and C-reactive protein. Secondary outcome measures are length of intensive care unit and total hospital stay, duration of ventilation, duration of catecholamine therapy, kidney injury as well as major adverse cardiac and cerebrovascular events. Interim analysis after 60 % of patients had been included revealed a well- balanced group allocation of patients. In the CytoSorb® group IL-6 values are decreased, whereas TNF-alpha values are comparable between the three groups. There was reduced sternal wound infections and lower usage of antibiotics in the CytoSorb® group. The use of the CytoSorb® filter during CPB is safe compared with standard procedure and without technical difficulties. CytoSorb® reduces cytokine load and seems to attenuate the inflammatory response.

[Link to Article](#)

Effect of hemoadsorption during cardiopulmonary bypass surgery - a blinded, randomized, controlled pilot study using a novel adsorbent

Bernardi MH, Rinoesl H, Dragosits K, Ristl R, Hoffelner F, Opfermann P, Lamm C, Preißing F, Wiedemann D, Hiesmayr MJ, Spittler A.

Crit Care 2016; 20(1):96

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Summary

Objective of this blinded, randomized, controlled single-center trial in 46 adult patients undergoing elective coronary artery bypass graft [CABG], valve surgery, or combined procedure with an expected CPB duration of more than 120 min, was to test CytoSorb® installed in the cardiopulmonary bypass (CPB) circuit (intraoperative usage) with changes in pro- and anti-inflammatory cytokines levels, inflammation markers, and differences in patients' perioperative course. The authors did not find any reduction in the pro-inflammatory response between patients and therefore no changes in their perioperative course. Of note, only the least sick cohort of patients undergoing relatively low-risk cardiac surgery were included in this study. Therefore the observed inflammatory response was only moderate even in the control group. The use and installation of the CytoSorb® adsorber in a CPB circuit was technically feasible, and no adverse device-related side effects occurred. The results showed that albumin and platelet levels are not significantly affected by CytoSorb®. There was a possible protective effect of the observed elevated IL-10 levels postoperatively, which have been associated with lower mortality in previous studies. After safety and feasibility have been demonstrated, patient groups

with the best clinical benefit from CytoSorb® need to be identified.

<http://www.ncbi.nlm.nih.gov/pubmed/27059056>

RECCAS - Removal of Cytokines during CArdiac Surgery: study protocol for a randomised controlled trial

Baumann A, Buchwald D, Annecke T, Hellmich M, Zahn PK, Hohn A.

Trials 2016; 17(1):137

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Summary

On-pump cardiac surgery triggers a significant postoperative systemic inflammatory response, sometimes resulting in multiple-organ dysfunction associated with poor clinical outcome. CytoSorb® may attenuate this inflammatory response. The aim of this single-center randomized, two-arm, patient-blinded RECCAS trial is to assess the efficacy of intraoperative CytoSorb® use during cardiopulmonary bypass (CPB) to reduce the pro-inflammatory cytokine (i.e. IL-6) burden during and after on-pump cardiac surgery, as well as to evaluate the effects on postoperative organ dysfunction and outcomes in high risk patients. Differences in secondary outcome variables between the study groups may give rise to further studies and may lead to a better understanding of the mechanisms of CytoSorb® treatment.

www.ncbi.nlm.nih.gov/pubmed/26971164

1.1.3 Liver

Correlation between Bilirubin Elimination with the Cytokine Adsorber CytoSorb® and Mortality in Critically Ill Patients with Hyperbilirubinemia

Grafe C, Paal M, Winkels M, Irlbeck M, Liebchen U, Scharf C.

Blood Purif 2023; 52(11-12):849-856

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Summary

This retrospective study investigated whether the extracorporeal elimination of bilirubin with CytoSorb® (CS) reduced mortality in patients with hyperbilirubinemia (bilirubin concentrations >10 mg/dL). Thirty patients treated with CytoSorb® at the physician's discretion in their clinical routine were compared to 52 control patients over the same time period. The patients had numerous reasons for their hyperbilirubinemia including sepsis, multi-organ failure, acute liver failure, acute on chronic liver failure, cardiac shock, secondary sclerosing cholangitis and liver transplant rejection. The authors found no significant differences in patients with and without CS treatment. Patients in the CS arm received on average 2 adsorbers for 24 hours each. A significantly higher median bilirubin reduction between day 0 and day 1 was observed in patients allocated to the CS group compared to the control group, however, there was no significant effect of the application of CS on the 30-day mortality. As noted by the authors, "the reasons for liver failure were numerous and to improve this complex disease pattern with only one device is nearly inconceivable." The authors conclude that the use of CS in patients with hyperbilirubinemia did not result in a significant reduction in 30-day mortality.

<https://www.ncbi.nlm.nih.gov/pubmed/37820591>

Artificial Liver Support with CytoSorb and MARS in Liver Failure: A Retrospective Propensity Matched

Analysis

Popescu M, Corina D, Marcu A, Olita MR, Mihaila M, Tomescu D.

Journal of Clinical Medicine 2023; 12(6):2258

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Summary

The aim of this retrospective study was to compare 15 patients who received Molecular Adsorbent Recirculating System (MARS) therapy with 15 patients receiving CytoSorb® therapy in liver failure. Twelve patients had acute on chronic liver failure (4 treated with CytoSorb®, 8 treated with MARS) and 18 patients were diagnosed with ALF (11 patients in the CytoSorb® group and 7 patients in the MARS group). The patients were matched in regards to demographic, biochemical, organ dysfunction and severity scores. Clinical and paraclinical data obtained after each individual session, after the course of treatment, as well as at the end of the intensive care unit stay were compared between the two groups. *Single sessions* of CytoSorb® and MARS were both associated with a significant decrease in bilirubin ($p = 0.04$ and $p = 0.04$) and ammonia levels ($p = 0.04$ and $p = 0.04$), but only CytoSorb® therapy was associated with a decrease in lactate dehydrogenase (LDH) levels ($p = 0.04$) and in platelet count ($p = 0.04$, no bleeding complications noted). However, after the *course of treatment*, only CytoSorb® (median 3 sessions) was associated with a significant decrease in lactate ($p = 0.01$),

bilirubin ($p = 0.01$), ammonia ($p = 0.02$), and LDH levels ($p = 0.01$), while patients treated with MARS (median 2 sessions) did not show any improvement in paraclinical liver tests. Only the CytoSorb® treatment was associated with a significant 10-point decrease, meaning improvement in the Model for End-Stage Liver Disease (MELD) Score ($p = 0.04$). In conclusion, the use of CytoSorb® was associated with an improvement in paraclinical liver functional tests demonstrated by a significant decrease in bilirubin, ammonia, lactate, transaminase, and LDH levels that were more pronounced compared to the MARS group and thus CytoSorb® may provide a more extensive biochemical control of liver failure compared to MARS. However, their impact on hospital length of stay and patient survival needs further evaluation in large-scale randomized control trials. <https://www.ncbi.nlm.nih.gov/pubmed/36983259>

Hemoadsorption in ‘Liver Indication’—Analysis of 109 Patients’ Data from the CytoSorb International Registry
Ocskay K, Tomescu D, Faltlhauser A, Jacob D, Friesecke S, Malbrain M, Kogelmann K, Bogdanski R, Bach F, Fritz H, Hartjes A, Kortgen A, Soukup J, Utzolino S, van Tellingen M, Träger K, Schumacher U, Brunkhorst FM, Molnar Z.

Journal of Clinical Medicine 2021; 10(21):5182

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Summary

This article reports on the results of the ‘liver indication’ subset of patients from the multi-centre CytoSorb® International Registry run by the Centre for Clinical Studies Jena, Jena University Hospital, Germany. In total 1434 patients were included in the Registry, of which 109 were identified as having treatment for ‘liver indication’ i.e. hyperbilirubinemia. This indication was the third largest cohort after sepsis/septic shock ($n = 936$) and cardiac surgery ($n = 239$). Treatment characteristics and changes from Time 1 (baseline, up to 24 h before treatment) to Time 2 (up to 24 h after the last CytoSorb® therapy) were evaluated with a special focus on bilirubin. Patients received a median of two treatments for a median of 46 hrs in total. 98% of adsorbers were administered together with continuous renal replacement therapy. APACHE II-predicted mortality was $49.6 \pm 26.8\%$. In the study, 91% of patients were alive at the termination of hemoadsorption and improvement was observed by the physicians in 75/109 cases. Overall 60 (55.0%) patients died in the ICU, and 65 (59.6%) died in the hospital. Baseline serum bilirubin levels were 12.0 mg/dl (3.9 – 24.7), which reduced significantly by 4.6 mg/dL (95% CI: 6.329 to 2.8). Thrombocytopenia was reported in four patients, without any bleeding complications. This is the largest case series on hemoadsorption for ‘liver indication’ thus far. The authors note that the observation of significant bilirubin removal could have a substantial impact in daily practice as well as designing and executing further studies on the effects of hemoadsorption in liver dysfunction.

<https://pubmed.ncbi.nlm.nih.gov/34768702/>

1.1.4 Myoglobinemia

NEW; Kidney replacement and conservative therapies in rhabdomyolysis: a retrospective analysis

de Fallois J, Scharm R, Lindner TH, Scharf C, Petros S, Weidhase L.

BMC Nephrol 2024; 25(1):96

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Summary

This retrospective analysis aimed to identify differences between conservative therapy and different modalities of kidney replacement therapy (KRT) regarding myoglobin elimination and clinical outcome in patients with rhabdomyolysis (myoglobin $>1000 \mu\text{g/l}$). From 328 included patients 157 had conservative treatment and 171 required KRT. Health condition on admission of this group was more critical compared to patients with conservative therapy. The various forms of KRT included; continuous veno-venous hemofiltration (CVVH – 41 pts), continuous veno-venous hemodialysis with high cut off filter (CVVHD–HCO – 44 pts), continuous veno-venous hemodialysis and CytoSorb adsorption (CVVHD – adsorber 9 pts), continuous veno-venous hemodiafiltration (CVVHDF – 14 pts, continuous veno-venous hemodialysis and sustained low-efficiency daily dialysis (CVVHD/SLEDD – 48 pts), combination (9 pts) and KRT during their ICU stay (6 pts). The decision to start KRT and choice of treatment modality was made by the attending intensivist. Comparison between various extracorporeal procedures showed no significant differences concerning mortality. When comparing specific KRT’s, no benefit was demonstrated for any treatment modality. Life span of the extracorporeal circuit was shorter with CVVH compared to that of others. The authors conclude that acute kidney injury requiring KRT following rhabdomyolysis is accompanied by high mortality rate. Differences in myoglobin reduction rate between various KRTs could not be confirmed, but CVVH was associated with reduced filter lifetime compared to other KRTs.

<https://www.ncbi.nlm.nih.gov/pubmed/38486159>

Rapid and Effective Elimination of Myoglobin with CytoSorb® Hemoadsorber in Patients with Severe Rhabdomyolysis

Albrecht F, Schunk S, Fuchs M, Volk T, Geisel J, Fliser D, Meiser A.
Blood Purif 2024; 53(2):88-95

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Summary

In this randomized control trial on patients with severe rhabdomyolysis (myoglobin > 30,000 µg/l or myoglobin > 10,000 µg/l plus GFR < 40 ml/min), four patients in the control group received continuous veno-venous hemodiafiltration (CVVHD) with a high cut-off hemofilter (EMIC®2) using high blood and dialysate flows for 48 h. Four patients in the CytoSorb® group received the same treatment, but in addition, CytoSorb® was inserted in front of the hemofilter and replaced once after 24 h (2 adsorbers in total). Blood samples were drawn simultaneously before (pre) and after (post) the hemofilter in the control group or the adsorber in the CytoSorb® group, after 5 and 30 min, as well as after 2, 4, 8, and 24 h. All measurements were repeated the next day after the hemoadsorber had been renewed in the CytoSorb® group. The primary outcome was the area under the curve (AUC) of the relative myoglobin concentrations as a percentage of the baseline. Patients in the CytoSorb® group had a significantly lower AUC during the first 24 h (42 +/- 10% vs. 63 +/- 6%, p = 0.029) as well as during the observation period of 48 h (26 +/- 7% vs. 51 +/- 12%, p = 0.029). The relative reductions for myoglobin were considerably higher in the CytoSorb® group compared to the control group during the first 8 h. In the CytoSorb® group, mean values as high as 76% at 5 min fell to 10% at 8 h, while in the control group mean relative reductions for Mb remained below 10% at all time points. The authors conclude that myoglobin concentrations declined considerably faster when CytoSorb® was added to CVVHD. When compared to a high-cut-off hemofilter, efficacy of CytoSorb® for myoglobin elimination was much better. They advise, that because of saturation CytoSorb should be renewed after 8–12 h if further Mb elimination is indicated.

<https://www.ncbi.nlm.nih.gov/pubmed/37918366>

The effect of CytoSorb® application on kidney recovery in critically ill patients with severe rhabdomyolysis: a propensity score matching analysis

Grafe C, Liebchen U, Greimel A, Maciuga N, Bruegel M, Irlbeck M, Weidhase L, Zoller M, Paal M, Scharf C.
Ren Fail 2023; 45(2): 2259231

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Summary

This propensity score matched study investigated whether the application of CytoSorb® (CS) led to an increased rate of kidney recovery in patients with kidney replacement therapy (KRT) due to severe rhabdomyolysis from various etiologies. Adult patients with myoglobin-concentrations >10,000 ng/ml and KRT were included while excluding those with chronic kidney disease. Groups 1 and 2 were defined as KRT (high-flux dialysis) with and without CS, respectively. The primary outcome was independence from KRT after 30 days. 35 pairs of patients could be matched from a total of 95 patients with a mean myoglobin of 27,218 vs. 26,872 ng/ml. In the CS group, CytoSorb® therapy was started within 24 h after starting continuous (C)KRT and a median of three adsorbers were used for a median duration of 2 days with changes of the adsorber every 12-24 hours. The probability of kidney recovery was significantly (p = .04) higher in the CS group 1 (31.4 vs. 11.4%) with a mean risk reduction of 20.0%, and a number needed to treat of five. Considering patients who survived to 30 days, kidney recovery was also significantly (p = .03) higher in patients treated with CS (61.1 vs. 23.5%) with the mean risk reduction being 37.5%, and 2.7 the number needed to treat. Furthermore, a significant decrease of myoglobin in the blood on days 1 and 2 was observed in patients treated with CS, whereas no significant change was detected in those with standard care (continuous venovenous hemodialysis or continuous venovenous hemodiafiltration - CVVHD or CVVHDF). In conclusion, the use of CS might positively affect renal recovery in patients with severe rhabdomyolysis and dialysis-requiring acute kidney injury, establishing the idea that CytoSorb® use in such patients may be beneficial. A prospective randomized controlled trial is needed to confirm this hypothesis.

<https://www.ncbi.nlm.nih.gov/pubmed/37728069>

1.1.5 Other indications

NEW; CytoSorb® in burn patients with septic shock and acute kidney injury on continuous kidney replacement therapy was associated with improved clinical outcome and survival

Mariano F, Greco D, Depetris N, Mella A, Sciarrillo A, Stella M, Berardino M, Rizzo D, Gambino R, Biancone L.

Burns 2024; epub

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Summary

In this retrospective observational study, 35 patients with severe burns underwent continuous kidney replacement therapy (CKRT) for acute kidney injury (AKI) associated septic shock. CytoSorb was used in 11 patients as an adjunctive therapy and the other 24 patients acted as controls. CytoSorb was given for a minimum of 2 cycles of 24 hrs, and a maximum of 6 sessions according to clinical need. Time to first use of CKRT and then CytoSorb was quite diverse. After the first two sessions, the indication for CytoSorb was evaluated daily and stopped when the conditions of septic shock and severe hemodynamic instability were reversed (vasopressor decreased to below 20% of the initial dose) or if there was no response to treatment. In two patients who improved then subsequently deteriorated a new cycle of CytoSorb was instigated. Overall mortality at 270 days was 45.4% for CytoSorb treated patients and 70.8% for the controls ($p=0.044$). A significant difference was seen between the groups for pH, white blood cell count (WBC) and norepinephrine requirements. The authors conclude that repetitive use of CytoSorb as an adjunctive therapy for severe burn patients with AKI-CKRT and septic shock was associated with an improvement clinically, and a lower mortality rate compared to patients treated with CKRT alone. These results should be considered a starting point for further research.

<https://www.ncbi.nlm.nih.gov/pubmed/38494395>

Cytokines Removal During Ex-Vivo Lung Perfusion: Initial Clinical Experience

Boffini M, Marro M, Simonato E, Scalini F, Costamagna A, Fanelli V, Barbero C, Solidoro P, Brazzi L, Rinaldi M. *Transplant Int* 2023; 36(36):10777

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Summary

The aim of the study was to investigate the feasibility and safety of cytokine adsorption with CytoSorb® during ex-vivo lung perfusion (EVLP) in high-risk donor lungs. From July 2011 to March 2020, 54 EVLP procedures were carried out, 21 grafts treated with CytoSorb® and 33 without. Of the CytoSorb® treated lungs, 16 (76%) were able to be transplanted and of the non CytoSorb treated lungs, 22 (67%) were able to be transplanted. Comparing the grafts perfused during EVLP, the use of CytoSorb® significantly decreased the levels of interleukin -IL 10 and granulocyte colony stimulating factor (GCSF) at the end of the procedure. Among the 38 transplanted patients, the CytoSorb® group (16) experienced a significant decreased IL6, IL10, monocyte chemotactic protein (MCP1) and GCSF concentrations compared to the non-adsorption group (22 pts). There was also a significantly lower in-hospital (0 v 5, $p = 0.03$) and 1-year mortality rate (0 v 8, $p = 0.01$) in the CytoSorb® treated group. This interventional study confirms the safety and efficacy of CytoSorb® for reducing the level of inflammatory mediators during EVLP. The authors conclude that EVLP not only represents a reliable platform to evaluate and preserve graft before transplant but can be potentially used to manipulate organs and to achieve proper reconditioning. The inflammatory response has a central role on graft function after transplant and active treatment using such as CytoSorb® adsorption to remove cytokines during perfusion is very attractive as it increases the potential for increasing the number of donor lungs available.

<https://www.ncbi.nlm.nih.gov/pubmed/37645241>

Nothing but NETs: Cytokine adsorption correlates with lower circulating nucleosomes and is associated with decreased primary graft dysfunction

Lindstedt S, Niroomand A, Mittendorfer M, Hirdman G, Hyllen S, Pierre L, Olm F. *J Heart Lung Transplant* 2023; 42(10):1358-1362

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Summary

Elevated levels of neutrophil extracellular traps (NETs) have been reported in primary graft dysfunction following lung transplantation, making methods to reduce or remove them highly valuable as they are related to higher rates of acute and chronic rejection. In this study, two patients were randomized to receive CytoSorb® adsorption during bilateral lung transplantation via integration into extracorporeal life support (ECLS) circuits and two received standard care. Circulating nucleosome levels as a measure of neutrophil extracellular traps were made. CytoSorb® treated patients showed reduced levels of circulating nucleosomes and remained free from primary graft dysfunction and histopathological signs of acute rejection at 1-and 3-month post-transplant. In contrast, both the patients treated without the adsorber experienced higher levels of circulating nucleosomes, primary graft dysfunction grades 1 and 3, and histopathological signs of acute rejection. In summary, according to the authors the present work is promising for

both the safe and effective intraoperative use of cytokine adsorption in lung transplant recipients. They conclude that using a cytokine adsorber (CytoSorb®) during lung transplantation may provide a reduced systemic inflammatory state with lower levels of NETs and consequently support graft acceptance.

<https://www.ncbi.nlm.nih.gov/pubmed/37348689>

Hemoadsorption in the critically ill – final results of the International CytoSorb Registry

Hawchar F, Tomescu D, Träger K, Joskowiak D, Kogelmann K, Soukup J, Friesecke S, Jacob D, Gummert J, Faltlhauser A, Aucella F, van Tellingen M, Malbrain M, Bogdanski R, Weiss G, Herbrich A, Utzolino S, Nierhaus A, Baumann A, Hartjes A, Henzler D, Grigoryev E, Fritz H, Bach F, Schröder S, Weyland A, Gottschaldt U, Menzel M, Zachariae O, Novak R, Berden J, Haake H, Quintel M, Kloesel S, Kortgen A, Stecher S, Torti P, Nestler F, Nitsch M, Olboeter D, Muck P, Findeisen M, Bitzinger D, Kraßler J, Benad M, Schott M, Schumacher U, Molnar Z, Brunkhorst FM.

PLoS One 2022; 17(10):e0274315

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Summary

This paper summarizes the final results of the International CytoSorb® Registry that was open between 2015 and 2021. 1434 patients were enrolled in total from 46 centres, with the main indication for the use of CytoSorb® being sepsis / septic shock (936 pts, 65%), intraoperative use in cardiac surgery (172 pts, 12%), postoperative use after cardiac surgery (67 pts, 5%), and other – like e.g. liver failure, pancreatitis, rhabdomyolysis, drug overdose or ticagrelor / rivaroxaban removal and hemophagocytic lymphohistocytosis (259, 18%). For inclusion in the Registry, there were no specific interventions apart from the use of CytoSorb®. Data collection was at four time points – baseline, before treatment with CytoSorb®, up to 24 hrs following treatment and hospital discharge. APACHE-II predicted mortality was 62.0±24.8%, whereas observed hospital mortality was 50.1%. Overall Sequential Organ Failure Assessment (SOFA) scores did not change but cardiovascular and pulmonary SOFA scores decreased significantly by 0.4 [-0.5;-0.3] and -0.2 [-0.3;-0.2] points, respectively. Serum procalcitonin and C-reactive protein levels showed significant reduction: -15.4 [-19.6;-11.17] ng/mL; -17,52 [-70;44] mg/L, respectively. In the septic cohort PCT and IL-6 also showed significant reductions: -18.2 [-23.6;-12.8] ng/mL; -2.6 [-3.0;-2.2] pg/mL, respectively. Evaluation of the overall effect by the treating physicians was: minimal improvement (22%), much improvement (22%) and very much improvement (10%), no change observed (30%) and deterioration (4%). In conclusion, this study represents the largest systematic data collection on the clinical use of CytoSorb® to date. Although there was no significant difference in mortality when comparing actual mortality with APACHE II predicted (primary outcome), there were significant improvements in cardiovascular and pulmonary components of the SOFA score and reductions in the inflammatory parameters, PCT, CRP and IL-6. Registry data also suggests that the use of CytoSorb® is safe.

<https://www.ncbi.nlm.nih.gov/pubmed/36282800>

Influence of extracorporeal cytokine adsorption on hemodynamics in severe acute pancreatitis: Results of the matched cohort pancreatitis cytosorbents inflammatory cytokine removal (PACIFIC) study

Rasch S, Sancak S, Erber J, Wiessner J, Schulz D, Huberle C, Algul H, Schmid RM, Lahmer T.

Artif Organs 2022; 46(6):1019-1026

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Summary

This study included 16 patients with severe acute pancreatitis (SAP), presenting within 7 days from onset of pain, an APACHE-II score of ≥ 10 and ≥ 1 marker of poor prognosis (includes for e.g. hematocrit $>44\%$ for males, $>40\%$ females, age >55 , C-Reactive Protein - CRP > 10 mg/dl, blood glucose >125 mg/dl). Patients received 2 consecutive 24-h treatments with CytoSorb® extracorporeal cytokine adsorption (intervention group) inserted into the continuous venovenous hemo(dia)filtration set up. Hemodynamics, organ failure, and mortality were compared with an APACHE-II score-matched retrospective control group of 32 patients. The primary objective (20% decrease in the vasopressor dependency index – VDI, or 20% increase in the cardiac index for patients with no vasopressor use at baseline) was reached in 68.8% of the intervention and 28.1% of the control patients ($p = 0.007$), respectively. Use of CytoSorb® significantly reduced IL-6 (-1998 pg/ml, $p = 0.005$) and resulted in stable C-Reactive Protein (CRP, $p = 0.101$) and decreased Procalcitonin (PCT, $p = 0.003$) levels in contrast to increased CRP ($p = 0.014$) and stable PCT levels ($p = 0.695$) in the control group. While mortality and improvement in respiratory failure were similar in both groups, renal failure significantly improved (change of KDIGO classification 72 hrs post-cytokine adsorption [-1 vs. 0, $p = 0.005$]) and the sequential organ failure assessment (SOFA) score significantly decreased in the intervention group compared to an increase in the

control group (day 5: -1.8 ± 2.0 vs. 1 ± 3.8 , $p = 0.013$). The authors conclude that Cytokine adsorption might be an effective treatment option to stabilize hemodynamics in SAP as it decreases levels of the pro-inflammatory marker IL-6 and stabilizes organ function according to serial SOFA score assessments. According to the authors this study provides highly significant results and paves the way for a randomized controlled trial to gain higher levels of evidence.

<https://www.ncbi.nlm.nih.gov/pubmed/35182395>

Pancreatitis CytoSorbents (CytoSorb) inflammatory cytokine removal: A Prospective Study (PACIFIC)

Huber W, Algül H, Lahmer T, Mayr U, Lehmann M, Schmid RM, Faltlhauser A.

Medicine 2019; 98(4):e13044

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Summary

Severe Acute Pancreatitis (SAP) has a mortality rate of around 42% with outcome closely related to the development of systemic inflammation and consecutive organ failures. In this article the authors describe the protocol for a study that intends to evaluate the effectiveness of two consecutive 24 hr treatments with CytoSorb® on hemodynamics in patients with early SAP. The primary endpoint is changes in the vasopressor dependency index (VDI) - derived from mean arterial pressure (MAP) and catecholamine dosage - compared to matched controls from recent studies within the same setting and same centres. Several other parameters will also be measured including cytokine levels. Ultimately it is hoped that the study will show that CytoSorb® could be a therapeutic option in the early treatment of SAP by providing a pathophysiological rationale.

<https://www.ncbi.nlm.nih.gov/pubmed/30681551>

International registry on the use of the CytoSorb® adsorber in ICU patients: Study protocol and preliminary results

Friesecke S, Traeger K, Schitter GA, Molnar Z, Bach F, Kogelmann K, Bogdanski R, Weyland A, Nierhaus A, Nestler F, Olboeter D, Tomescu D, Jacob D, Haake H, Grigorjev E, Nitsch M, Baumann A, Quintet M, Schott M, Kielstein JT, Meier-Hellmann A, Born F, Schumacher U, Singer M, Kellum J, Brunkhorst FM.

Med Klin Intensivmed Notfallmed 2019; 114(8):699-707

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Summary

This is the third interim analysis from the CytoSorb® clinical registry where the aim is to record the use of CytoSorb® adsorbers in critically ill patients under real-life conditions. It records all relevant information in the course of product use, including diagnosis, comorbidities, course of the condition, treatment, concomitant medication, clinical laboratory parameters, and outcome. Data available from the start of the registry on May 18, 2015 to November 24, 2016 (122 centers; 22 countries) were analyzed, of whom 20 centers from four countries provided data for a total of 198 patients (mean age 60.3 ± 15.1 years). In all, 192 (97.0%) had 1 to 5 CytoSorb® adsorber applications. Sepsis was the most common indication for CytoSorb® treatment (135 patients). Mean APACHE II score in this group was 33.1 ± 8.4 [range 15-52] with a predicted risk of death of 78%, whereas the observed mortality was 65%. There were no significant decreases in the SOFA scores after treatment, however interleukin-6 levels were markedly reduced after treatment (median 5000 pg/ml before and 289 pg/ml after treatment, respectively). This third interim report demonstrates the feasibility of the registry with excellent data quality and completeness from 20 study centers. Patient numbers are still small; however disease severity is remarkably high and suggest that adsorber treatment might be used as a potentially beneficial treatment in life-threatening situations. Treating physicians rated the condition of the patients as much or very much improved in approximately 50% of cases and reported a very favorable safety profile with no device-associated side effects.

<https://www.ncbi.nlm.nih.gov/pubmed/28871441>

Feasibility study of cytokine removal by hemoadsorption in brain-dead humans

Kellum JA, Venkataraman R, Powner D, Elder M, Hergenroeder G, Carter M.

Crit Care Med 2008; 36(1):268-272

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Summary

Through numerous mechanisms, brain death is associated with a massive release of proinflammatory cytokines, detectable both in blood and transplantable organs. This increased inflammatory response has been

associated with poor allograft function before and after transplantation. Therefore, this *in vivo* study examines the feasibility of hemoadsorption (using CytoSorb®) to remove cytokines in 8 brain-dead humans.

<http://www.ncbi.nlm.nih.gov/pubmed/18090355>

1.1.6 COVID-19

Extracorporeal hemoadsorption in critically ill COVID-19 patients in VV ECMO: The CytoSorb Therapy in COVID-19 (CTC) Registry

Hayanga JWA, Song T, Durham L, Garrison L, Smith D, Molnar Z, Scheier J, Deliangryis EN, Moazami N.
Crit Care 2023; 27(1):243

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Summary

This is the final analysis of the CytoSorb® Therapy in COVID-19 (CTC) Registry data which included 100 patients from 5 US centres treated with veno-venous extracorporeal membrane oxygenation (VV ECMO) and CytoSorb® for COVID-19 related acute respiratory distress syndrome (ARDS)*. Patients were treated according to the Emergency Use Authorization (EUA), whereby the adsorber was changed every 12 hours in the first 24 hrs, and then 24 hrly thereafter. Patients were followed until death or hospital discharge. Survival rates were high at 30 days (86%), and at 90 days (74%), which is particularly compelling when considering the extremely high risk population, and markedly higher than survival rates reported by the Extracorporeal Life Support Organization (ELSO) COVID-19 registry data (52% at 90 days). From a sub-group analysis, patients were grouped according to the median time delay until start of ECMO and CytoSorb®. When compared to patients with late treatment start (measured from time of ICU admission, >87h), those with early start of treatment (≤87 hours) had significantly shorter need for organ support (including mechanical ventilation) and ICU stay. No device-related adverse events were reported from any of the sites. In summary, to date, this multicentre registry is the largest systematically collected, published dataset looking at the use of CytoSorb® in VV ECMO patients. Results confirm that the approach is easy-to-implement, safe, and associated with high survival rates in ECMO patients. Early start of VV ECMO together with hemoadsorption may further improve outcomes by reducing organ support requirements and length of ICU stay in this extremely sick population. These observations support the concept of “enhanced lung rest”, i.e. the combination of CytoSorb® and ECMO, whereby CytoSorb® addresses systemic hyperinflammation during ECMO therapy.

*Data from the first 52 pts is already published (Song T et al., *Front Med* 2021; 8:773461)

<https://www.ncbi.nlm.nih.gov/pubmed/37337243>

Effect of hemoadsorption Therapy in Critically Ill Patients with COVID-19 (CYTOCOV-19): A Prospective Randomized Controlled Pilot Trial

Jarczak D, Roedel K, Fischer M, de Heer G, Burdelski C, Frings DP, Sensen B, Boenisch O, Tariparast PA, Kluge S, Nierhaus A.

Blood Purif 2023; 52(2):183-192

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Summary

In this single center randomized control pilot study patients with severe COVID-19 and refractory shock (norepinephrine ≥ 0.2 $\mu\text{g}/\text{kg}/\text{to}$ maintain a mean arterial pressure ≥ 65 mmHg), interleukin 6 ≥ 500 ng/L and an indication for either renal replacement therapy (RRT) or extracorporeal membrane oxygenation – ECMO) were randomized to receive either standard medical therapy (SMT) or additional hemoadsorption therapy with CytoSorb® (HT). Twenty-four patients were finally assigned to the two groups (12 pts each). In the CytoSorb® group, the adsorber was replaced every 18 – 24 hrs for up to 5 days, or less if shock reversal was observed for at least 24 hrs. Both groups had a similar severity of illness at baseline. Shock resolution (primary endpoint) was reached in 33% (4/12) versus 17% (2/12) in the HT and SMT groups, respectively ($p = 0.640$). The time to shock reversal was 6.3 (3.7 - 10.0) days in the HT and 9.2 (5.1 - 15.9) days ($p = 0.110$) in the SMT group. Although 28 day mortality was similar in both groups, during the treatment period of 5 days, only 1 patient died in the CytoSorb® group compared to 6/12 in the standard therapy group. The authors did not observe any device-related adverse or serious adverse events. The authors conclude that there was a non-significant trend towards clinical improvement in the intervention period in the CytoSorb® (HT) group with early mitigation of multiple organ dysfunction. They suggest that in selected patients CytoSorb® could be used as an option for stabilization before transfer and further therapeutic decisions.

<https://www.ncbi.nlm.nih.gov/pubmed/36075200>

Blood purification therapy in patients with severe COVID-19 requiring veno-venous ECMO therapy: a retrospective study

Akil A, Ziegeler S, Rehers S, Ernst EC, Fischer S.

Int J Artif Organs 2022; 45(7):615-622

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Summary

This retrospective series included 26 patients with COVID-19 requiring veno-venous extracorporeal membrane oxygenation (VV ECMO) due to severe acute respiratory distress syndrome (ARDS). Sixteen patients were also treated with CytoSorb® and compared to the other 10 patients (control group). CytoSorb® was inserted into a continuous renal replacement therapy (CRRT) circuit in 10 patients, and in a VV ECMO circuit in 6 patients. Patients received on average 6 treatments (range 2 – 21). In both settings there were no device related adverse events during or after treatment. CytoSorb® patients appeared to have a higher initial disease severity (Interleukin – IL-6 1067.9 vs. 134.8 pg/ml, procalcitonin 16.8 vs. 1.4 ng/ml, norepinephrine requirement 0.2 vs. 0.05 µg/kg/min in CytoSorb® vs. control groups). Despite this, combined treatment with CytoSorb® resulted in a significant reduction in IL-6 at 24, 48 and 72 hrs which was not the case in the control group where IL-6 tended to increase (pre 134.8 vs. 595.5 pg/ml at 72 hrs). Despite the fact that the initial dose was 4-fold the control group, all CytoSorb® treated patients had a significantly lower norepinephrine requirement at 48 hours, compared to only 40% of the controls. This hemodynamic stabilization also resulted in significantly lower levels of lactate. Lung function and oxygenation also improved. In summary, the authors note that treatment of a critically ill COVID-19 ARDS patient with combined VV ECMO support and hemoadsorption therapy led to rapid and sustained hemodynamic stabilization, control of the uncontrolled inflammatory response and an improvement in oxygenation. These findings point towards a patient-oriented benefit of extracorporeal hemoadsorption therapy, “future controlled, randomized studies should focus on the investigation of the appropriate timing and dosing of this promising treatment modality”.

<https://www.ncbi.nlm.nih.gov/pubmed/35695200>

CytoSorb Rescue for COVID-19 Patients With Vasoplegic Shock and Multiple Organ Failure: A Prospective, Open-Label, Randomized Controlled Pilot Study

Stockmann H, Thelen P, Stroben F, Pigorsch M, Keller T, Krannich A, Spies C, Treskatsch S, Ocken M, Kunz JV, Kruger A, Khadzhynov D, Kron S, Budde K, Eckardt KU, Enghard P, Lehner LJ.

Crit Care Med 2022; 50(6):964-976

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Summary

The objective of this prospective, randomized controlled pilot study was to investigate the effect of extracorporeal cytokine reduction by CytoSorb® on COVID-19 associated vasoplegic shock in eight ICUs located at three sites of the university hospital Charite, Berlin. To be included, patients had to have COVID-19 with vasoplegic shock, defined as a norepinephrine requirement greater than 0.2 microg/kg/min, C-reactive protein (CRP) greater than 100 mg/L, and indication for hemodialysis. Patients were randomized to receive either CytoSorb® for 3-7 days or standard therapy. In the end 23 patients were randomized to receive CytoSorb® and 26 patients to receive standard of care. Median time from admission to ICU was 15 days in the CytoSorb® group and 10 days in the control group. All patients had respiratory failure requiring invasive mechanical ventilation. Median norepinephrine dose at inclusion was 0.32 µg/kg/min in the CytoSorb® and 0.3 µg/kg/min in the control group. Both groups demonstrated markedly elevated CRP levels with 260.3 mg/dL and 237.2 mg/dL and serum IL-6 levels with 591.0 ng/L and 552.5 ng/L in the CytoSorb® and control groups, respectively. The primary outcome, time until resolution of vasoplegic shock, was similar between the groups with 5 days in the CytoSorb® and 4 days in the control group. Resolution of vasoplegic shock was observed in 13 of 23 patients (56.5%) in the CytoSorb® and 12 of 26 patients (46.2%) in the control group. Mortality rates showed no marked difference between the groups. Also the effects on inflammatory markers, catecholamine requirements, and the type and rates of adverse events were similar between the groups. There were no unexpected device- or procedure-related adverse events. The authors discuss that given the severity of disease with vasoplegic shock and multiple organ failure, it is possible that their intervention was applied too late during the disease course. They conclude that in severely ill COVID-19 patients, CytoSorb® did not improve resolution of vasoplegic shock or predefined secondary endpoints.

<https://www.ncbi.nlm.nih.gov/pubmed/35135967>

CytoSorb Therapy in COVID-19 (CTC) Patients Requiring Extracorporeal Membrane Oxygenation: A Multicenter, Retrospective Registry)

Song T, Hayanga J, Durham L, Garrison L, McCarthy P, Barksdale A, Smith D, Bartlett, R, Jaros M, Nelson P, Molnar Z, Deliargyris E, Moazami N.

Frontiers in Medicine 2021; 8:773461

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Summary

This multicenter (5 site) registry in the USA retrospectively recorded the use of CytoSorb® in 52 COVID-19 patients (between April 2020 and April 2021) under the Emergency Use Authorization (EUA) issued by the FDA. The primary outcome of the registry was ICU mortality. CytoSorb® was inserted in the veno-venous extracorporeal membrane oxygenation (vvECMO) circuit. CRP and ferritin were markedly elevated in patients at the start of therapy. At least four CytoSorb® adsorbers were used per patient (2 for 12 hrs, then 2 for the next 24hrs) on average 7 days into the intensive care unit stay. Results showed that ICU mortality was 17.3% (9/52) on day 30, 26.9% (14/52) on day 90, and 30.8% (16/52) at final follow-up on 153 days. C-Reactive Protein (CRP) and ferritin decreased from 144 ± 189.1 mg/L to 98 ± 90.0 ($p = 0.299$, $n = 22$) and 1768.0 ± 1815.89 to 1314.8 ± 970.02 ng/mL ($p = 0.260$, $n = 17$), respectively. There was a trend toward lower baseline SOFA scores, earlier initiation of CytoSorb® therapy after ICU admission, and lower rates of pharmacologic hemodynamic support pre-CytoSorb® in survivors compared to non-survivors. Survivors also had a trend toward lower baseline D-Dimer levels (2.3 ± 2.5 vs. 19.8 ± 32.2 $\mu\text{g/mL}$, $p = 0.056$) compared to non-survivors and a logistic regression analysis suggested a borderline association between baseline D-Dimer levels and mortality with a 32% increase in the risk of death per 1 $\mu\text{g/mL}$ increase ($p = 0.055$). So according to the authors the presence of very high D-Dimer levels may reflect an advanced process of extensive microangiopathy and thrombosis with broad tissue hypoxia and ischemic injury that is less likely to respond to cytokine removal. CytoSorb® was well-tolerated without any device-related adverse events reported. The authors conclude that CytoSorb® therapy for critically ill COVID-19 patients on ECMO was associated with high survival rates suggesting a potential therapeutic benefit. Elevated baseline D-Dimer levels may suggest increased risk of mortality. Prospective controlled studies are warranted to substantiate these results.

<https://pubmed.ncbi.nlm.nih.gov/34988092/>

Cytokine adsorption in patients with severe COVID-19 pneumonia requiring extracorporeal membrane oxygenation (CYCOV): a single centre, open-label, randomised, controlled trial

Supady A, Weber E, Rieder M, Lothar A, Niklaus T, Zahn T, Frech F, Müller S, Kuhl M, Benk C, Maier S, Trummer G, Flügler A, Krüger K, Sekandarezad A, Stachon P, Zotzmann V, Bode C, Biever PM, Staudacher D, Wengenmayer T, Graf E, Duerschmied D.

The Lancet Respiratory Medicine 2021; 9(7):755-762

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Summary

This single-centre, open-label, randomised, controlled trial investigated cytokine adsorption in adult patients with severe COVID-19 pneumonia requiring veno venous extracorporeal membrane oxygenation (vv ECMO). Patients were randomly assigned to receive cytokine adsorption or not. The CytoSorb® device was incorporated into the ECMO circuit and replaced every 24 hrs and removed after 72 h. 34 patients were assessed for eligibility, and 17 (50%) were treated with cytokine adsorption and 17 (50%) without. Median interleukin (IL)-6 decreased from 357.0 pg/mL to 98.6 pg/mL in patients randomly assigned to cytokine adsorption and from 289.0 pg/mL to 112.0 pg/mL in the control group after 72 h. One patient in each group died before 72 h (during treatment). Survival after 30 days was three (18%) of 17 with cytokine adsorption and 13 (76%) of 17 without cytokine adsorption with most patients dying between day 10 and 20, so several days after the end of the 72-h period of cytokine adsorption. Causes of death were respiratory failure, pulmonary hemorrhage, septic shock, multiorgan failure and intracranial hemorrhage. The authors summarize that early initiation of cytokine adsorption in patients with severe COVID-19 and vv ECMO did not reduce serum IL-6 and had a negative effect on survival and that therefore cytokine adsorption should not be used during the first days of ECMO support in COVID-19.

<https://pubmed.ncbi.nlm.nih.gov/34000236/>

Cytokine adsorption in patients with severe COVID-19 pneumonia requiring extracorporeal membrane oxygenation: protocol for a randomised, controlled, open-label intervention, multicentre trial

Rieder M, Schubach F, Schmoor C, von Spee-Mayer C, Wengenmayer T, Rilinger J, Staudacher D, Bode C, Duerschmied D, Supady A.

BMJ Open 2021; 11(1);e043345

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Summary

This is the published protocol of a 1:1 randomised, controlled, parallel group, open-label intervention, superiority multicentre trial to evaluate the effect of extracorporeal cytokine adsorption using CytoSorb® in severe COVID-19 related acute respiratory distress syndrome (ARDS) patients treated with veno-venous Extracorporeal Membrane Oxygenation (v-v ECMO). The hypothesis is that use of CytoSorb® in these patients effectively reduces interleukin (IL)-6 levels by 75% or more after 72 hours compared with the baseline measurement, and also reduces time to successful v-v ECMO explantation. The adsorber is usually installed in the system as part of the preparation of the ECMO system before the system is connected to the patient circuit, but at the latest within 4 hours after initiation of the ECMO. A total of 80 patients at nine centres in Germany are planned. The protocol of this study was approved by the ethical committee of the University of Freiburg as the leading institution (EK 285/20) with additional votes to be obtained at all participating centres. Trial registration numbers are NCT04385771 and DRKS 00021248.

<https://pubmed.ncbi.nlm.nih.gov/33455938/>

Cytokine adsorption in patients with severe COVID-19 pneumonia requiring extracorporeal membrane oxygenation

Rieder M, Wengenmayer T, Staudacher D, Duerschmied D, Supady A.

Crit Care 2020; 24:435

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Summary

In this letter to the editor, the randomized controlled data from four patients with COVID-19 on veno-venous (vv) Extracorporeal Membrane Oxygenation (ECMO) and CytoSorb® adsorbers was compared to 4 control patients on vvECMO without CytoSorb®. The adsorber was exchanged every 24 hrs and integrated into the ECMO circuit which was found to be both feasible and safe. Results showed that the reduction in interleukin (IL)-6 was more pronounced in the CytoSorb® group, although the initial level was much higher in this group. The letter then goes on to describe the planned multicentre randomized control trial established to compare cytokine adsorption in ECMO treatment plus CytoSorb® for COVID-19 with a control group receiving standard care without CytoSorb® (CYCOV-II study (Cytokine adsorption in patients with severe COVID-19 pneumonia requiring extracorporeal membrane oxygenation, ClinicalTrials.gov number NCT04385771).

<https://www.ncbi.nlm.nih.gov/pubmed/32664996>

1.2. Case series

1.2.1 Septic Shock

Catastrophic *Streptococcus pyogenes* Disease: A Personalized Approach Based on Phenotypes and Treatable Traits

Ruiz-Rodriguez JC, Chiscano-Camon L, Maldonado C, Ruiz-Sanmartin A, Martin L, Bajana I, Bastidas J, Lopez-Martinez R, Franco-Jarava C, Gonzalez-Lopez J, Ribas V, Larrosa N, Riera J, Nuvials-Casals X, Ferrer R.

Antibiotics (Basel) 2024; 13(2):187

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Summary

This case series included 13 patients with Streptococcal toxic shock syndrome (STTS) due to invasive *Streptococcus pyogenes* infections. The primary infections were community-acquired pneumonia (61.5%) and skin/soft tissue infection (30.8%). All patients received prompt antibiotic treatment with clinical source control. Organ support involved invasive mechanical ventilation, vasopressors, and continuous renal replacement therapy as per guidelines. Of note, 76.9% of patients also had septic cardiomyopathy, and 53.8% required extracorporeal membrane oxygenation (ECMO). In total, 10 patients also received hemoadsorption as part of their care. Hemoadsorption (HA) was guided by interleukin (IL)-6 and/or Endotoxin Activity Assay (EAA). This resulted in CytoSorb being used in 9 cases, Toraymyxin in 6 cases, and oXiris in 2 cases. Sequential HA (CytoSorb followed by endotoxin HA) was implemented in six (46.2%) cases. Specifically, patients had plasma concentrations of IL-6 of >100,000pg/mL and an Endotoxin Activity (EAA) of 0.93, respectively. The study identified three distinct phenotypic profiles; hyperinflammatory, low perfusion, and hypogammaglobulinemic

which could guide personalized therapeutic approaches. Hemoadsorption is useful for the recovery of immune homeostasis, however, for certain patients, endotoxin-only adsorption may be insufficient so that sequential HA (endotoxin HA and cytokine HA) may need to be implemented in highly selected patients as a way of removing the primary stimulus that induces the dysregulated inflammatory response. The authors note that candidates for sequential HA include patients experiencing septic shock, multiorgan dysfunction, elevated endotoxin activity, and hypercytokinemia (particularly extremely high levels of IL-6). Continuous monitoring of plasma cytokines (IL-6, IL-10) can provide guidance to clinicians for therapy management. The authors present cytokine HA as a safe procedure and they did not observe any adverse effects. They conclude that integrating these strategies with prompt antibiotics and efficient source control offers a potential avenue to mitigate organ failure, enhancing patient survival and recovery in the face of this severe clinical condition.

<https://www.ncbi.nlm.nih.gov/pubmed/38391573>

Potential correlation between hemodynamic improvement and an immune-modulation effect in pediatric patients with septic shock treated with renal replacement therapy and CytoSorb®: an insight from the PedCyto study

Bottari G, Cecchetti C, Serpe C, Grimaldi D, Taccone FS.

Crit Care 2024; 28(1):25

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Summary

In this additional analysis of the PedCyto study*, the authors investigated if the hemodynamic improvement in pediatric septic shock patients treated with CytoSorb® was associated with an incidence of less immune-dysfunction. The authors measured the time course of interleukin – IL-6, IL-10 and tumor necrosis factor alpha (TNF- α) from onset of hemoadsorption therapy till 24 hours after the end of treatment. The removal rate of cytokines was also calculated as well as changes in leukocyte count and in the class II major histocompatibility complex molecule (HLA)-DR. Results showed a significant reduction in IL-6 and IL-10 but not TNF α , and no significant differences in HLA-DR antigen and leukocyte counts indicating that hemodynamic improvements occurred in parallel with an immune modulatory effect on cytokine hyperproduction in these pediatric septic shock patients on continuous renal replacement plus CytoSorb® with no rebound effect post use. There was also no evidence of immune-paralysis or evidence of an impact on cellular immune function in these patients. The authors suggest these potential beneficial effects of hemoadsorption on leukocyte reprogramming be confirmed in a larger cohort of patients with a control group.

*Bottari et al., Impact of CytoSorb and CKRT on hemodynamics in pediatric patients with septic shock: the PedCyto study. *Front Pediatr* 2023; 15(11):1259384

<https://www.ncbi.nlm.nih.gov/pubmed/38233883>

Impact of CytoSorb Hemoadsorption Therapy on Fluid Balance in Patients with Septic Shock

Kogelmann K, Hübner T, Drüner M, Jarczak D.

Journal of Clinical Medicine 2024; 13(1); 294

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Summary

This multicentre, retrospective study of 124 septic shock patients who received CytoSorb hemoadsorption in the intensive care unit (ICU), analyzed data on administered fluid volumes within different time periods to obtain an assumption on the stability of the vascular barrier / endothelial function. Fluid balance, administered fluid volumes, and catecholamine demand in regard to treatment time with hemoadsorption for the first 72 h were defined as the primary objectives. Regarding the entire study cohort, findings revealed a significant reduction in fluid balance at 72 h (T72) compared to both baseline (T0) and the 24 h mark (T24). Fluid balances from T72–T0 were significantly lower in hospital survivors compared with non-survivors. Patients who received a second catecholamine had a significantly lower in-hospital mortality. The study findings show for the first time in such a focused manner, that the treatment regimen applied with these patients, including hemoadsorption therapy with CytoSorb, is associated with a reduced positive fluid balance paralleled by reductions in vasopressor needs, suggesting a potential positive effect on endothelial integrity / glycocalyx stability. These results, derived from a large cohort of patients, provide valuable insights on the multiple effects of hemoadsorption treatment in septic shock patients.

<https://www.ncbi.nlm.nih.gov/pubmed/38202301>

Post VV-ECMO Weaning Hyperinflammation—Can Prophylactic Hemoadsorption Treatment Prevent Complications?)

Kovacevic P, Dragic S, Jandric M, Momcicevic D, Topolovac S, Malesevic V, Kovacevic T, Matejic-Spasic M, Knezevic T, Zlojutro B.

Medicina 2023; 59(10):1818

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Summary

This three patient case series describes for the first time in the literature the use of CytoSorb® for reducing systemic hyperinflammation (SHI) post veno-venous extracorporeal membrane oxygenation (vvECMO) use in patients with acute respiratory distress syndrome (ARDS). CytoSorb® was used prophylactically for between 12 to 24 hrs immediately following decannulation from the vvECMO as a part of the clinical practice to prevent possible SHI. In all patients there was no evidence of the anticipated SHI, no patients required any vasopressor support throughout their treatment and the inflammatory parameters (including procalcitonin and C-reactive protein) demonstrated an absence of hyperinflammation. The authors believe that the use of CytoSorb® to control the (anticipated) excessive inflammatory response contributed to the patients' stabilization and prevented the occurrence of post-cannulation SHI.

<https://pubmed.ncbi.nlm.nih.gov/37893535/>

Impact of Continuous Kidney Replacement Therapy and Hemoadsorption with CytoSorb on Antimicrobial Drug Removal in Critically Ill Children with Septic Shock: A Single-Center Prospective Study on a Pediatric Cohort

Bottari G, Goffredo BM, Marano M, Maccarrone C, Simeoli R, Bianco G, Vallesi L, Beetham JCC, Mazzeo AT, Cappoli A, Cairoli S, Labbadia R, Cecchetti C, Bernaschi P, Corsetti T, Morabito S, Taccone FS, Guzzo I.

Antibiotics (Basel) 2023; 12(9):1395

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Summary

This is a prospective observational study of 10 children admitted to the pediatric intensive care unit (PICU) with a diagnosis of sepsis/septic shock. All critically ill children received hemoadsorption treatment with CytoSorb® (CS) in combination with continuous kidney replacement therapy (CKRT). Therapeutic drug monitoring (TDM) was done, testing four antimicrobial molecules: meropenem, ceftazidime, amikacin and levofloxacin. In order to evaluate the total and isolated CKRT and CS contributions to antibiotic removal, blood samples at 3 points along the circuit were performed: post-hemofilter (=CS inflow), CS outflow and effluent line. Therefore, the clearance and mass removal of the hemofilter and CS were calculated. There was a different impact of CS on these target drugs removal: CS clearance and mass removal mean values for meropenem were both negative, CS clearance was low for amikacine (6-12%), moderate for ceftazidime (43%) and moderate to high for levofloxacin (52-72%). Higher mass removal and clearance were observed with CKRT compared to CS. This is the first report regarding pharmacokinetic dynamics in critically ill children treated with CKRT and CS for septic shock. In the studied population, no significant clinical burden was observed, neither on ongoing infections nor on the occurrence of new infections, as a result of appropriate antibiotic coverage during treatments. However, more evidence is needed to confirm our data in a larger pediatric population.

<https://www.ncbi.nlm.nih.gov/pubmed/37760692>

Effect of CytoSorb Coupled with Hemodialysis on Interleukin-6 and Hemodynamic Parameters in Patients with Systemic Inflammatory Response Syndrome: A Retrospective Cohort Study

Persic V, Jerman A, Malgaj Vrecko M, Berden J, Gorjup V, Stecher A, Lukic M, Jereb M, Taleska Stupica G, Gubensek J.

J Clin Med 2022; 11(24):7500

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Summary

This retrospective analysis included 118 patients with hyperinflammation (systemic inflammatory response syndrome - SIRS) treated with CytoSorb® in the intensive care units (ICU) of University Medical Center Ljubljana, Slovenia. In the analysis 81 patients (69%) had septic shock, 19 (16%) post-resuscitation shock, 7 (6%) acute pancreatitis, and 11 (9%) 'other' indications. CytoSorb® was inserted into the renal replacement therapy in all but 1 patient, and on average, 1 CytoSorb® adsorber (range 1 – 7) was used for a median of 12 hrs. No device-related adverse events were observed during the treatment time. Median baseline values were 5000 ng/L for IL-6 (upper measurable limit), 70 for the VIS (vasoactive-inotropic score), 14 for the SOFA (Sequential Organ Failure Assessment) and 33 for APACHE II (Acute Physiology and Chronic Health Evaluation) score. Results already showed a statistically significant decrease in interleukin-IL-6 and VIS, and an increase in pH and mean arterial pressure after only 6 hrs of treatment. The reduction in lactate became significant at 48 h. Results were similar in the subgroup of 68 patients with septic shock. Observed ICU

and in-hospital mortalities were lower than predicted by SOFA (61% vs. 79%, $p = 0.005$) and APACHE II (64% vs. 78%, $p = 0.031$) scores. To conclude, the study shows that hemoadsorption in shocked patients with hyperinflammation was associated with a rapid decrease in IL-6 and a hemodynamic improvement, with improved observed vs. predicted survival.

<https://www.ncbi.nlm.nih.gov/pubmed/36556116>

Immunomodulation by Hemoadsorption—Changes in Hepatic Biotransformation Capacity in Sepsis and Septic Shock: A Prospective Study

Praxenthaler J, Schwier E, Altmann S, Kirchner C, Bialas J, Henzler D, Köhler T.

Biomedicines 2022; 10(10):2340

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Summary

This prospective case series included 21 patients with sepsis (7) or septic shock (14), treated with CytoSorb®, who also had their liver function tested by the dynamic LiMAX® test which was compared with the more traditional static liver function tests. The points of measurement for the LiMAX® test were T1: diagnosis of sepsis or septic shock, T2 and T3: 24 hrs and 48 hrs after start of CytoSorb®, and T4: 24 hrs after termination of CytoSorb®. CytoSorb® was integrated into the renal replacement therapy and replaced after 8 – 24 hrs depending on the patients' clinical course (vasopressor dose, inflammatory parameters, clinical condition). To maximize the CytoSorb® dose (ABP – amount of blood purified) a maximum blood flow rate of 200 mL/min with citrate anticoagulation was always targeted. On average patients received 5 adsorbers. In patients with septic shock, 9 (64%) had severely impaired liver function according to the LiMAX® test, and 5 (36%) had impaired liver function. Pre- adsorber (T1), 38% ($n = 8$) of all patients had limited liver injury, 57% ($n = 12$) had severe liver injury and 5% ($n = 1$) had normal liver function according to LiMAX®. For all patients, vasopressor support decreased continuously from T2 to T4. Interleukin – IL 6 levels were higher in the septic shock patients (4713 pg/mL) which decreased to 128.75 post adsorber. In these patients, between T1 and T2, IL6 reduced by 90% ($p 0.0004$). For septic patients IL6 reduced from 1402 pg/mL preadsorber to 68.3 pg/mL post adsorber. In these patients, between T1 and T2, IL6 reduced by 73% ($p 0.016$). All patients with sepsis were alive at 90 days, whereas 43% of septic shock patients survived to 90 days. There were no significant differences in static liver parameters between these patients, for all 4 time points. According to the LiMAX® score, liver function was still impaired post CytoSorb® use, highlighting the need for ongoing liver-protective measures to avoid further damage. The authors conclude that use of CytoSorb® resulted in both hemodynamic stabilization, and rapid control of the inflammatory situation, assuming rapid shock reversal in these patients. They postulate that use of CytoSorb® has a positive impact on the liver, especially hepatic metabolism and functional capacity. In this regard static liver parameters do not adequately reflect hepatic dysfunction and impaired hepatic metabolism. The LiMAX® test can reliably help to assess the severity and the course of hepatic dysfunction at the subcellular level and to make therapeutic decisions faster, individualized, and thus optimized.

<https://pubmed.ncbi.nlm.nih.gov/36289602/>

Does the cytokine adsorber CytoSorb® reduce vancomycin exposure in critically ill patients with sepsis or septic shock? a prospective observational study

Scharf C, Weinelt F, Schroeder I, Paal M, Weigand M, Zoller M, Irlbeck M, Kloft C, Briegel J, Liebchen U.

Annals of Intensive Care 2022; 12(1):44

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Summary

This prospective observational study looked at 160 serum samples from 7 patients with septic shock, all of whom were receiving the antibiotic vancomycin. Twenty CytoSorb® treatments had been performed in these patients and 15% of the samples ($n=24$) were collected during CytoSorb® treatment. Vancomycin pharmacokinetics were characterized using population pharmacokinetic modelling and the adsorption of vancomycin by CytoSorb® investigated as a linear or saturable process. The final model was used to derive dosing recommendations based on stochastic simulations. All patients received vancomycin as a continuous infusion with a preceding loading dose over 2 h (median loading dose: 1500 mg. range: 250–2000). The median infusion rate was 58 mg/h (range: 20–125 mg/h). Steady-state concentrations between 20 and 25 mg/L were defined as the therapeutic target range. Vancomycin concentrations during CytoSorb® were found to be significantly lower than without CytoSorb® (median concentration during vs. without CytoSorb®: 16.7 vs. 20.4 mg/L, $p < 0.001$), although the infusion rate was significantly higher during CytoSorb® (median infusion rate during vs. without CytoSorb®: 70 vs. 40 mg/h, $p < 0.001$). However, it was noted that 48.9% of the concentrations without CytoSorb® were also in the subtherapeutic range. In conclusion, the use of CytoSorb® leads to a clinically significant adsorption of vancomycin (max. 572 mg) in critically ill patients with sepsis or

septic shock. The authors recommend the administration of an additional dose of 500 mg vancomycin over 2 h to avoid subtherapeutic vancomycin exposure.

<https://www.ncbi.nlm.nih.gov/pubmed/35599248>

Benefit of Hemoadsorption Therapy in Patients Suffering Sepsis-Associated Acute Kidney Injury: A Case Series

Hakemi MS, Nassiri AA, Nobakht A, Mardani M, Darazam IA, Parsa M, Miri MM, Shahrami R, Koomleh AA, Entezarmahdi K, Karimi A.

Blood Purif 2022; 51(10):823-830

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Summary

This 3 centre retrospective study included 17 patients with sepsis associated acute kidney injury (AKI) treated with continuous renal replacement therapy (CRRT) in combination with CytoSorb®. Inclusion criteria were an APACHE II score of more than 25 and a diagnosis of septic shock based on the SEPSIS-3 criteria. If there was no decrease in norepinephrine demand even after an additional corticoid treatment, and if the patient fulfilled the minimum criteria for AKI stage II at this stage, CRRT in combination with CytoSorb® therapy was initiated. Demand for norepinephrine, mean arterial pressure (MAP), lactate, and procalcitonin (PCT) levels, as well as intensive care unit (ICU) length of stay, were measured. Patients received on average 2 CytoSorb® adsorbers which were changed every 12 or 24 hours depending on clinical effect and continued until catecholamine demand was stopped or until shock reversal. The blood lactate levels decreased by around 32 % comparing mean levels before and after treatment. All patients who survived (n = 14) had a reduction in vasopressor demand to 68.96% of their initial dose before the start of treatment. Predicted APACHE II mortality was 79.9%, whereas, observed ICU mortality was only 31%. In summary treatment with CytoSorb® and CRRT was associated with a considerable reduction in the SOFA score, paralleled by improved hemodynamic stability, reduction in vasopressor usage, and normalization in metabolic markers such as lactate. The authors conclude that applying CytoSorb® in combination with CRRT in septic patients with AKI is related to a significant decrease in mortality, particularly if the integrity and continuity of the treatment is kept, as much as possible. CytoSorb® was found to be well tolerated and safe. Finally, this study presents an effectively positive outcome with cytokine adsorber treatment as an adjuvant along with standard treatment in a high-risk mortality case of septic shock with organ failure.

<https://www.ncbi.nlm.nih.gov/pubmed/35108714>

Effects of the timing and intensity of treatment on septic shock patients treated with CytoSorb: Clinical experience

Berlot G, Samola V, Barbaresco I, Tomasini A, Di Maso V, Bianco F, Gerini U.

Int J Artif Organs 2022; 45(3):249-253

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Summary

In this single centre study a group of 51 septic shock patients treated with CytoSorb® hemoperfusion along with continuous veno-venous hemodialysis (CVVHD) were studied to determine (a) the effects of this technique on different clinical variables; and (b) the impact of the pre CytoSorb® interval and its intensity on the outcome. The catecholamine index (CI) and the pressure-catecholamine Index (PCAI = CI/MAP [mean arterial pressure]) were used to assess the amount of catecholamine administered at baseline and during the procedure, respectively. CytoSorb® was initiated in patients with at least two organ failures (SOFA score >2), who presented with a MAP <65 mmHg after 8 h from ICU admission, despite fluid resuscitation followed by the administration of norepinephrine in incremental dosages. Pre-treatment time was calculated from the onset of the septic-shock related hypotension and the initiation of the first session, and intensity was assessed by considering the total volume of blood processed as well as the duration of the hemoadsorption. From the 51 pts, 26 were discharged alive from the intensive care unit (ICU) and 25 died in ICU. In survivors (S), the time elapsing from the onset of symptoms and the start of CytoSorb® was shorter than in the non-survivors (NS), and the duration of treatment and volume of blood processed were significantly higher in this group too. The use of CytoSorb® was associated with an increase of the MAP in both S and NS; however, in the S group the CI and the CPAI decreased but increased in NS patients. No relevant side effects, including thrombocytopenia and electrolyte disorders were observed during or immediately thereafter. The authors suggest that the variables 'pre-CytoSorb® interval' and 'CytoSorb® intensity' (overall volume of blood processed) should be taken into consideration in the design of future observational studies or RCT. They conclude that earlier initiation of CytoSorb®, longer duration and higher volume of blood processed were associated with better survival. They also recommend that intensity of treatment be frequently adjusted by evaluating both clinical and bio-chemical needs.

<https://www.ncbi.nlm.nih.gov/pubmed/35075942>

Observational case series: six neurosurgical patients with septic shock demonstrating clinical improvement after a combination of standard care and blood purification

Burov AI, Abramov TA, Kostritca NS, Korotkov DS, Danilov GV, Strunina YV, Savin IA.
European Journal of Medical Research 2021; 26(1):151

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Summary

In this case series, 6 patients post neuro-surgery who developed septic shock were treated with combined blood purification (CBP), including continuous renal replacement therapy in combination with a CytoSorb® adsorber for 24 hours. Clinical improvement over the course of CBP was registered in all patients. The median norepinephrine dose decreased from 0.89 – 0.19 µg/kg/min after 24 hrs. Three patients had a stable clinical improvement; the other three patients had only a transient improvement due to aggravation of their underlying neurological and cardiac deficits. Septic shock reversal was observed in four patients. There were significant decreases in multi-organ failure (MOF) as measured by the Sequential Organ Failure Assessment (SOFA) from 15 – 11, blood lactate, procalcitonin and interleukin-6 levels. Two patients demonstrated level of consciousness increase during their CBP therapy. There were no adverse events during the procedure. The authors write that their results suggest that combined blood purification (CBP) therapy may have a role in septic shock patients with primary brain injury.

<https://www.ncbi.nlm.nih.gov/pubmed/34930484>

No clinically relevant removal of meropenem by cytokine adsorber CytoSorb® in critically ill patients with sepsis or septic shock

Liebchen U, Scharf C, Zoller M, Weinelt F, Kloft C, CytoMero collaboration team.
Intensive Care Med 2021; 47(11):1332-1333

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Summary

In this letter to the editor, 25 patients with septic shock, on continuous veno-venous hemodialysis with and without CytoSorb® had their levels of the antibiotic meropenem measured (333 serum samples including 114 during CytoSorb® treatments). To assess whether clearance of meropenem differed during CytoSorb® treatment or not, three approaches were used: (1) Quantification of a possible proportional increase in clearance during CytoSorb® treatment, (2) Investigation of (non)saturable adsorption at the CytoSorb® adsorber using different adsorption submodels (constant adsorption, linear and hyperbolic decrease of adsorption); and (3) Model parameter re-estimation, excluding samples collected during CytoSorb® treatment and evaluation of how well these parameters predicted concentrations during CytoSorb® treatment. Results showed that none of these approaches revealed a significant ($p < 0.05$) or relevant effect of CytoSorb® therapy on meropenem concentrations. The authors conclude that overall, no clinically relevant adsorption of meropenem by CytoSorb® was observed in the investigated critically ill patient population so that consequently, neither additional dosing nor more frequent monitoring of meropenem was necessary. It is noted however that these findings do not generally translate to other drugs, as every drug needs to be investigated separately.

<https://www.ncbi.nlm.nih.gov/pubmed/34519848>

Role of Hemoperfusion With CytoSorb Associated With Continuous Kidney Replacement Therapy on Renal Outcome in Critically Ill Children With Septic Shock

Bottari G, Lorenzetti G, Severini F, Cappoli A, Cecchetti C, Guzzo I.
Front Pediatr 2021; 9:718049

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Summary

This retrospective analysis looked at renal outcomes in a cohort of eight critically ill children with septic shock treated with continuous kidney replacement therapy (CKRT) plus hemoperfusion with CytoSorb®. Children were aged between 11 days and 14 years (weight 3.130 – 45kg). The main reasons for CKRT plus CytoSorb® use were acute kidney injury (AKI), fluid overload and acidosis. CytoSorb® was performed as a rescue therapy within 24h after the proved or suspected diagnosis of septic shock in case of an inadequate response to standard therapy after an observational period of a maximum of 6h or immediately in parallel to standard therapy in patients with refractory septic shock. Results showed that there was a significant reduction in interleukin (IL)-6 (1801 – 203 pg/ml) and IL-10 (179 – 23 pg/ml) after CytoSorb® use (average 3 x 24 hr

treatments). There was also a significant improvement in creatinine and blood urea nitrogen after blood purification and at pediatric intensive care unit (PICU) discharge. None of the patients required CKRT 30 days after PICU discharge (PICU-D) and none developed chronic kidney disease, so the authors postulate that together with CKRT the adjunctive action of hemoperfusion played a significant role on renal outcome. In conclusion hemoperfusion with CytoSorb® is described as a valuable therapeutic option in combination with CKRT in sepsis associated AKI. The use of adsorption columns is attractive, since these devices can be combined with CKRT for the concomitant treatment of fluid overload and AKI, and at the same time, play an important role in managing cytokine storm associated with organ damage in septic shock.

<https://www.ncbi.nlm.nih.gov/pubmed/34504817>

Hemadsorption as rescue therapy for patients with multisystem organ failure in pediatric intensive care -two case reports and review of the literature

Steurer LM, Schlager G, Sadeghi K, Golej J, Wiedemann D, Hermon M.

Artif Organs 2021; 45(12):1582-1593

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Summary

This two patient clinical series presents the cases of two pediatric patients successfully treated with a combination of the CytoSorb® hemoadsorber, continuous renal replacement therapy (CRRT) and extracorporeal membrane oxygenation (ECMO) due to multiple organ failure following different underlying medical conditions. Patient 1 was a seven-month-old, 7 kg male with Down's syndrome admitted to the Pediatric Intensive Care Unit (PICU) after congenital heart surgery, who developed antimicrobial-resistant septic shock and severe acute respiratory distress syndrome (ARDS). After 12 hours with ECMO, CRRT and CytoSorb® there was a rapid clinical improvement in his respiratory system, hemodynamically and in his laboratory parameters. His interleukin (IL)-6, procalcitonin (PCT) and C-Reactive Protein also significantly decreased. Vasopressors were halved in the first 12 hours and ceased after 40 hours of combined treatment. Patient 2 was a two-year-old, 14 kg male admitted to the PICU with influenza A-associated acute liver failure resulting in hyperammonemia, lactate acidosis, hemodynamic instability and acute kidney failure. CytoSorb® was inserted into his CRRT circuit, and within 12 hours, bilirubin had reduced from 26.2 – 6.6 mg/dl. After two adsorbers (24 hours each) his hemodynamic and respiratory situation had improved, and catecholamines had been stopped. The authors confirm that in both patients, hemoadsorption with CytoSorb® was initiated as an adjunctive rescue therapy to treat refractory multisystem organ failure with improvement of laboratory and clinical parameters observed within hours of treatment initiation. The authors also include a review of literature on the general use of CytoSorb® as well as a summary of published pediatric cases with CytoSorb® application including over 25 patients. They conclude that their observations suggests that CytoSorb® hemoadsorption contributed to the favourable outcomes of their two patients suffering from multisystem organ failure following refractory septic shock and acute liver failure. Its application was safe, efficient and did not cause any notable complications.

<https://www.ncbi.nlm.nih.gov/pubmed/34331775>

Standard renal replacement therapy combined with hemoadsorption in the treatment of critically ill septic patients

Popescu M, Dima S, David C, Tudor A, Simionescu M, Tomescu D.

Ther Apher Dial 2021; 25(5):663-670

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Summary

The aim of this prospective observational study was to assess clinical and paraclinical effects that hemadsorption with CytoSorb® had on organ dysfunction, severity scores and 28 days survival in 55 septic intensive care patients. Each patient underwent three consecutive 24-hour sessions of renal replacement therapy in combination with hemoadsorption, with clinical and paraclinical variables measured after the treatment. Use of hemoadsorption was associated with a significant increase in the PaO₂ /FiO₂ ratio, urine output and Glasgow Coma Score and a significant decrease in white blood cell count, C-reactive protein, procalcitonin levels and platelet count. Overall, the use of hemoadsorption was associated with an improvement in neurological and renal function and a decrease in inflammatory markers. Acute Respiratory Distress Syndrome (ARDS) improved significantly, based on relevant improvements in one third of the patients.

<https://www.ncbi.nlm.nih.gov/pubmed/33270367>

Effect of a novel extracorporeal cytokine apheresis method on endocan, copeptin And interleukin-6 levels in sepsis: An observational prospective study

Kaya Ugur B, Cicek H, Kul S, Mete O, Yilmaz M.

Transfus Apher Sci 2020; 59(6):102919

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Summary

The aim of the study was to evaluate the effect of each CytoSorb® hemoadsorption therapy course on several blood levels of inflammatory biomarkers of sepsis (endocan, copeptin, interleukin-6, procalcitonin, C-reactive protein). A total of 178 samples belonging to 34 sepsis patients who received CytoSorb® therapy either in hemoperfusion mode or as part of the renal replacement circuit were analysed. Arterial blood samples were obtained both before and after each CytoSorb® course (8 hours per session, range of adsorbers per patient 1 – 19). Levels of copeptin, interleukin-6, procalcitonin, C-reactive protein, erythrocyte sedimentation rate, white blood cell count, and creatinine were measured and all were significantly decreased after the CytoSorb® course when compared with levels before therapy ($p = 0.039, 0.001, 0.010, 0.001, 0.002$ and 0.001 , respectively). There was no significant difference between white blood cell count and creatinine levels before and after CytoSorb® courses. The authors speculate that decreasing plasma levels of inflammatory cytokines may help alleviate the cytokine storm and may have a role in improving outcomes.

<https://www.ncbi.nlm.nih.gov/pubmed/32912735>

Elimination of glycopeptide antibiotics by cytokine hemoadsorption in patients with septic shock: A study of three cases

Dimski T, Brandenburger T, MacKenzie C, Kindgen-Milles D.

Int J Artif Organs: 2020; 43(12):753-757

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Summary

In this short case series, glycopeptide antibiotic serum levels (vancomycin and teicoplanin) of three patients were measured pre and post CytoSorb® adsorber which was inserted into a hemodialysis circuit in hemoperfusion mode in all cases for one 8 hour cycle. All patients had septic shock and were critically ill. In two patients, teicoplanin and vancomycin were given via a 60-min infusion and, in the third patient vancomycin was given via a continuous infusion. Results for the short infusions (60 min bolus), showed that both vancomycin and teicoplanin were removed immediately by the adsorber. However, the adsorptive capacity of the device was saturable with serum levels of vancomycin, but not teicoplanin, decreasing to subtherapeutic levels. With the continuous infusion of vancomycin, removal was less and serum levels remained in the therapeutic range. After 240 mins a difference between pre and post adsorber concentrations was not detectable. This information shows that the dose of these antibiotics should be adjusted appropriately, and early therapeutic drug monitoring is highly recommended. The authors suggest administering these antibiotics at the upper limit of recommended dosing regimens. Vancomycin should be administered as a high loading dose followed by a continuous infusion. The adsorptive capacity of the device (for the investigated substances) seems limited and saturation occurs within 120– 240 min.

<https://www.ncbi.nlm.nih.gov/pubmed/32342769>

Hemoperfusion with Cytosorb in pediatric patients with septic shock: A retrospective observational study

Bottari G, Guzzo I, Marano M, Stoppa F, Rava L, Di Nardo M, Cecchetti C.

Int J Artif Organs 2020; 43(9):587-593

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Summary

This retrospective case series included eight consecutive pediatric patients who received CytoSorb® with standard Continuous Renal Replacement Therapy (CRRT) within 24 hours of proven or suspected septic shock refractory to standard treatment. The ages of the children ranged from 1-13 years, and weight from 10-45 kg. The source of the septic shock included three with secondary hemophagocytic lymphohistocytosis. Four of patients also received extracorporeal membrane oxygenation (3 VA-ECMO, 1 VV-ECMO). The Vasoactive-Inotropic Score (VIS) was measured before and after CytoSorb® treatment. Time course of cytokines IL-6, IL-10, and tumor necrosis factor-alpha (TNFa) were measured at time 0, then every 12 h until the end of blood purification treatment (72 or 96 h). CytoSorb® use with CRRT was associated with a rapid and significant decrease in catecholamine demand and hemodynamic stabilization with an improved VIS following CytoSorb® (pre: 40.00 post: 8.89 $p=0.0076$). Overall the pediatric intensive care unit survival was 88.75%. Measurement of

cytokine levels showed a significant reduction of IL-6 (7977.27-210.18 pg/mL, p=0.0077) and IL-10 (from 687.19 to 36.95 pg/mL, p=0.0180). There were no adverse events noted during the use of CytoSorb therapy.

<https://www.ncbi.nlm.nih.gov/pubmed/32003289>

Experience with hemoadsorption (CytoSorb) in the management of septic shock patients

Mehta Y, Mehta C, Kumar A, George JV, Gupta A, Nanda S, Kochhar G, Raizada A.

World J Crit Care Med 2020; 9(1):1-12

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Summary

This retrospective case series included 100 adult patients who were admitted to intensive care between 2016 and 2018 in an Indian hospital following the diagnosis of sepsis or septic shock, who had been treated with dialysis and CytoSorb® combination therapy. The authors used a new CytoSorb® scoring (CS) system that was developed by a group of Indian clinicians for initiating CytoSorb® therapy on the basis of their practical experience so far. The scoring system was derived from five parameters (hemodynamic, renal, respiratory, lab and sepsis scores), representing five different organ system which get affected in sepsis patients. This study proposes that the CytoSorb® therapy should be recommended to the patients with scores between 8-13. In summary, results showed a reduction in the vasopressor dose, a significant reduction in cytokine levels, remarkable reduction in diagnostic markers such as PCT, CRP, bilirubin and serum lactate after the usage of CytoSorb® therapy. Early (preferably within <48 h after onset of septic shock) initiation could result in better clinical outcomes. CytoSorb® was found to be safe and a well-tolerated rescue therapy option in patients with septic shock.

<https://www.ncbi.nlm.nih.gov/pubmed/32104647>

Hemadsorption by extracorporeal cytokine adsorption therapy (CytoSorb) in the management of septic shock: A retrospective observational study

Singh YP, Chhabra SC, Lashkari K, Taneja A, Garg A, Chandra A, Chhabra M, Singh GP, Jain S.

Int J Artif Organs 2020; 43(8):372-378

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Summary

This retrospective, observational study included 36 patients with septic shock who also received CytoSorb therapy. After CytoSorb® therapy there was a significant decrease in procalcitonin (PCT) within 24 hours of therapy. The leucocyte count also decreased within this time frame. The sepsis related organ failure assessment (SOFA) score decreased after the use of CytoSorb®. Shock reversal was seen in 8 patients within 24 hrs of treatment. The authors confirm that CytoSorb® may be a safe, effective and well tolerated rescue therapy, decreasing vasopressor requirements and stabilizing hemodynamics in septic shock patients.

<https://www.ncbi.nlm.nih.gov/pubmed/31868078>

A retrospective analysis of efficacy of hemoadsorption (CytoSorb®) in refractory septic shock patients as an adjuvant

Surendra M, Cherukuri B, Kumar S, Harithra N, Kantham L, Silpa, Bhavya, Srikanth, Jyothi Y.

Int Journal of Scientific Research 2019; 8(19):1-3

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Summary

This retrospective study included eight patients with refractory septic shock (defined as unresponsive to inotropic and vasopressor support – dopamine ³15mcg/kg/min, noradrenaline ³0.25 mcg/kg/min) treated with CytoSorb®. Patients were relatively young (age range 19 – 39 yrs) with a variety of causes for their sepsis. Six out of the 8 patients could be stabilized after 24hrs of CytoSorb® treatment, completely recovered and survived. CytoSorb® treatment appeared to be well tolerated in this patient population. Total leucocyte count, mean arterial blood pressure, lactate and vasopressor requirements all improved after 24 hours of CytoSorb® therapy. This study reports that the use of CytoSorb® as an adjunctive therapy along with standard therapy in a high risk group of septic shock patients with organ damage appears to improve their outcome.

[Link to Article](#)

Changes in Cytokines, Haemodynamics and Microcirculation in Patients with Sepsis/Septic Shock Undergoing Continuous Renal Replacement Therapy and Blood Purification with CytoSorb

Zuccari S, Damiani E, Domizi R, Scorcella C, D'Arezzo M, Carsetti A, Pantanetti S, Vannicola S, Casarotta E, Ranghino A, Donati A, Adrario E.

Blood Purif 2020; 49(1-2):110-113

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Summary

This prospective observational pilot study evaluated changes in cytokines, hemodynamics and microcirculation during blood purification with CytoSorb® adsorber in nine septic patients who were on renal replacement therapy (RRT) for acute renal failure. Measurements were taken at baseline, after 6 and 24 hrs and included hemodynamic parameters, arterial and central venous blood gases, plasma levels of tumour necrosis factor alpha, and interleukin (IL) 1-beta, IL-6, IL-8 and IL-10. The sublingual microcirculation as well as tissue oxygenation and microvascular reactivity were also assessed. Despite being hemodynamically stable, microvascular perfusion was significantly impaired at the time of enrolment. Hemodynamics remained stable throughout the observation, however, microvascular perfusion improved over time with a significant increase in microvascular density and a trend towards an improvement in blood flow quality. Plasma levels of IL-8 decreased at 24 h ($p < 0.05$ versus 6 h). The Sequential Organ Failure Assessment (SOFA) score decreased from 12 to 10 at 24 hrs ($p = 0.039$). This study shows that in septic patients undergoing RRT, use of CytoSorb® seems to show a potential beneficial effect of treatment on the microcirculatory perfusion going beyond just cytokine removal, with a decrease in plasma levels of IL-8, and an improvement in the microcirculation despite no significant variation in macro-hemodynamics in this study.

<https://www.ncbi.nlm.nih.gov/pubmed/31434083>

Feasibility and safety of combined cytokine adsorption and continuous veno-venous hemodialysis with regional citrate anticoagulation in patients with septic shock

Dimski T, Brandenburger T, Slowinski T, Kindgen-Milles D.

Int J Artif Organs 2020; 43(1):10-16

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Summary

In this article the feasibility, efficacy, and safety of CytoSorb® with regional citrate-anticoagulated continuous veno-venous hemodialysis (CVVHD) in 11 patients with septic shock and stage 3 acute kidney injury was recorded. Twelve cycles of CytoSorb® were included with parameters of citrate anticoagulation, circuit lifetime, laboratory parameters, hemodynamics, and vasopressor demand recorded. Ten out of 12 adsorber/CVVHD circuits reached the target of 24 hrs runtime (one system clotted and one was stopped as the patient needed emergency surgery). Nine of the remaining continuous renal replacement circuits reached their 72 hr lifetime. Using the standard citrate protocol, serum ionized calcium and pH remained in the normal range, urea and creatinine were significantly reduced, and norepinephrine dose significantly decreased from 0.47 to 0.16 µg/kg/min ($p = 0.016$) after 24 h. This study shows that combined CytoSorb®/CVVHD is safe and effective for controlling pH, reducing urea and creatinine, and improving hemodynamics by significantly reducing norepinephrine doses in patients with septic shock. It can be applied safely with standard settings of regional citrate anticoagulation rendering sufficiently long filter lifetimes for the CytoSorb® adsorber and the CVVHD circuit.

<https://www.ncbi.nlm.nih.gov/pubmed/31379256>

Use of hemoadsorption in sepsis-associated ECMO-dependent severe ARDS: A case series

Kogelmann K, Scheller M, Drüner M, Jarczak D.

Journal of Intensive Care Society 2020; 21(2):183-190

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Summary

This case series included seven consecutive patients admitted to the ICU with septic shock and acute respiratory distress syndrome (ARDS) who were treated with combined therapy of CytoSorb®, continuous renal replacement therapy (CRRT) and veno-venous ECMO. On admission to ICU patients had an APACHE II score of 39 (predicted mortality rate of 90.8%). All patients received at least 3 CytoSorb® treatments (average 24 hrs per adsorber) installed into the CRRT depending on their clinical response. The combined treatment for these patients was associated with a significant stabilization in hemodynamics and a clear reduction in hyperlactatemia. Patients also showed a significant improvement in lung function and ventilation invasiveness. Additionally, severity of illness and overall organ dysfunction showed a considerable decrease during the course of the combined treatment while observed mortality was only half as predicted by APACHE II. The

authors conclude that CytoSorb® might represent a potentially promising therapy option for patients with refractory ECMO-dependent ARDS in the context of septic shock. There were no CytoSorb® device related adverse events or problems running the adsorber in conjunction with the two additional extracorporeal treatments.

<https://pubmed.ncbi.nlm.nih.gov/32489416/>

Effect of hemoadsorption for cytokine removal in pneumococcal and meningococcal sepsis

Leonardis F, De Angelis V, Frisardi F, Pietrafitta C, Riva I, Martino Valetti T, Broletti V, Marchesi G, Menato L, Nani R, Marson F, Fabbris M, Cabrini L, Colombo S, Zangrillo A, Coniglio C, Stalteri L, Giuliani G, Dalmastrì V, Gordini G, La Manna G.

Case Reports in Critical Care 2018; 1205613

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Summary

In this case series five patients with pneumo (n=2) or meningo-coccal sepsis (n=3) were treated with a CytoSorb® adsorber for cytokine removal. In these patients bacteria enters the blood stream, proliferate and provoke an immune and inflammatory reaction which may rapidly lead to fulminant septic shock. These bacteria may also cross the blood brain barrier causing bacterial meningitis. Due to the severity of the disease process including coagulation disorders, poor outcome, typically including necessity for extensive amputation of extremities, and a high mortality rate is not uncommon. All patients showed progressive stabilization in hemodynamics along with rapid and marked reduction of catecholamine dosages, stabilization in metabolic disorders and less than expected loss of extremities. None of the patients died within the first 28 days. In these patients, use of CytoSorb® for cytokine removal seemed to be a valid and safe therapy in the management of meningococcal and pneumococcal diseases and may contribute to patient stabilization and prevention of severe sequelae.

<https://www.ncbi.nlm.nih.gov/pubmed/30018829>

Hemoadsorption by CytoSorb in septic patients – a case series

Kogelmann K, Jarczak D, Scheller, M, Drüner M.

Crit Care 2017; 21(1):74

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Summary

In this case series the authors evaluated the impact of CytoSorb®, used as adjunctive therapy, on hemodynamics and clinically relevant outcome parameters in 26 septic shock patients with a need for renal replacement therapy. Treatment was associated with hemodynamic stabilization and a reduction in blood lactate levels. Actual mortality was lower than that predicted by the APACHE II score. This effect was more pronounced in patients where therapy was started within 24 hours after the diagnosis of sepsis. Medical patients seemed to benefit more than post-surgical patients in terms of survival. Treatment with the CytoSorb® was safe and well tolerated with no device related adverse events during or after the treatment sessions.

<https://www.ncbi.nlm.nih.gov/pubmed/28343448>

Case series of patients with severe sepsis and septic shock treated with a new extracorporeal sorbent

Laddomada T, Doronzio A, Balicco B.

Crit Care 2016; 20(Suppl 2):P193

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Summary

In this case series of 8 patients with severe sepsis and septic shock treated with CytoSorb®, the influence of CytoSorb® on clinical outcomes such as mean arterial pressure (MAP), vasopressor need and inflammatory markers, e.g. procalcitonin (PCT) was analyzed. There was an overall improvement in MAP with a rapid reduction in vasopressor dosages. Moreover, CytoSorb® treatment in combination with CRRT was associated with a marked decrease in PCT levels and an improvement in renal function. In non-survivors, MAP was hard to stabilize and decreased, and there was an aggravation in the patients overall condition. The authors conclude that the timely use of CytoSorb® in combination with standard therapy may have benefits in improving hemodynamics and help with more rapid stabilization.

[Link to Article](#)

Early report: The use of Cytosorb haemabsorption column as an adjunct in managing severe sepsis: initial experiences, review and recommendations

Morris C, Gray L, Giovannelli M.

Journal of Intensive Care Society 2015; 16(3):257-264

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Summary

In this article the authors describe the use of CytoSorb® hemoabsorption device in 2 patients with overwhelming sepsis following community acquired pneumonia. In addition, the authors consider the experience and evidence supporting the use of CytoSorb® in clinical practice. They state that while CytoSorb® haemoabsorption is mechanistically distinct from other extracorporeal therapies in sepsis and appears effective in reducing inflammatory cytokines during sepsis, much of the basic science and clinical benefits remain unclear. Suggestions for future research and how CytoSorb® could be incorporated into practice are provided.

<https://www.ncbi.nlm.nih.gov/pubmed/28979423>

Clinical experience of using a novel extracorporeal cytokine adsorption column for treatment of septic shock with multiorgan failure

Sathe P, Sakhavalkar P, Kumar S, Choudhary S.

Crit Care 2015; 19(Suppl 1):P130

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Summary

In aim of this retrospective case series in 19 ICU patients treated with standard care plus CytoSorb® as an adjuvant therapy was to analyze clinical safety. In a subgroup of patients where CytoSorb® was used, selection of timing for initiation, number of CytoSorb® devices required per patient, and selective markers to identify its initiation was studied. All of the patients had high predicted mortality (APACHE II >17, SOFA >11). Four patients survived with use of CytoSorb® therapy. Importantly, three of them were treated early (<24 hours of admission). APACHE scores decreased >5 points in five patients after a single application of CytoSorb® therapy. Of those patients who died, the majority (n = 11) were given CytoSorb® treatment only once and seven were treated late (>24 hours). The authors state that a better outcome could be expected if therapy was initiated earlier (<24 hours). However, future studies are needed to clarify the role of CytoSorb® in patients with MOF/septic shock.

[Link to Article](#)

1.2.2 Cardiac

Impact of CytoSorb on kinetics of vancomycin and bivalirudin in critically ill patients

Scandroglio AM, Pieri M, Nardelli P, Fominskiy E, Calabro MG, Melisurgo G, Ajello S, Pappalardo F.

Artif Organs 2021; 45(9):1097-1103

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Summary

This retrospective case series included 89 critically ill patients treated with 109 CytoSorb® adsorbers. Reasons for treatment included 1. hyperinflammation caused by out of hospital - and in hospital - cardiac arrest, 2. acute respiratory distress syndrome, and both 3. post-cardiotomy and acute-cardiogenic shock. To assess the impact of CytoSorb® on two commonly used drugs (the antibiotic vancomycin and the thrombin inhibitor bivalirudin) blood plasma levels were recorded daily and 8 hourly respectively. During treatment with CytoSorb®, a decrease in lactate dehydrogenase (LDH, p=0.007), troponin T (p=0.022) and creatine phosphokinase (CPK, p=0.013) was seen. The vancomycin dose required significant adjustments during treatment (p<0.001), but no significant change was necessary after the first 3 days which was similar for the requirements of bivalirudin. Furthermore, it is reported that from a total of 11 patients that were brain dead after extracorporeal cardiopulmonary resuscitation (eCPR) and considered for organ donation, that all transplanted organs (kidneys in 7 patients and liver in 4 patients) showed good functional status after transplant. In conclusion, CytoSorb® therapy did not significantly modify the administered dose of vancomycin and bivalirudin after reaching initial stabilization in a large population of severely critically ill patients. The authors conclude that CytoSorb® treatment appears to have further application also in the context of organ donation and may be worth further evaluation as an adjunctive tool to reduce ischemic damage and cytokine burden in potential organ donors, as it might contribute to end-organ preservation and ultimately affect outcome.

<https://www.ncbi.nlm.nih.gov/pubmed/33686696>

Extracorporeal cytokine adsorption: Significant reduction of catecholamine requirement in patients with AKI and septic shock after cardiac surgery

Boss K, Jahn M, Wendt D, Haidari Z, Demircioglu E, Thielmann M, Ruhparwar A, Kribben A, Tyczynski B.
PLoS One 2021; 16(2):e0246299

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Summary

The purpose of this retrospective large case series was to investigate the effects of extracorporeal cytokine adsorption with CytoSorb® on hemodynamic parameters in 98 patients with acute kidney injury (AKI) on continuous renal replacement therapy (CRRT) who developed septic shock after cardiac surgery (44 emergency and 54 elective cases with 92 requiring cardiopulmonary bypass). All patients were initially treated following the Surviving Sepsis Guidelines. If there was no decrease in catecholamine demand after maximum standard therapy, extracorporeal cytokine adsorption was applied within 24 h of septic shock diagnosis. CytoSorb® was then used for at least 15 hours and at least one adsorber was used per patient (range 15 – 40 hours, 1 – 4 adsorbers). To compare cumulative catecholamine dose to maintain a mean arterial pressure (MAP) of ≥ 65 mmHg, the vasoactive score (VAS) was recorded for each patient before and after CytoSorb® use. Before CytoSorb® the mean VAS was 56.7 points and after use it was 27.7 points ($p < 0.0001$). Before use, the mean noradrenaline dose to reach a MAP of ≥ 65 mmHg was 0.49 $\mu\text{g}/\text{kg}/\text{min}$. This decreased to 0.24 $\mu\text{g}/\text{kg}/\text{min}$ ($p < 0.0001$) post CytoSorb® use. The mean adrenaline dose also decreased significantly. There was also a significant reduction in serum lactate after treatment (7.2 – 3.5 mmol/l, $p < 0.0001$). The mean predicted in-hospital mortality rate based on the mean SOFA-score was 77%, and 73% on APACHE II-score, while the all-cause in-hospital mortality rate of the patients in this study was 59.2%. In conclusion, the present study showed a stabilization in hemodynamic parameters in patients with AKI on CRRT and sepsis after cardiac surgery with a significant reduction in the catecholamine requirements and serum lactate level. This was also observed in patients with very high predicted mortality scores. Additionally, observed versus predicted in-hospital mortality SOFA- and APACHE II-score rates were decreased.

<https://www.ncbi.nlm.nih.gov/pubmed/33556101>

Hemoadsorption treatment with CytoSorb in patients with ECLS therapy – a case series

Traeger K, Skrabal C, Fischer G, Schroeder J, Marenski L, Liebold A, Reinelt H, Datzmann T.
Int J Artif Organs 2020; 43(8):422-429

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Summary

This retrospective case series described the use of extracorporeal life support (ECLS, specifically veno-arterial extracorporeal membrane oxygenation – VA ECMO) and CytoSorb® hemoadsorption in 23 cardio-thoracic intensive care patients with a wide range of complex disease states. The trigger for initiation of CytoSorb® was presence of renal replacement therapy (RRT) and the presence of one or more of the following - severe hyperinflammatory activation, severe reperfusion injury, extended cardiopulmonary bypass times with post-cardiotomy low cardiac output, and refractory vasoplegic response with rapid progressive organ dysfunction. The CytoSorb® was integrated into the renal replacement therapy system, and patients had, on average 2 x 24 hour treatments (range 1-3). APACHE II and SOFA scores were high for these patients (28 and 13 respectively), representing a very severely sick patient population. Both interleukin (IL)-6 and IL-8 decreased pre and post CytoSorb® as did procalcitonin (PCT). Patients stabilized hemodynamically, with a reduction in vasopressor requirements (epinephrine, norepinephrine) and a sustained mean arterial pressure (MAP). ECLS flow rate was maintained, and lactate, pH, and base excess could all be stabilized and normalized during and after the treatment period. The combination of CytoSorb® hemoadsorption and RRT in ECLS patients appeared to be well tolerated and there were no device related technical issues or adverse events during or after treatment.

<https://www.ncbi.nlm.nih.gov/pubmed/31868089>

Comparison of intra-operative versus intra- plus postoperative hemoadsorption therapy in cardiac surgery patients with endocarditis

Kühne L-U, Binczyk R, Rieß FC.
Int J Artif Organs 2019; 42(4):194-200

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Summary

In this study the use of CytoSorb® therapy in 20 endocarditis patients was investigated in two groups:

intraoperative use only (10 pts - group 1) versus intra- plus post-operative use (10 pts – group 2). The decision whether to continue CytoSorb® therapy postoperatively was made on clinical grounds, including the indication for renal replacement therapy, hence the patients in group 2 had more pronounced disease severity (higher EuroSCORE, higher reoperation rates, longer cardiopulmonary bypass times, worse inflammatory status and higher incidence of acute renal failure). Patients in both groups had a marked decrease in the requirement for vasoactive drugs and in their inflammatory parameters in the postoperative course. Despite being sicker and having a higher rate of postoperative complications as well as a longer ICU stay, patients in group 2 showed equal ICU and 90-day survival compared to group 1 patients who were only treated intraoperatively. This data suggests that the postoperative continuation of CytoSorb® might be beneficial for patients with endocarditis who develop perioperative renal failure and hemodynamic instability.

<https://www.ncbi.nlm.nih.gov/pubmed/30803290>

Blood Purification With CytoSorb in Critically Ill Patients: Single-Center Preliminary Experience

Calabro MG, Febres D, Recca G, Lembo R, Fominskiy E, Scandroglio AM, Zangrillo A, Pappalardo F.
Artif Organs 2019; 43 (2):189-194

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Summary

In this retrospective case series study in 40 critically ill cardiac surgery patients with multiple organ failure the use of CytoSorb® therapy inserted into either the extracorporeal membrane oxygenation (ECMO) circuit (19 pts), or as standalone hemoperfusion (21 pts) was evaluated for clinical outcomes. The series included patients with cardiogenic shock (28), septic shock (2), acute respiratory distress syndrome (9), and liver failure (1). Of the 19 patients who underwent ECMO, 11 had an intra-aortic balloon pump, 9 with Impella, and 6 had a ventricular assist device. Patients received at least one CytoSorb® treatment (median number of filters used 2). After CytoSorb® treatment, total bilirubin, lactate, Creatinine phosphokinase (CPK) and lactate dehydrogenase (LDH) all decreased significantly as did the vasoactive-inotropic score. Thirty-day mortality was 55% and ICU mortality was 52.5% with an expected ICU mortality of 80% according to the sepsis-related organ failure assessment (SOFA) score. This case series shows that CytoSorb® treatment is effective in reducing bilirubin, lactate, CPK and LDH, in critically ill patients mainly due to cardiogenic shock. No device related adverse events were observed.

<https://www.ncbi.nlm.nih.gov/pubmed/30156308>

Hemoadsorption treatment of patients with acute infective endocarditis during surgery with cardiopulmonary bypass - A case series

Traeger K, Skrabal C, Fischer G, Datzmann T, Schroeder J, Fritzler D, Hartmann J, Liebold A, Reinelt H.
Int Art Organs J 2017; 40(5):240-249

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Summary

In this retrospective case series, the authors describe 39 cardiac surgery patients with proven acute infective endocarditis undergoing valve replacement during cardiopulmonary bypass surgery in combination with intraoperative CytoSorb® hemoadsorption. In comparison an historical group of 28 similar patients treated without the use of intraoperative CytoSorb® were evaluated. CytoSorb® treatment was associated with a reduction in postoperative cytokines (IL6, IL8) and clinical metabolic parameters (lactate and base excess). Moreover, in comparison to the non-CytoSorb® group, the CytoSorb® patients showed hemodynamic stability (higher mean arterial pressure) during and after the operation with the need for vasopressors (norepinephrine and epinephrine) being lower within hours after completion of the procedure. The authors conclude that these improvements in patient outcome could be attributed to the use of the CytoSorb® adsorber treatment and that its use is a potentially promising therapeutic option for this group of critically ill patients leading to cytokine reduction, improved hemodynamic stability and organ function.

<https://www.ncbi.nlm.nih.gov/pubmed/28525670>

Treatment of post-cardiopulmonary bypass SIRS by hemoadsorption: a case series

Traeger K, Fritzler D, Fischer G, Schröder J, Skrabal C, Liebold A, Reinelt H.
Int J Artif Organs 2016; 39(3):141-146

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Summary

Objective of this case series in 16 adult patients undergoing standard or emergency cardiothoracic surgery procedures with prolonged CPB time, developing post-CPB SIRS over the course of the first post-operative 24 hours was to test the effect of CytoSorb® on changes of inflammatory cytokines levels, metabolic parameters hemodynamic variables, and patient outcome. Treatment of these patients with CytoSorb® in conjunction with CVVHD was associated with decreases in the proinflammatory cytokines, IL-6 and IL-8, as well as a clear stabilization of hemodynamic, metabolic and organ function parameters. All patients with an APACHE score of up to 30 survived. This is the first case series reporting the use of CytoSorb® therapy in patients with post-CPB SIRS. Due to a modulation of the cytokine response, CytoSorb® may offer a potentially promising new treatment option for severe post-CPB SIRS that presents with hemodynamic instability and requires high doses of vasopressors.

<http://www.ncbi.nlm.nih.gov/pubmed/27140295>

Systemic Inflammatory Response Syndrome in der Herzchirurgie: Neue Therapiemöglichkeiten durch den Einsatz eines Cytokin-Adsorbers während EKZ?

Born F, Pichlmaier M, Peterß S, Khaladj N, Hagl C.

Kardiotechnik 2014; 2:42-46

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Summary

In this retrospective observational study in 40 patients undergoing a major cardio-surgical procedure with the use of Cardio-Pulmonary-Bypass (CPB) (n=20 with CPB, n=20 with CPB and an additional CytoSorb®-adsorber in the circulation) the authors tested whether intraoperative treatment with CytoSorb® has a positive effect on the development of post-operative SIRS. Results showed that CytoSorb® contributes to a significant reduction in post-operative SIRS in these patients and emphasizes the reliability and safety of CytoSorb® in the setting of cardiac surgery.

[Link to Article](#)

1.2.3 Liver

Extracorporeal adsorption of protective and toxic bile acids and bilirubin in patients with cholestatic liver dysfunction: a prospective study

Greimel A, Habler K, Grafe C, Maciuga N, Brozat CI, Vogeser M, Zoller M, Happich FL, Liebchen U, Frank S, Paal M, Scharf C.

Ann Intensive Care 2023; 13(1): 110

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Summary

The prospective observation study (Cyto-SOVLE - NCT04913298) included 20 intensive care patients with cholestatic liver dysfunction, on continuous kidney replacement therapy, with total bilirubin concentrations > 10 mg/dl and the application of CytoSorb® into the dialysis circuit. Bilirubin and different bile acids (BAs) were measured pre- and post-CS at defined timepoints (10 min, 1, 3, 6, and 12 h after initiation). Relative reductions (RR %) were also calculated. The median RR for total and conjugated bilirubin after initiation was - 31.8% and - 30.3%, respectively, and decreased to - 4.5% and - 4.8% after 6 h showing adsorber saturation. A high initial RR was observed for the toxic BAs as well as the protective hydrophilic BAs after initiation. There were high inter-patient differences in the concentrations and distributions of different BAs, so the authors recommend that the use of CytoSorb® should be based on the concentration of toxic BAs in the blood, rather than total bilirubin or total BA concentrations. The authors conclude that CytoSorb® can adsorb bilirubin and toxic as well as protective BAs. A fast saturation of the adsorber resulting in rapid decrease in the RR was observed. The clinical benefit or harm of the BA adsorption needs to be evaluated in the future.

<https://www.ncbi.nlm.nih.gov/pubmed/37943350>

Liver-Support Therapies in Critical Illness—A Comparative Analysis of Procedural Characteristics and Safety

Göth D, Mahler CF, Kälble F, Speer C, Benning L, Schmitt FCF, Dietrich M, Krautkrämer E, Zeier M, Merle U, Morath C, Fiedler MO, Weigand MA, Nussbag C.

Journal of Clinical Medicine 2023; 12(14):4669

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Summary

In this retrospective comparative analysis, procedural characteristics and safety of the three liver-support therapies CytoSorb®, Molecular Adsorbent Recirculating System (MARS) and therapeutic plasma exchange

(TPE) were investigated in critically ill patients with acute liver failure. 21 patients were treated with 60 CytoSorb® treatments, 14 pts were treated with 61 MARS treatments, and 18 patients had 80 TPE treatments. Whereas TPE had its strengths with shorter treatment duration, for clearing larger molecules, affecting platelet levels less, and improving systemic coagulation and hemodynamics, CytoSorb® and MARS were associated with a superior reduction in particularly small protein-bound and water-soluble substances. Data showed that CytoSorb® therapy is most effective for eliminating total bilirubin. The clearance magnitude was concentration-dependent for all three therapies, but additionally related to the molecular weight for CytoSorb® and MARS therapy. Severe complications were not observed for any treatment modality, so all three liver-support therapies were seen as safe. The authors conclude that TPE may be beneficial in patients at high risk for bleeding complications and impaired liver synthesis and hemodynamics, while CytoSorb® and MARS may be considered for patients in whom the elimination of smaller toxic compounds is a primary objective.

<https://www.ncbi.nlm.nih.gov/pubmed/37510784>

Extracorporeal Liver Support Techniques: a comparison

Riva I, Valetti TM, Marchesi G, Fabretti F.

J Artif Organs 2023; epub

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Summary

This is a retrospective comparative analysis in 39 patients who presented with liver failure and were treated with different extracorporeal techniques. Seventeen patients had CytoSorb® (28 treatments), 19 patients had Coupled Plasma Filtration Adsorption (CPFA - 37 treatments), 1 patient Molecular Adsorbent Recirculating System (MARS - 3 treatments), 1 patient Prometheus (5 treatments) and 1 patient plasma adsorption perfusion (PAP - 2 treatments). The main objective of the study was to assess and compare the detoxification capacity of the systems in terms of total bilirubin (TB), direct bilirubin (DB) and total bile acids (BA). To verify the effectiveness of the treatments, mass balance (MB) and adsorption per hour were calculated. Serum samples were collected on average every 2 hours during the various treatments, directly before and after the adsorbent system to evaluate the absolute reduction in toxins and their removal over time. Treatments were well tolerated hemodynamically, and no major procedure-related adverse events occurred. For all the markers, TB, DB and BA, the total adsorption obtained with CytoSorb®, expressed by the total MB value, was significantly higher compared with that obtained with CPFA ($p < 0.001$). This result was more pronounced for TB: 2850.05 (± 384.76) mg/dl with CytoSorb® versus 537.45 (± 33.71) mg/dl with CPFA ($p < 0.001$). The adsorption ability was also confirmed by the average adsorption per hour. CytoSorb® presented a significantly higher adsorption ability for TB and DB compared to CPFA ($p < 0.05$). When performing a comparison between all the techniques, CytoSorb® resulted the most efficient system, showing a total MB value for TB, DB and BA that was significantly higher than CPFA, MARS and PROM ($p < 0.05$). The authors conclude that CytoSorb® might represent the most suitable option as a liver support technique, considering the combination of hepatic toxins, cytokine adsorption ability and technical versatility, as it can easily be inserted in a continuous renal replacement therapy circuit.

<https://www.ncbi.nlm.nih.gov/pubmed/37335451>

The application of hemoadsorption for hyperbilirubinemia and its impact on bilirubin removal kinetics in critically ill children

Hui WF, Cheung WL, Hon KL, Ku SW.

Int J Artif Organs 2023; 46(4):241-247

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Summary

This retrospective case series included 6 children aged between 9 months to 18 years old (median 9.3 yrs) who received extracorporeal blood purification (EBP). Among the 14 episodes of EBP, 57.1% of them received hemoadsorption (HA) with CytoSorb® in 5 patients, 33.3% received single-pass albumin dialysis (SPAD), and 7.1% received combined SPAD and HA. The median (Interquartile range - IQR) pre-HA peak total bilirubin level was 406 (254) $\mu\text{mol/L}$ with saturation noted in most sessions within 12 hours of HA initiation. Patients received between 1 – 3 adsorbers. The overall bilirubin removal ratio by HA was 44.6 (14.5)%. A higher HA effective dose and a higher pre-HA bilirubin level were both associated with better bilirubin removal. A higher effective dose was also associated with a shorter saturation duration. No major EBP-specific complication was encountered. The liver enzymes showed improvement in all children. No patients required liver transplantation. There was no EBP-related mortality, but the overall PICU mortality of the cohort was 50%. The authors conclude that HA with CytoSorb® was a safe and effective modality for bilirubin removal among children. Future studies should investigate the impact of bilirubin removal on clinical outcomes and explore the factors

responsible for better removal efficacy. The ease of set-up, the ability to remove cytokines, and comparable bilirubin removal capacity certainly make the use of a hemoadsorption column attractive in critical care setting, and HA will be a promising alternative to conventional ECLS modality for selected children with acute liver failure or hyperbilirubinemia. <https://www.ncbi.nlm.nih.gov/pubmed/36964647>

The cytokine adsorber CytoSorb® does not reduce ammonia concentrations in critically ill patients with liver failure

Liebchen U, Paal M, Grafe C, Zoller M, Scharf C, Cyto Solve Study Group.
Intensive Care Med 2023; 49(3):360-362

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Summary

This letter presents some of the results of the Cyto-SOLVE study which investigated the adsorption capacity of CytoSorb® for different substances (NCT04913298). In a subgroup-analysis of 20 intensive care unit (ICU) patients with liver failure the authors explored whether the use of CytoSorb® led to relevant ammonia adsorption. Patients were on continuous kidney replacement therapy (CKRT) and had hyperbilirubinemia (total bilirubin in serum > 10 mg/dL). CytoSorb® was installed primarily for bilirubin elimination and was integrated post-dialyzer into the CKRT circuit. Ammonia concentrations were measured at baseline, after six and twelve hours in different blood samples taken from the arterial cannula or the CKRT circuit in post-dialyzer or post-CytoSorb® position respectively. The median ammonia serum concentration at baseline was 77 µmol/L. There was significant ($p < 0.001$) ammonia elimination by the dialyzer (pre- vs. post-dialyzer) at all time points, however there was no significant elimination of ammonia or correlation at any time points in the pre versus post CytoSorb® blood samples. The authors conclude that the elimination of ammonia was mainly achieved by the dialyzer with a constant clearance over time depending on blood flow and effluent rate. So the decreased ammonia plasma-concentration, that was also observed in their population, can most likely be attributed to the dialyzer, and not, as postulated by Dominik et al.,* to CytoSorb®.

*Dominik A & Stange J. *Blood Purif* 2021; 50(1):119-128

<https://www.ncbi.nlm.nih.gov/pubmed/36763124>

Successful elimination of bilirubin in critically ill patients with acute liver dysfunction using a cytokine adsorber and albumin dialysis: a pilot study

Scharf C, Liebchen Uwe, Paal M, Becker-Pennrich A, Irlbeck, M, Zoller M, Schroeder I.
Scientific Reports 2021; 11(1):10190

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Summary

In this retrospective case series, 39 patients with acute liver dysfunction (ALD) and corresponding high levels of bilirubin (>10 mg/dl) were given either CytoSorb® integrated into high flux dialysis (n. 33), or the advanced organ support system ADVOS (n. 6). The reasons for admission to the Intensive Care Unit in these extremely ill patients treated with CytoSorb® were: Acute Respiratory Dysfunction Syndrome (24.2%), septic shock (15.2%), polytrauma (15.2%), liver transplantation (12.1%), Acute Liver Failure (12.1%), lung transplantation (6.1%), cardiogenic shock (6.1%), and other reasons (9.0%). The reasons for admission in patients treated with ADVOS were acute liver failure (50.0%), cardiogenic shock (33.3%), and liver transplantation (16.7%). Laboratory parameters were evaluated before starting therapy (d-1 and d0) and 12–24 h thereafter (d1). The median bilirubin at d-1 was 14.2 and 18.5 mg/dl, at d0 16.9 and 17.7 mg/dl and at d1 13.2 and 15.9 mg/dl, in the CytoSorb® and ADVOS groups, respectively, showing a significant increase in total bilirubin in the period prior to CytoSorb® treatment. There was a significant bilirubin reduction during CytoSorb® treatment ($p < 0.001$) and during ADVOS treatment ($p = 0.028$). Significant decreases of AST (92 kDa), ALT (110 kDa), and GGT (64 kDa), observed during CytoSorb® treatment might reflect an improvement of liver function, as direct adsorption is unlikely due to molecular size. The authors note that in addition to the lower than expected mortality (92% v 82.2%), there was also a significant reduction in norepinephrine demand with the use of CytoSorb®, resulting in hemodynamic stabilization. The significant reduction in SAPS II during CytoSorb® is another indicator of an improvement in the patient's outcome. The authors conclude liver support systems play an important role in the supportive therapy of patients with ALD. While both ADVOS and CytoSorb® led to a significant and comparable decrease in bilirubin in critically ill patients, the easy use of CytoSorb® might be an advantage compared to other procedures. They note that because CytoSorb® is able to be easily integrated into high flux dialysis, for example, it may be possible to use in smaller, less resourced hospitals.

<https://www.ncbi.nlm.nih.gov/pubmed/33986443>

Haemoadsorption by CytoSorb in patients with acute liver failure: A case series

Tomescu D, Popescu M, David C, Sima R, Dima S.
Int J Artif Organs 2021; 4(8): 560-564

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Summary

The aim of this case series was to assess the clinical effects of CytoSorb® on a range of biochemical parameters in 28 patients with acute liver failure (ALF). Causes of ALF included acetaminophen (paracetamol) overdose, acute viral hepatitis, mushroom poisoning and Wilsons disease. Patients were treated with three consecutive 24 hr sessions of continuous venovenous haemodiafiltration (CVVHDF) in combination with CytoSorb®. Use of CytoSorb® was associated with a significant decrease in serum creatinine, bilirubin, ammonia and C-Reactive Protein (CRP). Twelve patients had a decrease in SOFA score after the use of CytoSorb® that was mostly due to a decrease in serum bilirubin levels. A decrease was also noted in the platelet count but this was not associated with any significant bleeding episodes. The authors note that the decrease in the platelet count in patients with ALF may be attributed to both the intrinsic mechanism in liver disease and to the use of renal replacement therapy. In accordance with previously published cases, the use of CytoSorb® can be considered as a therapeutic option for the management of liver impairment in patients with ALF, as providing biochemical control of liver function tests may aid in bridging such patients to liver transplantation, or until spontaneous remission is assured. Thrombocytopenia remains one of the side effects of this treatment requiring consideration on a patient by patient basis. A higher survival rate was observed in patients in whom a decrease in Sequential Organ Failure Assessment (SOFA) was observed.

<https://www.ncbi.nlm.nih.gov/pubmed/33302765>

Impact of Cytokine Adsorption Treatment in Liver Failure

Acar U, Gokkaya Z, Akbulut A, Ferah O, Yenidunya O, Acik ME, Tokat Y, Yentur E.
Transplant Proc 2019; 51(7):2420-2424

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Summary

This case series included four patients with sepsis / septic shock plus severe liver failure, and tested the effect of CytoSorb® use on liver function and liver toxins. In total, nine CytoSorb® cartridges were used with continuous venovenous hemodialysis in 12-hour sessions. The biochemical values of the patients before and after the use of the adsorber were recorded. According to the results the authors note that CytoSorb® can be considered as an option to lower bilirubin levels in cases of liver failure however, in their patients the authors were not able to detect a decrease in ammonia levels. Although further studies are needed, cytokine adsorption systems (including CytoSorb®) may be considered in the treatment of sepsis and hyperbilirubinemia in liver failure patients with sepsis.

<https://www.ncbi.nlm.nih.gov/pubmed/31405742>

Novel use of CytoSorb haemadsorption to provide biochemical control in liver impairment

Dhokia VD, Madhavan D, Austin A, Morris CG.
Journal of Intensive Care Society 2019; 20(2):174-181

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Summary

In this case series the use of CytoSorb® is described in the management of two patients with drug induced cholestasis and a third with alcoholic hepatitis and subsequent acute on chronic liver failure. CytoSorb® was used in these patients to remove bilirubin and bile acids by supporting impaired excretory hepatic function. The first two patients were admitted to the intensive care unit specifically for a trial of CytoSorb® therapy for alleviating their symptoms (including general malaise, anorexia and severe pruritus) and as a bridge to recovery of endogenous liver function. In all three cases, meaningful reductions in bilirubin (typically around 50% with 24 h CytoSorb® therapy) and even more impressive reductions in bile acids were observed and, in conscious patients, were associated with an improvement in symptoms. The authors conclude that for patients with liver impairment where recovery might be expected or where transplantation is not clinically appropriate, and especially where an existing CRRT extracorporeal circuit is in use (? in AKI), clinicians may wish to consider CytoSorb® as a convenient and effective means of reducing jaundice and clearing bile acids, although further studies are needed. The authors note that these cases suggest that CytoSorb® should also be evaluated as an adjunct to support liver excretory functions in other arenas, such as acute liver failure or drug overdose.

<https://www.ncbi.nlm.nih.gov/pubmed/31037112>

1.2.4 Myoglobinemia

Extracorporeal Removal of Myoglobin in Patients with Rhabdomyolysis and Acute Kidney Injury: Comparison of High and Medium Cut-Off Membrane and an Adsorber Cartridge

Jerman A, Andonova M, Persic V, Gubensek J.

Blood Purif 2022; 51(11):907-911

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Summary

In this single centre, retrospective case series, 15 pts with rhabdomyolysis (myoglobin >20,000 µg/L from various etiologies) were treated with either high cut-off (HCO), medium cut-off (MCO) dialysis membranes or the CytoSorb® adsorber. Overall, 28 procedures were performed with each patient only receiving one form of treatment (13 HCO, 9 MCO, and 6 adsorber treatments). Pre-treatment serum myoglobin levels were similar between the groups with myoglobin reduction significant in the HCO and MCO groups and borderline significant in the adsorber group, which was likely due to the small number of procedures in the adsorber group. Reduction rates were comparable between the groups. With routine albumin substitution in the HCO group only, serum albumin remained stable during the procedures in all subgroups. The authors note that in this small cohort of patients, the MCO membrane might represent the optimal mode of treatment of severe rhabdomyolysis-associated AKI. However, for patients with multiorgan failure requiring cytokine removal, CytoSorb® adsorption can simultaneously reduce cytokine and myoglobin levels, probably with a comparable effect on myoglobin reduction compared to the other two methods.

<https://www.ncbi.nlm.nih.gov/pubmed/35340002>

Successful Treatment of Rhabdomyolysis-Associated Acute Kidney Injury with Haemoadsorption and Continuous Renal Replacement Therapy

Hui WF, Hon KL, Lun KS, Leung KKY, Cheung WL, Leung AKC, Srivastava T.

Case Reports in Pediatrics 2021; 2148024

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Summary

This is a report of two children with rhabdomyolysis-associated acute kidney injury who were successfully treated with the CytoSorb® haemoadsorption column in addition to continuous renal replacement therapy (CRRT). In the 1st case a 14-year-old girl with multiorgan failure requiring extracorporeal membrane oxygenation (ECMO) developed rhabdomyolysis due to reperfusion injury. As her creatine kinase (CK) and lactate levels continued to escalate despite high-dose CRRT, CytoSorb® was added post CRRT filter which brought down the CK level from 264,500 IU/L to 97,436 IU/L after 8 hours of therapy. In the 2nd case a 4-year-old boy with epilepsy and cerebral palsy who was admitted for gastroenteritis with dehydration developed acute kidney injury and rhabdomyolysis with a peak CK level of 946,060 IU/L. He was initially treated with CRRT for 40 hours, which reduced his CK level to 147,580 IU/L. Two sessions of CytoSorb® were then performed in addition to the CRRT, which further lowered his CK level to 32,306 IU/L in 48 hours. The authors note that both patients demonstrated enhanced reduction of CK levels when CytoSorb® was used in addition to the CRRT, and no specific complication related to the haemoadsorption therapy was reported. The authors confirm that haemoadsorption can be considered as an adjunctive therapy for children with severe rhabdomyolysis-associated acute kidney injury, particularly those that show suboptimal response to standard therapies.

<https://www.ncbi.nlm.nih.gov/pubmed/34646583>

Blood purification with a cytokine adsorber for the elimination of myoglobin in critically ill patients with severe rhabdomyolysis

Scharf C, Liebchen U, Paal M, Irlbeck M, Zoller M, Schroeder I.

Crit Care 2021; 25(1):41

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Summary

This retrospective observational case series included 43 patients with anuric renal failure with the need of renal replacement therapy, who additionally received CytoSorb® therapy because they had rhabdomyolysis resulting in potentially damaging high levels of myoglobin (recognised as >5,000 ng/ml, study median was >25,000 ng/ml). The reason for the rhabdomyolysis included several factors including septic shock, trauma and hypovolemic or cardiogenic shock. Due to the severity of their illness (SOFA – sequential organ failure assessment score - on treatment day was 19 with an expected mortality of >90%), around 33% of all patients also needed ECMO (extracorporeal membrane oxygenation). Levels of myoglobin were measured pre- and post-CytoSorb® treatment. Patients were divided into those with persistent rhabdomyolysis (ongoing

creatinine kinase (CK) and myoglobin production from ongoing muscle injury) and those in which rhabdomyolysis was resolving (assuming that there is no direct removal of CK by CytoSorb® due its large molecular weight of 80kDa, as was indicated by decreasing CK levels). Overall, myoglobin levels decreased by 29% with a higher reduction of 38% seen in patients without ongoing rhabdomyolysis. Since all patients had anuric renal failure, renal elimination of myoglobin cannot be assumed and, in the authors' view, the reduction of myoglobin was largely due to the use of CytoSorb® and not due to the high-flux dialyzer. There was no significant difference in myoglobin elimination in patients with or without ECMO indicating that ECMO therapy might not have any impact on the elimination performance of the CytoSorb® adsorber. In hospital mortality was 67.4%. In summary, myoglobin removal with the CytoSorb® integrated into a high-flux dialyzer can be recommended for clinical routine due to its existing CE mark, ease of use and absence of side effects. This is the first case series in severe rhabdomyolysis patients showing the benefit of CytoSorb® therapy for removal of myoglobin, thereby averting permanent kidney damage.

<https://www.ncbi.nlm.nih.gov/pubmed/33509234>

1.2.5 Other indications

First Experience With Extracorporeal Cytokine Adsorption Therapy After Lung Transplantation

Peyneau M, de Chaisemartin L, Faille D, Messika J, Mal H, Castier Y, Mordant P, Carrasco JL, Tanaka S, Lortat Jacob B, Ferrari P, Arraul X, Ajzenberg N, Chollet-Martin S, Montravers P, Tran-Dinh A.

Transpl Int 2022; 35: 10319

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Summary

In this letter to the editor, 6 patients received CytoSorb® following admission to the intensive care unit (ICU) post lung transplantation (fibrosis - 4, chronic obstructive pulmonary disease - 1, silicosis - 1). CytoSorb® was integrated into the extracorporeal membrane oxygenation (ECMO) circuit and ran for 24 hrs. Blood samples were collected before CytoSorb® was installed (T0), after 24 hrs of treatment (T1), and 24 hours after cessation of treatment (T2). Membrane activation markers of neutrophils (CD66b and CD11b), monocytes (CD14 and HLA-DR), interleukin – IL6 and IL 8 and coagulation factors and lactate were collected. At T2 CD66B and CD11b were significantly decreased, as was lactate, with a downward trend noted for all other markers. The decrease in neutrophil and monocyte activation markers suggests a possible indirect immunomodulatory effect on phagocyte activation. The three patients with elevated IL-6 and/or IL-8 levels at T0 experienced a dramatic decrease at T1. There was no rebound effect at T2. Coagulation markers remain unaltered. Norepinephrine doses improved as did the P/F ratio during CytoSorb® treatment (so between T0 and T1). When compared to a 'control' group of 27 transplant pts, the ICU and hospital lengths of stay were longer for the CytoSorb® group, however at year 1 after transplant, all the CytoSorb® patients were alive, whereas the survival rate for the control group was 70.4%. The authors conclude that CytoSorb® appears to be a safe and promising device to fight post lung transplant inflammation.

<https://www.ncbi.nlm.nih.gov/pubmed/35387399>

Cytokine mass balance levels in donation after circulatory death donors using hemoadsorption: Case series report

Baroni S, Marudi A, Rinaldi S, Ghedini S, Magistri P, Piero Guerrini G, Olivieri T, Dallai C, Talamonti M, Maccieri J, Benedetto FD, Bertellini E.

Int J Artif Organs 2022; 45(7):642-646

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Summary

This observational case series includes 8 patients who were assessed for the donation after circulatory death (DCD) program for donation of either liver or kidneys. All DCD donor subjects were of a similar age (<60), without critical conditions, and had no known liver or kidney dysfunction. CytoSorb® was added to the extracorporeal membrane oxygenator (ECMO) prior to transplantation. Several inflammatory cytokine levels (interleukin – IL6, IL8, IL10, TNF-alpha) were measured before and after the CytoSorb® cartridge at various time points over nearly 3hrs, during the normothermic regional perfusion (NPR). Results showed a substantial reduction in IL-10 and TNF-alpha levels during the NPR period with hemoadsorption suggesting effective removal by the device with no evidence of a saturation effect. All livers and kidneys were transplanted from the DCD donors. Receiving patients spent less than 3 days in the intensive care unit and the mean number of days of hospitalization was below 14 days. None of these organs presented with signs of primary non-function or histological necrosis. None of the patients underwent renal replacement therapy during their hospital stay.

No apparent device-related adverse events occurred during normothermic perfusion. At the 1-year follow-up, there were no significant complications such as graft rejection or liver stenosis ducts. In summary, this study confirms the use of CytoSorb® during normothermic reperfusion in DCD donors where all donor organs could be transplanted without complications or primary non function, and, as the authors write, “may serve as a first in human validation towards a strategy to improve organs and to increase organ availability for donation and reduce the waiting list”.

<https://www.ncbi.nlm.nih.gov/pubmed/35426347>

Hemoperfusion with CytoSorb to Manage Multiorgan Dysfunction in the Spectrum of Hemophagocytic Lymphohistiocytosis Syndrome in Critically Ill Children

Bottari G, Murciano M, Merli P, Bracaglia C, Guzzo I, Stoppa F, Pardeo M, Nunziata J, Bufalo FD, Genuin L, De Benedetti F, Locatelli F, Cecchetti C.

Blood Purif 2022; 51(5):417-424

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Summary

In this cohort the authors evaluate the impact of hemoadsorption with CytoSorb® combined with continuous kidney replacement therapy used as an adjunctive therapy in six critically ill children with multiple organ dysfunction (MOD) due to HLH (hemophagocytic lymphohistiocytosis) caused by various etiologies. The age range of the children was 12 – 60 months, weight range was 10 – 29.5 kg, and they received on average 3 adsorbers for 24 hours each. Hemoadsorption with CytoSorb® (used in combination with CRRT) was started within 24 hours after pediatric intensive care unit (PICU) admission. Results showed that there was a reduction in inflammatory biomarkers pre and post treatment including: interleukin - IL 6 1,304 – 119 pg/mL, IL 10 140.7 – 31.59 mg/dL, C-Reactive Protein 23.1 – 0.59 mg/dL, procalcitonin 56.3 – 1.93 ng/mL. Ferritin, one of the most important bedside biomarkers of HLH, showed a reduction in five of the treated patients (59,280 – 1,578 ng/mL). The patients whose HLH trigger was infection showed hemodynamic stabilization as measured by the Vasopressor-Inotropic-Score, and reduction in the organ disease score measured with the Pediatric Logistic Organ Dysfunction score. Mortality was less than expected based on the Pediatric Index of Mortality 3 score at pediatric intensive care unit admission (expected mortality 47%, actual mortality 33%). The authors conclude that hemoperfusion with CytoSorb® could be a valuable therapeutic option in HLH. The advantage of CytoSorb® over the more commonly used plasma exchange is that it does not require plasma separation and that it allows for the concomitant treatment of fluid overload and acute kidney injury, both of which are commonly seen in MOD. Finally, the adsorber was safe and well tolerated with no device-related adverse events during or after the treatment sessions.

<https://www.ncbi.nlm.nih.gov/pubmed/34344006>

Multicentric Castleman's disease in HIV patients: a single-center cohort diagnosed from 2008 to 2018

Gliga S, Orth HM, Lubke N, Timm J, Luedde T, Jensen BO.

Infection 2021; 49(5):945-951

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Summary

This is a retrospective, descriptive study on a cohort of nine patients with multicentric Castleman's Disease (MCD) admitted to the infectious diseases or intensive care unit over a ten year period. Included patients had a previous or new HIV diagnosis and clinical signs resembling MCD. All patients received rituximab, and three also received tocilizumab. Other treatment options included: splenectomy (2/9), valganciclovir (2/9), vincristine and siltuximab (1/9), ruxolitinib and CytoSorb® (2/9). CytoSorb® was used to reduce cytokine levels associated with a cytokine storm, and control sepsis (in one of the patients). The authors conclude that the most effective first-line therapy and retreatment option remains rituximab and that the effectiveness of other treatment options such as splenectomy or different immunotherapeutic approaches require confirmation in larger-scale studies.

<https://www.ncbi.nlm.nih.gov/pubmed/33945103>

Use of CytoSorb in cases of acute amitriptyline intoxication

Paland M.

Journal of Clinical Pharmacy and Therapeutics 2021; 46(5):1476-1479

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Summary

This is a report of two patients with potentially lethal amitriptyline overdose levels. As treatment options for this type of tricyclic antidepressant overdose are limited, continuous renal replacement therapy was also

started along with CytoSorb® hemoadsorption. In the first patient three adsorbers were used over 22 hours with plasma levels assessed pre and post the adsorber. Measurements showed the direct and highly efficient removal of amitriptyline so that CytoSorb® treatment resulted in the rapid and sustained decrease in plasma levels to non-toxic levels within only a few hours (186 µg/l to 54.7 µg/l). In the second patient a toxic range of 844 µg/l at the start of treatment dropped to 290 µg/l at its discontinuation 8.5 hours later. As noted by the author, the ability of CytoSorb® to address hyperinflammation and/or to remove bilirubin and other liver toxins and myoglobin might also justify its use in intoxications in which clinical complications such as shock states, rhabdomyolysis or liver failure are present, despite the non-confirmed direct removal of the overdose substances. In cases presented here, CytoSorb® was primarily used with the idea of effective and early detoxification, which is thought to have prevented the occurrence of clinical complications. The author concludes that the use of CytoSorb® therapy in amitriptyline intoxication as a detoxification approach should be encouraged.

<https://www.ncbi.nlm.nih.gov/pubmed/33768556>

Use of Hemoadsorption in Patients With Severe Intoxication Requiring Extracorporeal Cardiopulmonary Support-A Case Series

Zickler D, Nee J, Arnold T, Schroder T, Slowinski T, Eckardt KU, Korner R, Kruse JM.
ASAIO J 2021; 67(11):e186-190

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Summary

This is a case series that includes four cases of acute intoxication requiring Venous Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) support used as extracorporeal cardiopulmonary resuscitation after intoxication-induced out-of-hospital cardiac arrest (OHCA). All patients were additionally treated with CytoSorb® hemoadsorption in combination with renal replacement therapy. Drugs included the anti-hypertensives - amlodipine, bisoprolol, and the antidepressant amitriptyline. The number of days of treatment ranged from 1 – 7. Combined treatment was associated with a considerable decrease in plasma levels of all the overdosed drugs. Additionally, the combination of applied techniques was safe, practical, and technically feasible with no adverse or any device-related side effects documented during or after the treatment sessions. Taking the pathophysiology of post cardiac arrest syndrome and its elevated levels of cytokines into account, CytoSorb®, might also have had some additional beneficial immunomodulatory properties in these cases next to potential detoxification effects. In summary and based on the reported dramatic decline in drug levels during treatment the authors strongly suggest to further investigate the potentially lifesaving role of CytoSorb® therapy in patients with acute intoxications requiring multiple organ support techniques.

<https://www.ncbi.nlm.nih.gov/pubmed/33587468>

First experiences of hemoadsorption in the Donation after Circulatory Death

Baroni S, Melegari G, Brugioni L, Gualdi E, Barbieri A, Bertellini E.
Clinical Transplant 2020; 34 (6):e13874

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Summary

In this letter to the editor, the authors describe a recent new application of the use of CytoSorb® with extracorporeal membrane oxygenation (ECMO) in cases of Donation after Circulatory Death (DCD). Particular to Italy, determination of death requires a 20-minute flat electrocardiogram, resulting in absence of circulation and any subsequent “Warm Ischemia Time (WIT)”, which results in high levels of cytokines, such as Tumor Necrosis Factor-Alpha (TNFα). This is a case report of three DCD donors. The abdominal organs were re-perfused using normothermic regional perfusion (nRP) in combination with CytoSorb® (included in the side arm of the regional ECMO circuit) in an attempt to increase the number of organs suitable for transplantation (liver and kidneys). Kidneys and liver were re-perfused with a blood flow always higher than 3 L/min, while blood flow through CytoSorb® was 300ml/min during extracorporeal circulation. Blood sampling from the circuit showed a significant removal of TNFα by CytoSorb®. During the first week after transplantation the creatinine serum mean value was almost 1.0 mg/dl, bilirubin 3.0 mg/dl, INR 1.2, only serum transaminase reached value upper 2000 U/L followed by physiological decrease. No cases of liver or kidney graft syndrome or recipient death at day 30 were reported. The authors state that nRP in combination with CytoSorb® has the potential to limit irreversible organ damage, to restore organ function and to be used as a bridge to transplantation, potentially mitigating cytokine release and harmful inflammatory mediators, especially TNFα, thereby reducing the risk of any adverse scenarios or graft dysfunction.

<https://pubmed.ncbi.nlm.nih.gov/32339334>

Cytokine Adsorption in Critically Ill Patients Requiring ECMO Support.

Lothar A, Benk C, Staudacher DL, Supady A, Bode C, Wengenmayer T, Duerschmied D.
Front Cardiovasc Med 2019; 6:71

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Summary

Systemic inflammation is a key characteristic of sepsis but also in non-infectious conditions such as post-cardiac arrest syndrome. Cytokine adsorption and extracorporeal membrane oxygenation are emerging therapies applied in these critically ill patients, but experience is limited. In this study the authors evaluated cytokine adsorption in critically ill patients requiring support with either veno-venous (vv) or veno-arterial (va) extracorporeal membrane oxygenation (ECMO) support. Data from the first six cases of a prospective single-center registry of patients was analysed (4 with sepsis, 2 post cardiac arrest). The CytoSorb® was incorporated directly into the ECMO circuit without interruption of continuous ECMO support. No relevant side effects attributable to the use of CytoSorb® were observed. Thirty-day mortality was 83% (predicted mortality 87%), indicating that the decision for adding cytokine adsorption may have been considered as an ultima ratio decision in severe cases with poor prognosis. Data suggest that incorporation of cytokine adsorption into the management of critically ill patients requiring continued ECMO support is feasible and easy to handle. Additional data regarding whether cytokine removal improves clinical outcome in ECMO-treated patients is now being gathered.

<https://www.ncbi.nlm.nih.gov/pubmed/31275944>

Application of hemoadsorption in neonatal and pediatric hyperinflammatory states: a case series

Milella L, Ficarella M, Calabrese G, Sisto M, Grieco N, Moliterni P, Raimondo P, Cito F, Bellino V, Ranieri M, Giordano M.

American Journal of Pediatrics 2019; 5(2):34-42

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Summary

This was a single center retrospective case series in ten patients (age range 1–312 months, weight 3.5 – 52 kgs) from a neonatal and pediatric general intensive care unit. The use of CytoSorb® in combination with standard therapy, continuous renal replacement therapy (CRRT) and plasmapheresis was observed for the treatment of multiple organ failures of various etiologies including sepsis and cardiac failure. The effect was reported on the inflammatory status, hemodynamics (reduction in catecholamine doses), clinically relevant outcome parameters, feasibility and safety of CytoSorb® application. The authors observed a marked decrease in inflammatory mediators (IL-6, IL-10, procalcitonin, C reactive protein, presepsin), a reduction in catecholamine (norepinephrine, epinephrine) and milrinone dosages and an improvement in organ functions, which was particularly pronounced in patients who survived. Early onset of treatment (within 24-48 hours after diagnosis of sepsis) seemed to be beneficial for eventual survival. In this neonatal and pediatric population, CytoSorb® was easy to implement and worked well in combination with simultaneous extracorporeal CRRT / plasmapheresis therapy.

[Link to Article](#)

Clinical Effects of hemoadsorption with CytoSorb in patients with severe acute pancreatitis: a case series

Tomescu D, Popescu M, Corina D, Dima S.

Intl J Artif Organs 2019; 42(4):190-193

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Summary

This prospective case series included 12 patients with severe acute pancreatitis who were treated with continuous venovenous hemodiafiltration (CVVHDF) and CytoSorb®. Clinical data including organ failure and level of vasopressor support were collected pre- and post CVVHDF and CytoSorb® treatment. All patients except one required three consecutive sessions. C Reactive Protein and procalcitonin (PCT) decreased from 242 – 180 mg/L (p=0.04) and 2.21 – 1.1 ng/ml (p=0.02) respectively. The mean vasopressor support was 0.1 mg/h at the start of treatment but was able to be discontinued in all cases post treatment (p=0.01). The number of organ dysfunctions decreased from four to three post treatment. No deaths were recorded during CytoSorb® therapy and the 24 hours thereafter, whereas 28 day survival was 66.7%. The therapy was well tolerated and no adverse outcomes were noted during the therapy or up to 24 hrs after the last session. In this first published case series of patients with severe acute pancreatitis, treatment with CytoSorb® and CVVHDF improved

hemodynamics, decreased vasopressor support, and appeared to re-balance the inflammatory response, as shown by the decrease in inflammatory markers.

<https://www.ncbi.nlm.nih.gov/pubmed/30638101>

1.2.6 COVID-19

Sequential Extracorporeal Blood Purification Is Associated with Prolonged Survival among ICU Patients with COVID-19 and Confirmed Bacterial Superinfection

Premuzic V, Situm I, Lovric D, Erceg A, Karmelic D, Mogus M, Jurjevic M, Nedeljkovic V, Mazar M, Mihaljevic S, Villa G, Ronco C.

Blood Purif 2023; 52(7-8):642-651

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Summary

This study investigated the impact of sequential extracorporeal blood purification (BP) treatments with oXiris® or CytoSorb® plus Seraph-100® on the clinical and laboratory parameters of critically ill patients in intensive care with COVID-19 and bacterial superinfection. Patients receiving standard care (SC), defined as BP with oXiris® or CytoSorb® (35 pts – 15 CytoSorb®, 20 oXiris®) was compared to SC plus sequential BP with the addition of Seraph-100® (33 pts – 14 CytoSorb®, 19 oXiris®). Results showed a significant reduction in the sequential organ failure assessment (SOFA) score 3 days after treatment in patients undergoing BP plus Seraph-100®. The difference between the observed and expected mortality rate based on APACHE IV was greater in the sequential BP group (42.4% vs. 81.7%) than the SC BP group (74.2% vs. 81.7%) which appeared to translate to longer term survival. The sequential approach may enhance the positive effect of BP on organ dysfunction, particularly respiratory status and decrease in vasoactive support, among critically ill patients with COVID-19 and bacterial superinfection.

<https://www.ncbi.nlm.nih.gov/pubmed/37482053>

Kinetics of SuPAR hemoadsorption in critical COVID-19 patients on renal replacement therapy

Vicka V, Januskeviciute E, Bartuseviciene I, Ringaitiene D, Aleknaviciene A, Serpytis M, Rimsevicius L, Miglinas M, Jancoriene L, Sipylaite J.

BMC Nephrol 2022; 23(1):371

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Summary

Soluble urokinase-type plasminogen activator receptor (suPAR) is a novel biomarker, both indicative of inflammation and propagating it. The aim of this prospective observational study was to determine suPAR kinetics during hemoadsorption in 18 patients with COVID-19. The CytoSorb® hemoadsorber was integrated into the continuous renal replacement therapy (CRRT) circuit. The first series of suPAR measurements was performed 10 minutes after the start of the session, sampling both incoming and outgoing lines of the adsorber. A second series of the measurements was performed before finishing the session with the same adsorber. At the beginning of the session the fraction of suPAR cleared across the adsorber was 29.5%, and in the end of the session it decreased to 7.2%, so 4 times lower, $p = 0.003$. The median length of session was 21 hours, with minimal duration of 16 hours and maximal duration of 24 hours. On average three adsorbers per patient were used. The median suPAR before the procedure was 8.71 [7.18-10.78] and after the session was 7.35 [6.53-11.28] ng/ml. There was no statistically significant difference in suPAR concentrations before and after the session ($p = 0.831$). This study concludes that in the beginning of the hemoadsorption procedure a significant amount of suPAR is removed from the circulation. However, by the end of the procedure there is a substantial drop in adsorbed capacity. Furthermore, despite a substantial amount of suPAR cleared there is no significant difference in systemic suPAR concentrations before and after the hemoadsorption procedure, suggesting an ongoing active production.

<https://www.ncbi.nlm.nih.gov/pubmed/36401202>

Cannulate, extubate, ambulate approach for extracorporeal membrane oxygenation for COVID-19

Hayanga JWA, Kakuturu J, Dhamija A, Asad F, McCarthy P, Sappington P, Badhwar V.

J Thorac Cardiovasc Surg; 2023; 166(4):1132-1142 e33

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Summary

This is a single centre, retrospective analysis from the hospital's extracorporeal membrane oxygenation (ECMO) registry, where patients with severe COVID-19 versus non-COVID-19-related acute respiratory distress

syndrome (ARDS) were compared using data from 2017 to 2021. The association of COVID-19 status (COVID-19-related ARDS vs non-COVID-19 ARDS) and survival to decannulation, discharge, tracheostomy, and extubation were compared. The authors also conducted a subgroup analyses to compare outcomes with patients that were also prescribed the use of extracorporeal cyto-reductive techniques (CytoSorb® and plasmapheresis). The decision to start cyto-reductive techniques was a threshold ferritin level of 1,000 and a D-dimer of 3,000. There were 128 patients in total (50 with COVID-19 and 78 with non-COVID-19 ARDS). Advancing age was associated with decreased probability of survival to decannulation. Compared with the non-COVID-19 ARDS group, patients with COVID-19 had a greater probability of survival to extubation and comparable survival to discharge. Use of CytoSorb® in line with the emergency use authorization protocol in the 25 COVID-19 pts did not result in any differences in outcome when compared to patient not receiving CytoSorb® but plasmapheresis. In conclusion, patients with COVID-19 managed with ECMO had comparable outcomes to patients with non-COVID ARDS. A strategy of early extubation and ambulation might be a safe and effective strategy to improve outcomes and survival, even for patients with severe COVID-19.

<https://www.ncbi.nlm.nih.gov/pubmed/35396123>

Cytokine Hemoadsorption as Rescue Therapy for Critically Ill Patients With SARS-CoV-2 Pneumonia With Severe Respiratory Failure and Hypercytokinemia

Ruiz-Rodríguez JC, Chiscano-Camón L, Ruiz-Sanmartin A, Palmada C, Paola Plata-Menchaca E, Franco-Jarava C, Pérez-Carrasco M, Hernández-González M, Ferrer R.

Frontiers in Medicine 2022; 8:779038

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Summary

This retrospective case series included six patients with SARS-CoV-2 pneumonia, acute respiratory failure (refractory to the use of prone positioning) and hypercytokinemia who received CytoSorb® during their intensive care treatment. Patients received on average 1 adsorber with a mean perfusion time of 16 hrs. All patients were mechanically ventilated. Inclusion criteria for the use of CytoSorb® were the presence of acute respiratory failure ($\text{PaO}_2/\text{FiO}_2$ ratio < 150) with poor response to the prone position, as well as a hyperinflammatory state, manifested as interleukin-6 (IL-6) hypercytokinemia ($\text{IL-6} > 1,000$ pg/ml), and increased levels of ferritin and D-dimers (DD). CytoSorb® was connected post-hemofilter to a CRRT circuit and anticoagulation was performed with citrate or heparin. A significant difference was found in the pre- and post CytoSorb® treatment: D-dimers (17,868 mcg/ml vs. 4,488 mcg/ml, $p 0.046$), C-reactive protein (12.9 mg/dl vs. 3.5 mg/dl, $p 0.028$), ferritin (1,539 mcg/L vs. 1,197 ng/ml, $p 0.04$) and interleukin- IL-6 (17,367 pg/ml vs. 2,403 pg/ml, $p 0.043$) levels. There was also a significant improvement in oxygenation pre and post adsorber use ($\text{PaO}_2/\text{FiO}_2$ ratio 103 – 222, $p 0.029$) and the sequential organ failure assessment score (SOFA) ($p 0.046$). In summary, the adjuvant use of CytoSorb® in this refractory group of patients with COVID-19 and acute respiratory failure was safe and effective, significantly reducing inflammatory biomarkers including IL-6, and improving oxygenation and multiorgan dysfunction.

<https://www.ncbi.nlm.nih.gov/pubmed/35083241>

Extracorporeal Cytokine Removal in Critically Ill COVID-19 Patients: A Case Series

Virág M, Rottler M, Ocskay K, Leiner T, Horváth B, Adam Blanco D, Vasquez A, Bucsi L, Sárkány A, Molnár Z.

Front Med 2021; 8: 760435

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Summary

This retrospective case series included 13 patients with COVID-19 viral pneumonia, requiring mechanical ventilation and renal replacement therapy who were also treated with hemoadsorption (HA) with CytoSorb®. According to the authors it is the first and largest comprehensive case series on COVID-19 patients treated with hemoadsorption from Eastern Europe. Clinical and laboratory data were collected on admission, and before and after HA therapy. On average 1.6 days elapsed from admission to the application of the first adsorber and patients received on average 3 adsorbers. From before to after HA there was a tendency of decreasing norepinephrine requirements (193.7 to 50.2 $\mu\text{g}/\text{kg}/\text{day}$) and increasing $\text{PaO}_2/\text{FiO}_2$ ratio (127.8 to 155.0 mmHg). All patients were alive at the end of HA and were still alive 72 hours after the initiation of therapy, therefore therapy was not terminated due to a deterioration in the patient's condition, however, only 3 survived their hospital stay. There were no treatment related adverse events reported. The authors discuss lack of human resources, including intensive care doctors and nurses, as highly relevant in Eastern European hospitals, which might result in a situation where even state-of-the art equipment and treatment strategies,

such as CytoSorb®, cannot make a difference. They conclude that hemoadsorption was well tolerated and helped to stabilise and overcome the initial critical phase of the severe COVID-19 infection.

<https://www.ncbi.nlm.nih.gov/pubmed/34869464>

Cytokine Adsorption Therapy during Extracorporeal Membrane Oxygenation in Adult Patients with COVID-19

Rodeia SC, Martins FL, Fortuna P, Bento L.

Blood Purif 2022; 51(9):791-798

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Summary

In this retrospective case series, five patients with respiratory failure and severe SARS-CoV-2 disease (COVID-19) were treated with standard therapy plus extracorporeal membrane oxygenation (ECMO) and cytokine adsorption therapy (CAT) with CytoSorb® if the interleukin – IL6 was >100 pg/ml. CytoSorb® was inserted within the ECMO circuit (2 adsorbers for 24 hrs use each) with no direct complications seen. CAT use with CytoSorb® helped control the inflammatory state (C-reactive protein, ferritin, and IL-6), and all patients were able to have their vasopressor support stopped within 72 hrs. In this case series of severe COVID-19 patients, due to the severity of their disease, eventually 3 patients died from irreversible lung fibrosis, complications of critical hypoxemia before ECMO induction and complications of systemic anticoagulation. Nonetheless the authors note that CytoSorb® appears to have a role in controlling the inflammatory response from multiple insults, as judged by the reduction in IL-6, lactate and vasopressor requirements. They conclude that cytokine adsorption therapy seems to be a safe therapy, and, albeit expensive, its costs may be offset by its efficacy in controlling the superinflammatory response seen in COVID-19 patients.

<https://www.ncbi.nlm.nih.gov/pubmed/34856539>

CytoSorb purification in critically ill SARS-CoV-2 patients

Pieri M, Fominskiy E, Nardelli P, Bonizzoni MA, Scandroglio AM.

Int J Art Organs 2022; 45(2):216-220

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Summary

This retrospective case series included 15 critically ill patients with refractory acute respiratory distress syndrome (ARDS) following SARS-CoV-2 infection. All patients were mechanically ventilated, 8 were also on venovenous extracorporeal membrane oxygenation (vvECMO) and 11 required inotropes for circulatory failure. CytoSorb® was used in either hemoperfusion mode or attached to the ECMO circuit with patients receiving on average 3 CytoSorb® cycles. Results showed a reduction in the levels of C reactive protein, total bilirubin, direct bilirubin, and D-dimers during CytoSorb® treatment and a trend toward reduction in lactate dehydrogenase, creatine phosphokinase, and fibrinogen. Respiratory parameters also tended to improve over the days of CytoSorb® treatment (PaO₂ / FiO₂ increase). Of the seven patients who were discharged from the ICU, five had recovery of their native lung function and two were successfully bridged to lung transplantation whilst on vvECMO support. In summary, CytoSorb® treatment was seen to be effective in reducing several laboratory parameters and inflammation, and no treatment related adverse events were recorded. According to the authors, CytoSorb® treatment long with vvECMO can provide time for the patients to benefit from hemodynamic stabilization and decreased use of inotropes and time for spontaneous recovery. In the light of the unique pathophysiology of SARS- CoV-2 infection, the treatment is described as being extremely promising as it might reduce both inflammation and activation of coagulation.

<https://www.ncbi.nlm.nih.gov/pubmed/34702109>

Hemoperfusion with CytoSorb in Critically Ill COVID-19 Patients

Peng JY, Li L, Zhao X, Ding F, Hou X, Peng Z.

Blood Purif 2022; 51(5):410-416

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Summary

In this case series, 10 patients with COVID-19 were included from three Chinese hospitals in the Spring of 2020. The median age of the patients was 67.7 years with an APACHE II score of 23.5 and SOFA score of 11.4. CytoSorb® was most commonly inserted into the renal dialysis circuit, and patients received a median of 3 adsorbers (range = 1-6 for 12 – 24 hrs per adsorber). The median CytoSorb® perfusion time was 47 h (12-92 h). The level of interleukin (IL)-6 significantly decreased after treatment (712.6 [145-5,000] vs. 136.7 [46.3-1,054] pg/mL, p = 0.005). This was particularly apparent in the two patients who were also on extracorporeal membrane oxygenation (initially IL-6 was 3,854.6 pg/ml with an 80% reduction after treatment). Significant

improvement was found in the PaO₂/FiO₂ ratio (118 [81-220] vs. 163 [41-340] mm Hg, p = 0.04) and lactate levels (2.5 [1-18] vs. 1.7 [1.1-10] mmol/L, p = 0.009). The hemodynamic situation as measured by norepinephrine/mean arterial pressure (MAP) also improved after treatment (17 [0-68] vs. 8 [0-39], p = 0.09). No significant changes were found in red blood cell counts, white cell counts, and platelets. The authors conclude that treatment with CytoSorb® in these critically ill COVID-19 patients was found to be safe and well tolerated with no device related adverse events, and its use was associated with a decrease in IL-6, reduction of catecholamine support and an improvement in oxygenation.

<https://www.ncbi.nlm.nih.gov/pubmed/34407530>

Use of CytoSorb therapy to treat critically ill coronavirus disease 2019 patients: a case series

Mehta Y, Mehta C, Nanda S, Kochar G, George JV, Singh MK.

J Med Case Rep 2021; 15(1):476

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Summary

This article presents three cases of severely ill adult patients with coronavirus disease 2019 admitted to intensive care unit who were treated with CytoSorb® therapy. All patients used a single CytoSorb® device for 24 hours. During their clinical course, all patients were also prescribed tocilizumab, antivirals, hydroxychloroquine, azithromycin, and other antibiotics and general antipyretic drugs. No vasopressor treatment was required. All patients showed significant improvement in biochemical parameters and clinical outcomes post CytoSorb® therapy, as well as a speedy recovery. The authors conclude that extracorporeal cytokine removal could be a useful adjuvant therapy to overcome hyperinflammation in critically ill patients and could also be considered as a potential therapeutic option to manage the serious complications of hyperinflammation and cytokine release syndrome in critically ill COVID-19-infected patients.

<https://www.ncbi.nlm.nih.gov/pubmed/34535189>

Adjuvant hemoadsorption therapy in patients with severe COVID-19 and related organ failure requiring CRRT or ECMO therapy – a case series

Wunderlich-Sperl F, Kautzky S, Pickem C, Hörmann C.

Int J Artif Organs 2021; 44(10):694-702

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Summary

This retrospective case series included thirteen patients with COVID-19 acute respiratory distress syndrome (ARDS) who received either extracorporeal membrane oxygenation (ECMO, around 60% of patients) and/or continuous renal replacement therapy (CRRT). Hemoadsorption with CytoSorb® was initiated once the patient had established or was at high risk of developing a hyperinflammatory state, including hemodynamic instability and/or progressive lung failure. CytoSorb® was used on average 7 days after intensive care admission for a median of four treatments. Change of the adsorber was planned every 24h, but could be adapted to every 12h if deemed appropriate by the treating physician (e.g. lack of hemodynamic stabilization or worsening organ failure after 12 h). CytoSorb® treatment was associated with a significant reduction in inflammatory parameters, such as C-Reactive Protein (CRP) and interleukin – IL-6. This was paralleled by hemodynamic stabilization with decreasing requirements for vasoactive substances. Lung function, oxygenation and level of ventilatory support also improved significantly during the treatment period, including P/F ratio 76 – 122.22 mmHg). Overall mortality was 38.5% at 21 days. The authors conclude that there was effective IL-6 removal, reduced norepinephrine requirements and improved lung function during adjuvant therapy with CytoSorb®. The authors did not observe any device-related adverse events, nor were there any problems installing the adsorber into the CRRT circuit (in pre-hemofilter position) or into the vvECMO circuit. They also present a protocol for CytoSorb® initiation used for decision making in their ICU, which may be a good foundation for the development of further prospective studies in this field and may eventually also be applied to other forms of hyperinflammatory ARDS.

<https://www.ncbi.nlm.nih.gov/pubmed/34256643>

Impact of CytoSorb Hemoadsorption on Sedation Requirements in Patients with Severe COVID-19 on Venovenous Extracorporeal Membrane Oxygenation

Lewis TC, Merchan C, Toy B, Goldenberg RM, Geraci TC, Chang SH, Galloway AC, Smith DE, Moazami N.

ASAIO J 2021; 67(8):856-861

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Summary

This is a retrospective review of patients with severe COVID-19 requiring veno-venous extracorporeal membrane oxygenation (VV-ECMO) for respiratory support. Eight patients who were enrolled in a clinical study of CytoSorb® were compared to 18 patients on VV-ECMO alone. Data was collected for the 72-hour CytoSorb® therapy and an additional 72 hours post-CytoSorb®. Sedative (midazolam) and analgesic (fentanyl) doses were totalled for each day. Sedation was monitored by the bedside nurse using the Richmond Agitation and Sedation Scale (RASS). There was no effect of CytoSorb® therapy on midazolam equivalents over the 72-hour therapy (p=0.71) or the 72 hours post-CytoSorb® use (p=0.11). In contrast, there was a significant effect of CytoSorb® therapy on fentanyl equivalents over the first 72 hours (p=0.01), but this was not consistent over the 72-hours post CytoSorb® (p=0.23). Median daily RASS scores were similar between groups. The authors conclude that the use of CytoSorb® therapy led to significant increases in analgesic requirements without impacting sedative requirements. Further research is needed to define the relevance of CytoSorb® hemoadsorption on critical care pharmacotherapy.

<https://pubmed.ncbi.nlm.nih.gov/34339400/>

Hemoadsorption for management of Patients on Venovenous ECMO Support for Severe COVID-19 Acute Respiratory Distress Syndrome

Geraci T, Kon Z, Moazami N, Chang S, Carillo J, Chen S, Fargnoli A, Alimi M, Pass H, Galloway A, Smith D. *J Cardiac Surg* 2021; 36(11):4256-4264

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Summary

This study reports outcomes in 10 patients with COVID-19 supported by veno-venous extracorporeal membrane oxygenation (VV-ECMO), who were chosen for the emergency use of CytoSorb® hemoadsorption integrated in the VV-ECMO circuit. Hemoadsorption was added to the circuit in selected patients based on severity of illness, so primarily those who had progressive clinical decline while supported on VV-ECMO received hemoadsorption treatment. Patients were supported on ECMO a median of 1 day before initiation of CytoSorb®. Various clinical data and inflammatory markers were assessed pre and post treatment to determine the safety and feasibility of using this system, and to evaluate clinical effect. CytoSorb® use was planned for 72 hrs (2 adsorbers for 12 hours each, then 2 adsorbers for 24 hrs each), which could be completed in 80% of patients. During treatment with CytoSorb® hemoadsorption median levels of interleukin (IL)-2R, IL-6, and IL-10 decreased by 54%, 86%, and 64% respectively. Reductions in other markers were observed for lactate dehydrogenase (LDH -49%), ferritin (-46%), D-dimer (-7%), C-reactive protein (-55%), procalcitonin (-76%) and lactate (-44%). Vasoactive-inotrope scores decreased significantly over the treatment interval (-80%). The median hospital length of stay was 53 days (36-85) and at 90-days post cannulation, survival was 90% which was similar to a group of patients without the use of hemoadsorption. The authors conclude that the addition of hemoadsorption into the VV-ECMO in patients with severe COVID-19 is feasible and reduces measured cytokine levels. However, in this small series, the precise impact on the overall clinical course and survival benefit still remains unknown.

<https://www.ncbi.nlm.nih.gov/pubmed/34219277>

Blood purification with CytoSorb in critically ill COVID-19 patients: A case series of 26 patients

Nassiri AA, Hakemi MS, Miri MM, Shahrami R, Koomleh AA, Sabaghian T. *Artif Organs* 2021; 45(11):1338-1347

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Summary

In this retrospective study, 26 patients with COVID-19 and acute respiratory distress syndrome (ARDS) were treated with CytoSorb® hemoadsorption therapy. On average patients received two hemoadsorption treatments (one for 12 hours and one for 24 hours) either in hemoperfusion (standalone) mode or inserted into a continuous renal replacement therapy (CRRT) circuit. When pre and post treatment levels were compared, there were significant decreases in norepinephrine requirements, and inflammatory marker plasma concentrations (procalcitonin, C-Reactive Protein, ferritin). Also PaO₂/FiO₂ improved significantly as did overall organ function (i.e. Sequential Organ Failure Assessment - SOFA score). Patients stayed on the ICU for a mean of 9 days and ICU mortality was 19.2% with 5 patients dying on the ICU. Time from onset of symptoms until start of CytoSorb® treatment was significantly shorter in the survivor group. This is one of the largest case series to date reporting early experiences on extracorporeal hemoadsorption therapy in SARS-CoV-2 positive patients with hyperinflammation and moderate ARDS. Treatment proved to be effective, technically feasible and well-tolerated.

<https://www.ncbi.nlm.nih.gov/pubmed/34152629>

Continuous hemadsorption with cytokine adsorber for severe COVID-19: A case series of 15 patients

Paisey C, Patvardhan C, Mackay M, Vuylsteke A, Bhagra SK.

Int J Artif Organs 2021; 50(6):976-978

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Summary

This is a retrospective case series of 15 patients with severe Covid-19 receiving adjunctive hemadsorption (HA) in our ICU. Ten patients received CytoSorb® and five Jafron HA330. In most cases patients received 4 adsorbers (2 in the first 24 hrs, and two over the next 48 hours). All patients were intubated, ventilated and required renal replacement therapy with 11/15 also supported on extracorporeal membrane oxygenation (ECMO). Significant differences were found in pre- and post- treatment ferritin 3622 ng/ml v 1682 ng/ml ($p = 0.022$), C-Reactive Protein - CRP 222 mg/ml v 103 mg/ml ($p = 0.008$, 95% CI 22.4-126.5), lactate 2 mmol/L versus 1.3 mmol/L ($p = 0.017$), and procalcitonin - PCT 15.3 ng/ml versus 4.2 ng/ml ($p = 0.023$). No significant difference in pre- and post- interleukin - IL-6, IL-10 IL1 beta, TNF alpha, or vasoactive inotrope score (VIS) were seen, however, a significant difference pre-HA and at 72h was noted for SOFA score 8 versus 6. At 6 month follow up, overall mortality was 8/15 pts. No safety concerns were identified. The authors conclude that the use of HA as an adjunctive treatment in a critically unwell group of COVID-19 patients led to a reduction in ferritin, CRP, PCT and lactate with no significant change in other parameters.

<https://www.ncbi.nlm.nih.gov/pubmed/34128416>

Extracorporeal Cytokine Hemadsorption in Severe COVID-19 Respiratory Failure

Damiani M, Gandini L, Landi F, Borleri G, Fabretti F, Gritti G, Riva I.

Respiratory Medicine 2021; 185:107477

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Summary

The letter to the editor reports on 11 patients admitted with COVID-19 over a 2 week period in March 2020. All patients were mechanically ventilated and admitted to intensive care. Along with standard therapy at the time, CytoSorb® was included in the continuous veno-venous hemodiafiltration circuit. Most patients had 2 x 24 hr treatment. After a median follow up of 16 days (range 6 – 30 days), nine patients survived (82%) and were discharged from intensive care. Inflammatory mediators (including interleukin – IL-6) were measured before and after treatment, and 7 days from treatment end. Markedly elevated levels in particular of IL6 and IL8 were observed, with a significant reduction in IL-6, IL-8, IL-10 and IL1β at treatment end. C-Reactive Protein also significantly reduced and median P/F ratio increased indicating improved respiratory function. CytoSorb® proved to be safe in these COVID-19 patients and no unexpected adverse events were observed. Clinical improvement was seen in most treated patients despite the severity of the disease.

<https://pubmed.ncbi.nlm.nih.gov/34102594/>

Longitudinal Cytokine Profiling in Severe COVID-19 Patients on ECMO and Haemoadsorption

Lebreton G, Dorgham K, Quentric P, Combes A, Gorochov G, Schmidt M.

Am J Respir Crit Care Med 2021; 203(11):1433-1435

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Summary

This letter to the editor included 22 COVID-19 patients who were put on extracorporeal membrane oxygenation (ECMO) due to the severity of their condition. The first group of 11 consecutive patients had a CytoSorb® adsorber placed in the ECMO circuit. These patients were unselected otherwise, as was the timing for the initiation of the CytoSorb® adsorber. These patients were then compared to the next 11 patients on ECMO who were not given CytoSorb® (control group). Various biomarkers for inflammation were recorded pre ECMO, 4 hours after ECMO start (before CytoSorb® start), then 12 and 48 hours after CytoSorb® and ECMO use (or ECMO alone for control group). Biomarkers included interleukin- IL-1β, IL-6, IL-8, IL-22, IL-10, IL-17A, IL-18, GM-CSF, IFN-α, IFN-γ, TNF-α, and IFN-β. Analysis of the cytokines tested did not show an increase after four hours of ECMO indicating that ECMO itself does not exacerbate cytokine release in COVID-19 patients. IL-10 and IFN-γ concentrations decreased significantly after 48 hours of CytoSorb®. IL-6 also decreased but not significantly. IL-6, IL-8 and IL-10 also decreased significantly in the control group. Eight patients survived to 60 days in the CytoSorb® group (73%), compared to seven patients in the control group (64%). In conclusion, ECMO does not exacerbate cytokine release in COVID-19 patients where IL-6, IL-8, and IL-10 decrease after 48 hours on ECMO with ultra-protective mechanical ventilation. To what extent combining a CytoSorb® adsorber

with ECMO could enhance the decrease of these cytokines and improve outcomes, warrants further investigations.

<https://pubmed.ncbi.nlm.nih.gov/33725469/>

Effects of tocilizumab versus hemoadsorption combined with tocilizumab in patients with SARS-CoV-2 pneumonia:

Preliminary results

Berlot G, Pintacuda S, Moro E, Paluzzano G, Scamperle A, Chillemi A, Longo I, Dattola R, Roman-Pognuz E, Tomasini A.

Int J Artif Organs 2022; 45(1):75-80

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Summary

In this retrospective analysis of four patients with SARS-CoV-2 pneumonia, two treated with Tocilizumab (TCZ) alone were compared to two patients treated with CytoSorb® hemoadsorption (HA) and TCZ. TCZ alone was administered in patients with only pulmonary involvement and blood levels of C-Reactive Protein (CRP) ≥ 100 mg/L and of interleukin (IL)-6 > 11 pg/m, whereas HA was added to the TCZ in the presence of arterial hypotension and/or signs of organ dysfunction (OD) other than the lung. In both of the two CytoSorb® patients, three procedures were performed for 24 hrs each. All patients were mechanically ventilated with the blood values of IL-6, CRP and PaO₂/FiO₂ ratio measured before, during and after treatment. In all patients, the IL-6 increased during the treatment; after its termination, its values sharply decreased only in those treated with HA. According to the authors the increase of the IL-6 of can be ascribed to its displacement from cellular and soluble receptors, whereas its decrease is likely due to the scavenging effect exerted by the HA. Conversely, CRP decreased in all patients; the PaO₂/FiO₂ increased in three patients and remained stable in one. Both the TCZ and CytoSorb® adsorber were well tolerated; all patients were weaned from the mechanical ventilation and discharged from the hospital. The authors note that although the use TCZ and HA could be valuable in the treatment of the Cytokine Release Storm (CRS) associated with SARS-CoV-2, that CytoSorb® could be more effective as it neutralizes a wider panel of inflammatory mediators.

<https://www.ncbi.nlm.nih.gov/pubmed/33573449>

Hemoperfusion with CytoSorb as Adjuvant Therapy in Critically Ill Patients with SARS-CoV2 Pneumonia

Rampino T, Gregorini M, Perotti L, Ferrari F, Pattonieri EF, Grignano MA, Valente M, Garrone A, Islam T, Libetta C, Albertini R, Bruno R, Belliato M.

Blood Purification 2021; 50(4-5):566-571

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Summary

In this article the authors conducted an observational study on nine consecutive COVID-19 positive patients hospitalized in their COVID Intensive Care Unit. Five of the patients were treated with hemoperfusion (HP) using a CytoSorb® adsorber. Due to the emergency overload it was impossible to deliver blood purification in the other four patients. All patients had severe pneumonia requiring continuous positive airway pressure. HP was started in all five patients 6–7 days after hospital admission. The treated patients (T) received 2 consecutive sessions of the CytoSorb® adsorber. The results showed a better clinical course for these CytoSorb® treated patients compared to the control patients (C). All five CytoSorb® patients except 1 survived, and only 2 of them had to be intubated, while all control patients required intubation and unfortunately died. Lymphocytopenia worsened in the controls but not in CytoSorb® treated patients. C-reactive protein decreased in both patients, but to a greater extent in the CytoSorb® group. Interleukin (IL)-6, IL-8, and TNF- α decreased after CytoSorb®, IL-10 did not change. Respiratory function remained stable and did not worsen in the CytoSorb® group compared to the controls. As the authors note, this experience suggests a potential therapeutic role of adjuvant CytoSorb® in the early course of COVID-19 pneumonia by improving respiratory function and lowering mortality. The authors are currently conducting a randomized clinical trial which is ongoing.

<https://www.ncbi.nlm.nih.gov/pubmed/33181508>

Continuous renal replacement therapy with the addition of CytoSorb® cartridge in critically ill patients with COVID-19 plus acute kidney injury: a case-series

Alharthy A, Faqih F, Memish ZA, Balhamar A, Nasim N, Shahzad A, Tamim H, Alqahtani SA, Brindley PG, Karakitsos D.

Artif Organs 2021; 45(5):E101-E112

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Summary

This case series retrospectively analyzed 50 patients with severe COVID-19 induced acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT) along with CytoSorb®. Patients also had to have sepsis /septic shock, acute respiratory distress syndrome (ARDS) and cytokine release syndrome (CRS). This was given in around 10% of all COVID-19 patients admitted to ICU in the study period of June 1 to July 30,2020. In addition to CRRT with CytoSorb® all received ARDS-net ventilation, prone positioning, plus empiric ribavirin, interferon beta-1b, antibiotics, hydrocortisone, and prophylactic anticoagulation. These patients were critically ill according to the ICU scores (mean APACHE II 22.5, SOFA 9.4) with a PaO₂/FiO₂ ratio of 117.46. Duration of mechanical ventilation was 17.38 days, ICU length-of-stay 20.70 days, and mortality at 28 days post-ICU admission being 30%. Non-survivors (30% of total patients) had higher levels of inflammatory biomarkers (interleukin – IL 6), and more unresolved shock, ARDS, AKI, and pulmonary emboli (8% vs. 4 %, p<0.05) compared to survivors (70% of patients). After 2±1 CRRT sessions with CytoSorb® (adsorber changed 24 hrly), survivors had decreased Sequential Organ Failure Assessment (SOFA) scores, lactate dehydrogenase, ferritin, D-dimers, C-reactive protein, and interleukin (IL)-6; and increased PaO₂/FiO₂ ratios, and lymphocyte counts (all p<0.05). Survivors were also able to have vasopressors weaned off and renal function improved. Statistical analysis showed that post therapy values of IL-6 (cutoff point > 620 pg/ml) predicted in-hospital mortality for these patients (AUC 0.87). No side effects of CytoSorb® therapy were recorded. The authors conclude that CytoSorb® provided a safe rescue therapy in life threatening COVID-19 associated sepsis, AKI, ARDS, and hyperinflammation and appears to mitigate hyperinflammation. <https://pubmed.ncbi.nlm.nih.gov/33190288/>

1.3 Case reports

1.3.1 Septic Shock

CytoSorb® in Combination with CRRT in A Patient Suffering from Septic Shock, Acute Respiratory Distress Syndrome (ARDS) and Acute Kidney Injury (AKI): A Case Report

Sharma GS, Narwal M.

Int J Health Sciences & Research 2023; 13(10):353-357

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Summary

In this case report, a 53 yr old female patient suffering from septic shock with acute kidney injury (AKI) and acute respiratory distress syndrome (ARDS) was treated with standard medical treatment, including mechanical ventilation and continuous renal replacement therapy (CRRT). Due to her refractory situation, adjuvant extracorporeal hemoadsorption with CytoSorb® was started on intensive care unit day 5 to address the cytokine storm. After two sessions of CytoSorb® (24 hrs each) there was a rapid improvement in her hemodynamic stability (norepinephrine decreased from 0.58 to 0.17 µg/kg/min, epinephrine from 0.08 – 0.025 µg/kg/min), improvement in her respiratory function (PaO₂ improved from 80.9 to 95.2 mmHg with a reduction of FiO₂ from 90 to 40 %) and decrease in the blood lactate (5 – 1.2 mmol/L). The authors conclude that the use of adjuvant CytoSorb® therapy in conjunction with standard treatment and CRRT was found to be a safe and effective therapeutic alternative in this patient suffering from septic shock, ARDS, and AKI. Adjuvant CytoSorb® therapy was associated with rapid hemodynamic stability, improvement in respiratory functions, reduction in vasopressor requirements, and decrease in blood lactate. It helped achieve immunological homeostasis, thus gaining treatment time in order for the standard therapies to work.

[Link to Article](#)

CytoSorb® Therapy in the Treatment of a Patient with Chronic Kidney Disease (CKD) Associated with Symptoms of Sepsis: A Case Report

Andrews R, Paul R, Sirga S, Panigrahi N.

Clinical Care Reports 2022; 5(4):234

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Summary

In this case a 37 yr old with chronic kidney disease (CKD) was admitted to hospital with suspected sepsis and cytokine storm. He was admitted to the intensive care unit (ICU) with respiratory and renal dysfunction. Two days after admission, CytoSorb® was started, inserted into a hemodialysis circuit. Two devices were used (16 hrs each) during which time his regular sessions of dialysis were continued. Post CytoSorb® therapy, procalcitonin, interleukin 6 and C-Reactive Protein all improved. Total bilirubin also decreased and his clinical condition improved considerably, including a decrease in lactate and increase in urine output. The patient was able to be discharged from ICU after 10 days and back home after 13 days for ongoing hemodialysis. The authors conclude that CytoSorb® therapy can be considered as a bridge to stabilize critically ill CKD patients,

until more definitive therapies take place. The therapy provides hemodynamic stability and improves organ dysfunction and with no significant adverse events.

[Link to article](#)

Veno-venous extracorporeal membrane oxygenation, cytokine removal and continuous renal replacement therapy in a severe burn adult patient

Bubenek-Turconi SI, Corneci D, Scarlat C, Baila S, Marinescu P, Valeanu L.
Int J Artif Organs 2023; 46(2):120-125

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Summary

This is a case report on a 41 yr old with 25% total body surface area, deep partial thickness burns to his upper body and grade II inhalational injury following an explosion, who, after an initial good recovery, went on to develop acute respiratory distress syndrome (ARDS), nosocomial pneumonia and septic shock. Veno-venous extracorporeal membrane oxygenation (VV ECMO) and continuous renal replacement therapy (CRRT) with hemoadsorption (CytoSorb®) were successfully used at different times to overcome critical situations. Significant hemodynamic improvement and reductions in inflammatory markers were observed during CRRT combined with hemoadsorption. The patient was eventually discharged from intensive care on day 71 and hospital on day 73, having fully recovered. The authors conclude that although debatable, the use of VV ECMO in burn patients with severe ARDS could be considered when conventional treatment fails. The use of CRRT combined with hemoadsorption may limit the proinflammatory response sustained by the combination of a major burn, ECMO and sepsis.

<https://www.ncbi.nlm.nih.gov/pubmed/36540045>

Successful Extracorporeal Blood Purification Therapy using Double Haemoadsorption Device in Severe Endotoxin Septic Shock: A Case Report

Ferraro S, Bianzina S, Mocka S, Cappadona F, Traverso GB, Massarino F, Esposito P.
J Crit Care Med (Targu Mures) 2022; 8(4): 292-295

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Summary

This is a case of a 70-year-old woman admitted to the intensive care unit (ICU) with a severe endotoxin septic shock due to *Neisseria meningitidis* serogroup C. Despite prompt medical intervention, including fluid resuscitation, high dose vasopressors, inotropic support, and broad-spectrum antimicrobial treatment, the patient's haemodynamic rapidly worsened and she developed multi-organ failure (MOF), including severe acute kidney injury (AKI), requiring continuous renal replacement therapy (CRRT). For CRRT the oXiris® hemofilter was used and CytoSorb® added to the circuit with the aim of improving the host immune response and haemodynamic status by intensively removing inflammatory mediators. Over the following 48 hours of this combined extracorporeal treatment, haemodynamic parameters improved, allowing a significant reduction in the vasoactive therapy, with a concomitant decrease in endotoxin and inflammatory markers serum levels. Over the subsequent days the patient's condition continued to improve and renal function recovered. The authors conclude they strongly believe that extracorporeal renal replacement therapy, associated with haemoadsorption blood purification techniques, may be useful in managing severe septic shock associated with MOF. They suggest that the personalization of therapy, the choice of appropriate timelines, and the adoption of hybrid methods can help in reducing the mortality rate of endotoxic septic shock.

<https://www.ncbi.nlm.nih.gov/pubmed/36474615>

Hemoadsorption as part of a multimodal therapy concept to treat *Capnocytophaga* sepsis with thrombocytopenia and multiple organ failure)

Kreutz J, Choukeir M, Chatzis G, Schieffer B, Markus B.
Int Journal Art Organs 2023; 46(1):52-57

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Summary

In this case report a 68-year-old presented at the hospital following a severe deterioration in his general condition, including fever up to 39°C, oliguria and repeated vomiting for a couple of days following a dog bite to his right foot whilst on holiday. On admission, the patient showed pronounced marbling and cyanosis to all extremities and ears. The reddened bite wound to the second toe did not appear infected so there was no medical or surgical intervention at this time. Despite standard therapy including antibiotics and multiple blood products he developed septic shock with acute renal failure, liver dysfunction, cognitive dysfunction and

respiratory deterioration so was started on continuous renal replacement therapy (CRRT), and eventually intubated and ventilated. Given the patient's hyperinflammatory condition a CytoSorb® hemoadsorber was additionally integrated into the CRRT circuit. In total 4 adsorbers were used during this 1st therapy interval (changed every 12 hrs). CytoSorb® was then stopped for 24 hrs as he improved clinically, however, due to a relapse in his clinical condition, CytoSorb® was then restarted for another 5 treatment sessions for 24 hours each (2nd therapy interval). All of the applied therapeutic measures led to rapid clinical stabilization, control of the hyperinflammatory situation, and improvement in his neurological status. The therapy was well tolerated with no complications encountered. The patient was able to be extubated after 3 days of mechanical ventilation and he was finally able to be transferred to a rehabilitation unit in a stable condition after a total hospital stay of 32 days. This is the first clinical case describing the successful application of a multimodal treatment approach including extracorporeal blood purification therapy in a patient with septic shock, acute renal failure and severe thrombocytopenia with signs of DIC and TMA due to Capnocytophaga infection following a dog bite.

<https://www.ncbi.nlm.nih.gov/pubmed/36401351>

Use of hemadsorption in pediatric meningococcal sepsis, Waterhouse-Friderichsen-Syndrome, and multiple organ failure

Mandilaras G, Dold SK, Dalla Pozza R.

Open Journal of Clinical & Medical Case Reports 2022; 8(12):1889

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Summary

Community-acquired bacterial meningitis still represents one of the most important infectious diseases worldwide and remains a substantial cause of mortality and morbidity, particularly in both the very young and the elderly patients. The disease is characterized by a hyperinflammatory response with a rapid and excessive production of inflammatory mediators, accompanied by disseminated intravascular coagulation (DIC) and development of Waterhouse–Friderichsen syndrome. Extracorporeal blood purification therapies represent a new therapeutic approach since they seem to be able to attenuate this detrimental process by lowering systemic cytokine levels. We herein report on an 18-year-old previously healthy male who had to be intubated and mechanically ventilated shortly after hospital admission followed by confirmation of *Neisseria meningitidis* infection. Antibiotic as well as catecholamine and volume therapy were initiated. Over time he developed excessive hyperinflammation, Waterhouse-Friderichsen-syndrome with purpura fulminans, hyperlactatemia and progressive renal failure, leading to the initiation of combined renal replacement and CytoSorb® hemoadsorption therapy. This resulted in significant decrease in inflammatory parameters and a progressive reduction in catecholamine and lactate levels while peripheral perfusion was restored preventing any loss of extremities. The patient could be extubated 10 days after PICU admission. No adverse or unwanted device-related side effects were documented. In conclusion, this case report is supporting other promising results in this highly sensitive patient cohort, by showing rapid hemodynamic stabilization and control of hyperinflammation being associated with the use of CytoSorb®, however, evidence on the application of the CytoSorb® adsorber in pediatrics remain rather sparse and more clinical data are needed.

[Link to Article](#)

Combined Application of Cytosorb and Sustained Low Efficiency Dialysis (SLED) in Critical Patients

Daza JL, Cruz YDL, Gutierrez G, Sarzuri H, Guarnizo N, Ariza A, Marin L.

Annals of Case Reports 2022; 7(2):807

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Summary

In this case report a 41 yr old patient with refractory septic shock and acute kidney injury (AKIN III) secondary to pancreatitis requiring pancreatectomy, colectomy and ileostomy, was given sustained low efficiency dialysis (SLED) plus CytoSorb®. Two consecutive SLED & CytoSorb® sessions were performed for 12 hrs each with a Genius 90 machine and blood flow rates around 120 ml/min. Over the following 48 hours, norepinephrine was able to be reduced from 1.2 µg/kg/min to 0.3 µg/kg/min after the first session and 0 after the second session. There was also a notable improvement in ventilatory parameters (paO₂/FiO₂ ratio up from 120 to 230 after the first session and up even further to 290 after the second session. Unfortunately, the patient presented with various complications over the following days including a massive pulmonary thromboembolism on day 29 from which he died. The authors then discuss the SLED modality which combines the benefits of continuous

renal replacement therapy (CRRT) and intermittent hemodialysis (IHD) and present some comparative studies in this regard. They conclude by stating that, to date, no dialysis therapy modality shows clear superiority over others in terms of survival and recovery of renal function. For clinical cases with multi-organ systemic involvement associated with acute renal dysfunction requiring dialysis therapy in the context of anuria, they propose the use of SLED modality daily, combined with CytoSorb®, pre-filter.

[Link to Article](#)

Sublingual Microcirculatory Evaluation of Extracorporeal Hemoadsorption with CytoSorb® in Abdominal Sepsis: A Case Report

Duran S, Miedema D, Ergin B, Ince C.

Blood Purif 2022; 51(7):634-638

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Summary

In this case report an 83 yr old man was admitted to intensive care after surgical repair of a colonic perforation for fecal soiling after a low anterior resection for a rectum carcinoma, with leakage of bowel content at the resection site. Despite adequate surgical treatment followed by optimal support in the ICU the patient developed symptoms consistent with septic shock. CytoSorb® was added to the continuous renal replacement therapy circuit for 48 hours (2 adsorbers for 24 hrs each) and sublingual microcirculatory imaging performed at regular intervals with measurement of total vessel density (TVD) and microvascular mean flow index (MFI) among the additional parameters. By the second day of CytoSorb® therapy lactate levels had decreased by 76% and the vasoactive-inotropic-score (VIS) had decreased by 87% which was associated with an improvement in the clinical condition. The functional parameters of the microcirculation also showed improvement within the first 12 hrs of treatment with CytoSorb® and normalized thereafter. The patient was eventually able to be discharged with normal renal function. The authors conclude that in their case report initiation of hemoadsorption together with standard of care improved the microcirculation and renal function along with a decrease in lactate levels. They suggest that non-invasive real-time evaluation of the microcirculation may be a sensitive diagnostic tool to monitor the effectiveness of hemoadsorption therapy.

<https://www.ncbi.nlm.nih.gov/pubmed/34535603>

Endotoxin and Cytokine Sequential Hemoadsorption in Septic Shock and Multi-Organ Failure

Ruiz-Rodriguez JC, Chiscano-Camon L, Palmada C, Ruiz-Sanmartin A, Perez-Carrasco M, Larrosa N, Gonzalez JJ, Hernandez-Gonzalez M, Ferrer R.

Blood Purif 2022; 51(7):630-633

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Summary

These two cases report on the sequential use of Polymyxin B (PMX) endotoxin-adsorbing column and CytoSorb® in 68 and 57 yr olds, both with severe septic shock and multi-organ dysfunction (SOFA score of 13 and 15 points, respectively). In both patients PMX was used for 2 hrs and then CytoSorb® for 24 hrs inserted into their renal replacement circuits. This resulted in a significant reduction in vasoactive drugs and lactate clearance. Interleukin -IL 6 and 10 also decreased significantly. There were no complications associated with the procedure. According to the authors this case report highlights that both techniques are complementary and without adverse effects. Rapid control of the inflammatory response, modulating not only the inducing stimulus but also the inflammatory mediators, can achieve an early improvement.

<https://www.ncbi.nlm.nih.gov/pubmed/34515070>

Immunoabsorption therapy for a meningococemia patient with myocarditis, adrenal hemorrhage, and purpura fulminans: a case report

Akcay N, Kihitir HS, Ozcelik G, Barlas UK, Petmezci MT, Sevketoglu E.

Braz J Anesthesiol 2022; 72(6):819-822

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Summary

In this case report a 10 year old patient with septic shock associated with Neisseria meningitidis (meningococcus) type B was admitted to the pediatric intensive care unit, unconscious and in a poor general condition. She received a combination of treatments including antibiotics, volume resuscitation, hydrocortisone, therapeutic plasma exchange and CytoSorb® treatments over 3 days (starting with two adsorbers over the first 24 hours). CytoSorb® was inserted into a hemodialysis circuit and pre and post clinical

parameters compared. Use of CytoSorb® resulted in an absolute decrease in inotrope need (including adrenaline, noradrenaline and milrinone) and stabilization in hemodynamics as also seen by improvements in systemic vascular resistance index (SVRI) and lactate levels. Extravascular Lung Water (ELWI) measurements with PiCCO monitoring showed reductions from elevated to (near) normal values. Her inflammatory markers also decreased (C-Reactive Protein and procalcitonin). The authors conclude that in this patient with meningococemia, the combined treatment including CytoSorb® therapy resulted in stabilization of hemodynamics, as well as control of the hyperinflammation. They state that in their opinion “use of CytoSorb® helped to bring the severe hyperinflammation under control and presumably helped the patient to overcome the acute phase by early intervention”. CytoSorb® was found to be safe and easy to use in combination with hemodialysis.

<https://www.ncbi.nlm.nih.gov/pubmed/34284056>

Hemoadsorption with CytoSorb and the early course of linezolid plasma concentration during septic shock

Köhler T, Schwier E, Kirchner C, Winde G, Henzler D, Eickmeyer C.

J Artif Organs 2022; 25(1):86-90

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Summary

This is a case of a 61-year-old female patient with Ulrich Turner syndrome who was treated with CytoSorb® and linezolid during her intensive care treatment for septic shock. The patient was admitted post operatively and after developing septic shock, CytoSorb® was started to stabilize her hemodynamic situation and provide liver support. Five adsorbers were used (18 hrs each) with good clinical results (norepinephrine reduced by 60%, and interleukin 6 levels decreased by 93%, stable bilirubin levels). However, after detection of staphylococcus epidermidis, it was necessary to start linezolid. After establishment of a new CytoSorb® adsorber, 600 mg of linezolid was administered over 1 h and levels measured before the adsorber inlet (cpre) and after the adsorber outlet (cpost) at 0, 15, 60, 120 and 480 mins after starting infusion. Linezolid plasma concentrations (cpre) after 60 min (3.25 mg/l) and 120 min (4.7 mg/l) showed sufficiently high linezolid levels (therapeutic range 3-9 mg/l), however, after 480 min, cpre had decreased to 2.8 mg/l. With cpost levels starting to increase over time after 60 minutes (up to 1.85 mg/l after 480 min), the calculated CytoSorb® clearance rate decreased to 67.86 ml/min (from 200 ml/min at 60 min). The authors recommend an additional loading dose of 600 mg and suggest that linezolid therapy under hemoadsorption with CytoSorb® requires a clear indication and close monitoring of levels to avoid underdosing.

<https://www.ncbi.nlm.nih.gov/pubmed/34047868>

Mechanical circulatory support with Impella 5.0 in septic shock

Haidari Z, Ruhparwar A, Weymann A.

Artif Organs 2021; 45(2): 183-184

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Summary

In this letter to the editor, the authors discuss the case of a 71 yr old male with chronic heart failure from dilated cardiomyopathy, and cardiac resynchronization therapy who presented with device related infective endocarditis. Hemoadsorption with CytoSorb® was first used intraoperatively. Post-operatively the patient was transferred to the intensive care unit in septic shock requiring high dose vasopressor support. CytoSorb® hemoadsorption was then inserted into the hemodialysis circuit. Due to continuing hemodynamic deterioration, the patient had an Impella 5.0 inserted, whereafter his vasopressor needs, and lactate levels dropped significantly. The authors write that the intra- and post-operative use of hemoadsorption ‘could have additionally contributed to the rapid stabilization of the inflammatory response which plays a major role in sepsis’.

<https://www.ncbi.nlm.nih.gov/pubmed/32929738>

Use of CytoSorb® as a therapeutic option in a critically ill patient with acute respiratory distress syndrome caused by influenza A (H1N1) pneumonia: A case report

Kovacevic P, Tomic B, Kovacevic T, Dragic S.

Int J Crit Illn Inj Sci 2020; 10(4):216-219

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Summary

This is a case of a previously healthy 29-year-old male patient who was admitted to the Medical Intensive Care Unit (MICU) with multiple organ dysfunction and pneumonia caused by influenza type A. Due to acute respiratory failure and altered state of consciousness, the patient was intubated and mechanically ventilated immediately after admission. The

initial computed tomography scan showed massive bilateral pneumonia, and few days later the patient's condition progressively worsened, and he developed signs of multi-organ failure. Given the patient's progressing hemodynamic instability (norepinephrine increased to 0.6 µg/kg/min) and systemic inflammatory response (C-Reactive Protein – CRP 519 mg/L, procalcitonin 1.28 ng/ml, leucocytes 14.8 x 10³/µl), a CytoSorb® adsorber was added into the continuous renal replacement therapy (CRRT) circuit on day 7. Immediately after the first session the norepinephrine requirement decreased to 0.15 µg/kg/min and was able to be discontinued 2 days later. However, the patient's condition started to deteriorate on day 10, so CytoSorb® was again used. Overall, the inflammatory markers decreased during combined CRRT plus CytoSorb® (CRP to 330 mg/L, PCT to 0.7 ng/ml, leucocytes to 9.2 x 10³/µl). Lactate also improved from 4.4 mmol/L to 0.7 mmol/L. The ventilation parameters and lung function also gradually improved. After 48 days in the MICU, he was discharged to the wards, and then to a rehab clinic a few days later. The authors conclude that the combination of pharmacotherapy, supportive measures, and application of CytoSorb® resulted in complete recovery of the patient with CytoSorb® use associated with rapid hemodynamic stabilization and control of inflammatory response. <https://www.ncbi.nlm.nih.gov/pubmed/33850832>

CytoSorb in the management of severe septic shock after coronary artery bypass graft surgery

Prakash A, Garg V, Mittal DK, Upadhyay AB.

Heart India 2020; 8:151-153

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Summary

This is a case of acute septic shock that developed post coronary artery bypass graft surgery in a 58 year old male. The patient was admitted to intensive care postoperatively on moderate inotropic support, however, within 12 – 24 hrs, he had developed refractory hypotension with signs of multiple organ failure. After the progressive deterioration in his hemodynamic state (requirement for epinephrine, norepinephrine and vasopressin), he was started on continuous renal replacement therapy (CRRT) with CytoSorb®. After a single 24 hr session, there was an improvement in end-organ dysfunction (decreased requirements for vasopressors, improved urine output, decreased ventilatory requirements, improved liver function, and normal temperature). Hence, inotropic and organ support could be gradually withdrawn and the hemodynamic status remained stable with improvements in the inflammatory and other laboratory parameters. The authors note that CytoSorb® was an effective, safe and easy option in the management of severe septic shock post cardiac surgery and seems to be a promising tool in stabilizing hemodynamics in refractor vasoplegia. In patients with known risk factors, CytoSorb® therapy could be used during surgery. They concluded that septic shock increases the risk of multiple organ failure and also adds to the financial burden, which was reduced by CytoSorb® therapy.

[Link to Article](#)

Sequential Extracorporeal Therapy Collaborative Device and Timely Support for Endotoxic, Septic, and Cardiac Shock: A Case Report

De Rosa S, Samoni S, Ronco C.

Blood Purif 2020; 49(4):502-508

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Summary

The authors report the case of a patient with a severe bacterial infection (*Neisseria meningitidis*) who was admitted to the ICU due to septic shock. In addition to the critical care management, 2 treatments with Polymyxin B hemoperfusion were performed. The treatment resulted in a marked decrease in the serum endotoxin level but without any improvement in tachycardia and circulatory insufficiency progressed. Therefore, considering the involvement of septic cardiomyopathy and cardiogenic shock, and aiming to reduce excessive levels of inflammatory mediators, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was initiated on day 3 from admission and CytoSorb® was integrated into the VA-ECMO circuit for 48 h without an evident considerable improvement. Therefore, a 72-h continuous veno-venous hemodialysis session was started in which a high cutoff filter was used. Tachycardia and myocardial dysfunction improved under the combined therapy and VA-ECMO was withdrawn. Subsequently, nutrition management and rehabilitation were performed, and the patient was transferred to the department of respiratory medicine on day 80, he was discharged from the hospital on day 113. The authors concluded that the sequential extracorporeal therapy may be beneficial when concomitant with circulatory assistance in uncontrollable cases of septic shock using catecholamines.

<https://www.ncbi.nlm.nih.gov/pubmed/31865323>

Cytokine adsorption as a promising option for septic shock and multiple organ failure due to Candida infection and decompensated type 1 diabetes mellitus

Klinkmann G, Stope MB, Meyer A.

Artif Organs 2020; 44(5):522-525

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Summary

This is the case report of a 19 year old female patient with type 1 diabetes mellitus (T1DM) and candidiasis associated with severe metabolic acidosis who was admitted to the intensive care unit in septic shock with hemodynamic instability. Continuous renal replacement therapy (CRRT) was initiated in the first 24 hrs due to the metabolic acidosis (initial pH 6.69) and increased retention parameters. When she remained hemodynamically unstable despite high dose catecholamine therapy, and because of the significantly elevated interleukin(IL) -6 levels (>1000 pg/ml), a CytoSorb® cartridge was inserted into the CRRT circuit for a 20 hr period. This resulted in a rapid improvement in her hemodynamics and resolution of the metabolic acidosis. The vasopressor support could be reduced during the treatment (norepinephrine 0.9 – 0.2 ug/kg/min). The hyperinflammation could also be rapidly controlled and all parameters reduced during the course of treatment (including procalcitonin and leukocytes). Treatment with CytoSorb® was found to be safe and feasible without technical problems. Notably, this is the first case description reporting on the effects of CytoSorb® in a patient with fungal septic shock and T1DM.

<https://www.ncbi.nlm.nih.gov/pubmed/31738446>

Successful application of CytoSorb® hemadsorption in an immunocompromised teenager with collapsing glomerulopathy, acute respiratory distress syndrome, and sepsis

Keles E, Fidan K, Yenicesu I, Kalkan G.

Int J Artif Organs 2019; 42(12):765-769

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Summary

In this case report, a 17-year-old male was admitted to the hospital with severe diarrhoea and was then found to have elevated creatinine levels and proteinuria consistent with collapsing glomerulopathy, a severe form of kidney injury. He was treated with multiple immunosuppressive agents including corticosteroids, mycophenolate mofetil, and rituximab as well as several courses of hemodialysis and plasmapheresis. *Stenotrophomonas maltophilia* bacteria was then found in his blood and catheter cultures. He was unresponsive to treatment (antibiotics, intravenous immunoglobulin, and supportive management including albumin, platelet and erythrocyte concentrations, and fresh frozen plasma), and severe sepsis and multi-organ dysfunction developed. CytoSorb® was then added to the hemodialysis for three consecutive days. The use of CytoSorb® resulted in an immediate attenuation of the inflammatory response which correlated with a clinical improvement. Specifically the authors reported an immediate recovery in renal parameters, respiratory status, and oxygen demand. The need for erythrocyte, platelet, and albumin transfusions decreased dramatically 24hrs after CytoSorb® therapy. Despite a high mortality risk (Pediatric Index of Mortality score (PIM II) of 100), the patient was able to be transferred from the intensive care unit to the general ward after the three sessions of CytoSorb®. In this immune-compromised patient with sepsis and collapsing glomerulopathy with multiorgan failure CytoSorb® was successfully used as a rescue therapy. The authors state that the use of CytoSorb® in this case was without any device related adverse events and there were no problems installing the adsorber.

<https://www.ncbi.nlm.nih.gov/pubmed/31277560>

Clindamycin clearance during CytoSorb hemoadsorption case report and pharmacokinetic study

Poli E, Simoni C, Andre P, Buclin T, Longchamp D, Perez M-H, Ferry T, Schneider A.

Int J of Artif Organs 2019; 42(5):258-262

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Summary

This is a case report of a severely sick 14-year-old boy with Panton-Valentine leucocidin producing methicillin-resistant *Staphylococcus aureus* infection (PVL-MRSA) and also Influenza B pneumonia requiring veno-arterial extra-corporeal membrane oxygenator (VA-ECMO) for refractory shock. In the absence of any response to conventional therapy, CytoSorb® was inserted directly into the VA-ECMO circuit resulting in, according to the authors, a spectacularly rapid and sustained decrease in vasopressor requirements (noradrenaline, vasopressin and dopamine). In total four adsorbers were used for 81 hours, and eventually, despite the severity of his initial condition the patient was discharged home on day 156. Since the antibiotic clindamycin which is a key component of PVL-MRSA treatment might be removed by CytoSorb® hemoadsorption, the authors developed a

pharmacokinetic model incorporating variable plasma clearance based on serial plasma concentrations measurements which were performed before, during and after CytoSorb® use. According to this model, use of CytoSorb® did not seem to result in significant clindamycin removal so therefore its use with CytoSorb® appears safe and feasible requiring no adaptation of dosage necessary.

<https://www.ncbi.nlm.nih.gov/pubmed/30819024>

First successful hemoadsorption using CytoSorb® in a septic pediatric patient in Kazakhstan: A case report

Saparov A, Sazonov V, Tobylbaeva Z, Isakov S, Bekpan A, Autilipov D, Muratbekova B, Manaybekova Z, Anikin V.

Int J Artif Organs 2019;42(6):315-317

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Summary

This is the first CytoSorb® treatment in Kazakhstan where CytoSorb® was used in an 8-month-old patient with a body weight of 5600 g. The patient was admitted with acquired severe laryngeal stenosis, chronic tracheal cannulation and protein energy malnutrition after being born at 34 weeks and previously requiring subsequent readmissions for pneumonia and cytomegalovirus infection. The patient underwent balloon dilatation of the larynx however then developed pneumonia, respiratory failure and bacterial and fungal infections. After an eight-day stay in the pediatric intensive care unit, and due to no improvement of the ongoing multi organ failure, continuous veno-venous hemodialysis (CVVHD) was started along with CytoSorb® which was run for 36 hours. CytoSorb® resulted in a reduction of inflammation markers IL-6, S100, procalcitonin, and C-reactive protein. Simultaneously, the level of transaminases, creatine kinase, and troponin were normalized. By the end of the treatment the patient's hemodynamics were stable, there was no further need for vasopressors, the acid-base balance was maintained, and the patient was weaned from mechanical ventilation onto spontaneous breathing. The patient was subsequently discharged to the ward and then home. The authors conclude that CytoSorb® treatment was safe and well-tolerated in this very small pediatric patient, easy to use with CVVHD, and has proven its practical value as an adjuvant therapy for sepsis in such populations. While it must be noted that CytoSorb® use in the pediatric population is currently 'off label', this is the smallest case reported so far in the peer review literature (5600g).

<https://www.ncbi.nlm.nih.gov/pubmed/30614343>

Successful use of combined blood purification techniques in splenectomised patient with septic shock in streptococcus pneumoniae infection - a case report

Sinkovic A, Kit B, Markota A.

BMC Infect Dis 2018; 18(1):433

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Summary

Septic cardiomyopathy, caused by the cytokine storm, is a severe cardiac impairment in sepsis and is completely reversible if the patient survives. This is a case of a 52 yr old woman with a history of chemotherapy for lymphoma, splenectomy and autologous bone marrow transplantation, who suffered acute severe pneumococcal sepsis, septic shock and septic cardiomyopathy, resistant to pharmacological therapy including fluids and vasopressors. After 36 hrs of maximum standard therapies, it was decided to add extended hemodynamic monitoring, and continuous veno-venous hemofiltration plus CytoSorb® therapy because of the persistently resistant shock, to try to improve the hemodynamic situation and modulate the inflammatory response. After 24 hours of therapy the hemodynamic situation stabilized (including left ventricular systolic function), her IL-6 level dropped from 114 pg/ml to 14.2pg/ml and vasopressors could be ceased. This case shows that early removal of inflammatory cytokines enabled the reversal of circulatory failure and significant improvement of the septic cardiomyopathy resulting in improved hemodynamic status, lactacidosis and clinical outcome in this patient.

<https://www.ncbi.nlm.nih.gov/pubmed/30157806>

Hemoadsorption in a Case of Severe Septic Shock and Necrotizing Fasciitis Caused by Nontraumatic Renal Rupture due to Pyelonephritis with Obstructive Uropathy

Kousoulas L, Wittel U, Fichtner-Feigl S, Utzolino S.

Case Rep Crit Care 2018: 5248901

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Summary

In this case a 25-year-old female presented with a four week history of acute worsening abdominal pain. She was found to have peritonitis, leukocytosis, severe lactic acidosis and pronounced anemia, with imaging consistent with nontraumatic renal rupture with retroperitoneal abscess, perforation of the colon, and severe necrotizing fasciitis of the right lower limb. She underwent a right nephrectomy, a right hemicolectomy, surgical debridement of the retroperitoneum, and upper thigh amputation. Due to severe septic shock and rhabdomyolysis with acute renal failure combined treatment of hemoadsorption using CytoSorb® (three cycles) and continuous venovenous hemodialysis (CVVHD) was started. Treatment was associated with rapid hemodynamic stabilization and decrease in IL-6 as well as myoglobin levels. Subsequently the patient recovered and was discharged home with no signs of infection and with normal renal function. The authors conclude that early treatment of the patient with CytoSorb® led to the rapid hemodynamic and metabolic stabilization and preservation of the renal function, suggesting that hemoadsorption might be a rescue therapy in patients with severe septic shock and traumatic rhabdomyolysis.

<https://www.ncbi.nlm.nih.gov/pubmed/29854478>

A case of viper snake bite presenting with gangrene and sepsis associated multi-organ failure, successfully treated with CytoSorb as an adjunct therapy – a clinical experience

Paul R, Jha BK, Shetty VK.

J. Evid Based Med Healthcare 2018; 5 (6):559-561

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Summary

This is a case of a 32-year old male patient bitten by a viper who developed cellulitis, acute renal failure, and disseminated intravascular coagulation (DIC), septicemia and acute respiratory distress syndrome (ARDS). Because of necrotizing fasciitis and gangrene he had to have his lower limb amputated and was admitted to Intensive Care post op in septic shock (APACHE II 29 and SOFA 15). On the third post op day, in view of the multi-organ failure, he was treated with CytoSorb®, along with standard care as per the International Sepsis Guidelines. After two CytoSorb® treatments each for 24-hours, renal, hemodynamic and respiratory parameters improved remarkably and returned to normal over 5 days. The authors state that CytoSorb® along with standard care can be a safe and advantageous extracorporeal therapy option to treat snake bite patients with multi organ failure to help them recover.

[Link to Article](#)

Use of CytoSorb in Traumatic Amputation of the Forearm and Severe Septic Shock

Stelzer H, Grieb A, Mustafa K, Berger R.

Case Reports in Critl Care 2017; 8747616

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Summary

This case study reports on a 49-year-old male patient admitted to hospital following traumatic amputation of his right forearm that was cut off at the elbow joint while working on a land fill site. After initial treatment for shock, he received immediate replantation and was transferred to the ICU. Due to the anticipated risk of a complex systemic infection, continuous renal replacement therapy in combination with CytoSorb® was initiated. The patient received 6 CytoSorb® treatments for 12 hrs each. During the course of the combined treatment, a rapid improvement in hemodynamics was noticed (noradrenaline dose could be halved during the first treatment), as well as a significant reduction in IL-6 (from >5000 to 43 pg/ml) and lactate levels (from 4 mmol/l to within the normal range). Despite recurring sepsis and the necessity for amputation, the patient clinically stabilized and underwent complete recovery 18 days after admission. Early treatment with a combination of CVVHDF and CytoSorb® was accompanied by an attenuation of the systemic inflammatory reaction, which subsided without major or permanent organ damage, despite the impressive pathogen spectrum and the pronounced local damage.

<https://www.ncbi.nlm.nih.gov/pubmed/29423323>

Use of Hemadsorption in a Case of Pediatric Toxic Shock Syndrome

Berkes A, Szikszay E, Kappelmayer J, Kerenyi A, Szabo T, Ujhelyi L, Bari K, Balla G, Balla J.

Case Rep Crit Care 2017; 3818407

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Summary

This case report describes the successful treatment of toxic shock syndrome (a potentially fatal disease mediated by

gram-positive bacterial toxins) in a 5 year old female pediatric Downs syndrome patient who presented with an inflamed area surrounding an insect bite, signs of systemic inflammation, and multiple organ failure. As attempts at resuscitation (including fluids, catecholamines and antibiotics), and immune modulatory therapies (including hydrocortisone, plasma exchange therapy and immunoglobulin therapy) were unsuccessful, renal replacement therapy supplemented with the CytoSorb® adsorber was started which was associated with a rapid and significant stabilization in the hemodynamic situation, and a decrease in inflammatory mediators within hours after the initiation of therapy. The application of CytoSorb® therapy was simple and safe. The use of CytoSorb® proved potentially beneficial for removing bacterial toxins and inflammatory mediators and could therefore play a role in the clinical management of toxic shock syndrome.

<https://www.ncbi.nlm.nih.gov/pubmed/28791185>

Effect of extracorporeal cytokine removal on vascular barrier function in a septic shock patient

David S, Thamm K, Schmidt BM, Falk CS, Kielstein JT.

J Intensive Care 2017; 5:12

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Summary

A 32-year-old female presented with septic shock and accompanying acute kidney injury to ICU. In spite of a broad anti-infective regimen, adequate fluid resuscitation, and high doses of inotropics and catecholamines, she remained in refractory hypotensive shock. The extraordinary severity of septic shock suggested an immense overwhelming host response assumingly accompanied by a notable cytokine storm. Thus, a CytoSorb® adsorber was added to the dialysis circuit. To analyze the endothelial phenotype in vitro before and after extracorporeal cytokine removal, the authors tested the patient's serum on human umbilical vein endothelial cells (HUVECs) and the effect on the endothelial integrity was assessed. The authors found severe alterations in cell-cell contacts, the cytoskeletal architecture, and profound functional permeability changes (in other words clinical vascular leakage syndrome) when blood from the patient taken prior to the CytoSorb® adsorber was added to the HUVECs. However, the endothelial barrier was protected from these profound adverse effects when blood serum was collected after the CytoSorb® adsorber (cytokine removal) and added to the HUVECs. In conclusion the benefit of extracorporeal cytokine removal with CytoSorb® in septic shock patients might-at least in part-be promoted via protection of vascular barrier function.

<https://www.ncbi.nlm.nih.gov/pubmed/?term=28127473>

Hemadsorption with Adult CytoSorb® in a Low Weight Pediatric Case

Cirstoveanu CG, Barascu I, Mc Kenzie Stancu S.

Case Rep Crit Care 2017; 6987167

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Summary

This case study describes a nine-month old male infant admitted to the Neonatal Intensive Care Unit due to sepsis post cardiac surgery (Fallot tetralogy), and multi-system organ failure (MSOF), including liver and renal failure which was successfully treated by a combination of continuous hemodiafiltration (HDF) and hemoadsorption with CytoSorb®. CytoSorb® was added to the set up on day 9 due to increasing bilirubin levels. Over the 49 hour period of hemoadsorption plus CytoSorb®, total bilirubin decreased from 54 to 14 mg/dl, the patient's general status improved considerably, accompanied by a rapid decrease in liver enzymes (aminotransferases). Hemodynamic status also improved and requirement for inotropes decreased rapidly during the two days of CytoSorb® treatment. The patient was discharged home after 34 days of hospitalization, in good general health. This is the first published case of the successful use of CytoSorb® treatment in such a young patient (9 months old, 9 kilos in weight).

<https://www.ncbi.nlm.nih.gov/pubmed/?term=28127437>

Cytokine Adsorption in Septic Shock and Multiorgan Failure Following Major Obstetric Hemorrhage

Withanage RK, Nilmini Wijesuriya N.

Journal of Case Reports 2017; 7(1):124-126

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Summary

In this case report a 38-year-old previously healthy patient developed septic shock with multi-organ failure following recurrent cardiac arrests due to massive obstetric hemorrhage. She had secondary hepatic impairment and acute kidney injury. Her medical care involved several surgical interventions and admission to intensive care. Continuous Renal

Replacement Therapy was started on day 3 in ICU and CytoSorb® was added to the hemofilter. Her liver enzymes (AST and ALT) and bilirubin started to decrease quite dramatically 12 hrs after the start of CytoSorb®, her white blood cell count and CRP also decreased, and her vasopressor and inotropic support could also start to be tailored off. This case shows how a patient with major obstetric hemorrhage leading to recurrent cardiac arrests complicated by ischemic hepatocellular and kidney injury with secondary sepsis was managed successfully with the cytokine adsorber.

[Link to Article](#)

Hybrid blood purification strategy in pediatric septic shock

Bottari G, Taccone FS, Moscatelli A.

Crit Care 2016; 20(1):366

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Summary

In this letter to the editor, the case of a 12 year old girl with a history of acute lymphatic leukemia and recent chemotherapy admitted with fever and fatigue is described (cause of which later found to be klebsiella pneumonia from a central line infection). She was given fluid resuscitation, empiric antibiotics and admitted to ICU. Because of ongoing hypotension, epinephrine and norepinephrine were initiated, however she remained severely hypotensive. Continuous renal replacement therapy was started with a high cut off filter (Septex) along with a CytoSorb® adsorber. After 48 hours a significant reduction in the vasopressors was observed, lactate decreased as did procalcitonin. The 'hybrid' extracorporeal blood purification - EBP (combination of CytoSorb® and Septex) was continued for 72 hours in total and the patient discharged after 10 days. No adverse events related to the procedure were observed. The authors state that the combination of 'hybrid' EBP might have a synergistic effect in the setting of pediatric septic shock.

<https://www.ncbi.nlm.nih.gov/pubmed/27832804>

Combination of ECMO and cytokine adsorption therapy for severe sepsis with cardiogenic shock and ARDS due to Panton-Valentine leukocidin-positive Staphylococcus aureus pneumonia and H1N1

Lees NJ, Rosenberg A, Hurtado-Doce AI, Jones J, Marczin N, Zeriuoh M, Weymann A, Sabashnikov A, Simon AR, Popov AF.

J Artif Organs 2016; 19(4):399 - 402

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Summary

Sepsis-induced cardiogenic shock in combination with severe acute respiratory failure represents a life-threatening combination that is often refractory to the conventional methods of treatment. Here the authors describe the case of a 33-year-old patient who developed acute cardiovascular collapse and ARDS secondary to superinfection of Panton-Valentine leukocidin-positive Staphylococcus aureus and H1N1 pneumonia who underwent successful combination therapy for severe sepsis-related cardiomyopathy and respiratory failure using extracorporeal membrane oxygenation and CytoSorb® therapy. Use of the CytoSorb® appeared to result in rapid resolution of neutropenia, reversal of toxic shock and rapid weaning off of the high dose vasopressors.

<http://www.ncbi.nlm.nih.gov/pubmed/27436098>

First case of toxic shock treated with haemoadsorption by CytoSorb in the Netherlands

van der Linde GW, Grootendorst A.

Neth J Crit Care 2016; 24(2):27-29

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Summary

This case study reports on a 17-year-old male who reported a local rural hospital with complaints of pretibial pain in his right leg, after he accidentally cut his leg while in the fields a few days earlier. He was diagnosed with having a phlegmon with an abscess followed by surgical debridement with wound nettoyage with no clinical signs of subcutaneous emphysema or necrotising fasciitis. Postoperatively the patient's condition deteriorated and after admission to ICU he developed erythema, spreading from the right lower leg to the right upper leg, abdominal wall and the left leg, consistent with toxic shock syndrome and subsequent development of septic shock due to invasive S. aureus infection with respiratory failure, hemodynamic instability treated with vasopressors, hydrocortisone, antibiotic therapy. Due to disease severity, CRRT was initiated with a CytoSorb® adsorber with the only goal to remove cytokines (despite absence of acute kidney injury and no need for renal replacement therapy). Within six hours the erythema progression stopped and after 12 hours the need for vasopressors diminished. The erythema diminished after a few hours and had disappeared after 24 hours. After

cessation of CytoSorb® physicians concluded that the patient was no longer septic and diuretics were started because of fluid overload. Respiration improved, the ventilator support was weaned and the patient was extubated on day 5 after admission, within 72 hours of cessation of CRRT. In the authors opinion, the patient would have survived without CytoSorb®, but they felt that his stay in the ICU might have been shortened by the use of the CytoSorb® adsorber.

[Link to Article](#)

Cytokine Reduction in the Setting of an ARDS-Associated Inflammatory Response with Multiple Organ Failure

Traeger K, Schuetz C, Fischer G, Schroeder J, Skrabal C, Liebold A, Reinelt H.

Case Reports in Crit Care 2016; 2016:9852073

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Summary

This case study reports on a 45-year-old male admitted with a small bowel obstruction due to torsion who was immediately scheduled for surgical intervention. At anesthetic induction, the patient aspirated and subsequently developed severe systemic inflammatory response syndrome with acute respiratory distress syndrome, and multiple organ failure requiring the use of ECMO, CRRT, antibiotics, and low dose steroids. Due to the rapid deterioration in his clinical status and a concurrent surge in inflammatory biomarkers, CytoSorb® was added to the CRRT circuit. The combined treatment resulted in a rapid and significant reduction in the levels of circulating inflammatory mediators. This decrease was paralleled by marked clinical stabilization of the patient including a significant improvement in hemodynamic stability and a reduced need for norepinephrine and improved respiratory function, and indirect measures of capillary leak syndrome. The authors attribute the clinical improvement to the rapid control of the hyperinflammatory response and the reduction in the inflammatory mediators using a combination of CytoSorb® and other therapies. CytoSorb® treatment was safe and well tolerated, with no device-related adverse effects observed.

<http://www.hindawi.com/journals/cricc/2016/9852073/>

CytoSorb, a novel therapeutic approach for patients with septic shock: a case report

Hinz B, Jauch O, Noky T, Friesecke S, Abel P, Kaiser R.

Int J Artif Organs 2015; 38(8):461-464

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Summary

This case study reports on 72-year-old male patient with periodically recurring infectious episodes admitted with suspected urosepsis. Over the following hours his hemodynamic situation deteriorated markedly, with respiratory-metabolic acidosis, elevated inflammatory markers, severely disturbed coagulation, increased retention parameters, liver dysfunction, and confirmation of bacteria and leucocytes in his urine. After admission to the ICU in septic shock the patient received renal support with additional hemoadsorption using CytoSorb®. Three CytoSorb® sessions were run over the following days resulting in reductions in procalcitonin, C-reactive protein and bilirubin and a markedly reduced need for vasopressors and corresponding hemodynamic improvement (i.e., cardiac index, extravascular lung water). Due to a recurring inflammatory "second hit" episode, another CytoSorb® session was run, resulting in the marked decrease in leukocytosis and liver (dys)function parameters. The rapid hemodynamic stabilization with reduction in vasopressor needs and reduction of the capillary leak as well as the quick reduction in infection markers were the main conclusions drawn from the use of CytoSorb® in this patient. Additionally, treatment appeared to be safe and was well tolerated. Further studies are necessary to elucidate to what extent these favorable consequences are attributable to the adsorber itself.

<http://www.ncbi.nlm.nih.gov/pubmed/26349530>

CytoSorb-friend or foe!!

Pattnaik SK, Panda B.

Indian J Crit Care Med 2015; 19(5):296

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Summary

In this letter to the editor the authors refer to the case report by Basu et al. (PMID 25538418), share their experiences with a similar patient treated with CytoSorb® and discuss some of the intriguing points of their treatment. A 79-year-old male patient with severe septic shock (urosepsis) and multi-organ failure and an APACHE II score of 32, was started on CytoSorb® therapy plus sustained low effusion dialysis along with

standard surviving sepsis guidelines treatment. Within 3 days, hemodynamic parameters, ventilator requirements and urine output improved. APACHE II score improved after day 3 of therapy, and IL-6 levels reduced after the last session. Since the patient started to deteriorate clinically from day 5 despite ongoing supportive care, the authors bring up a possible immunosuppressive effect and express their concern as to whether CytoSorb® therapy could be the cause of this. They note that randomized controlled trials are necessary to check the risk-benefit ratio of hemadsorption therapy in severely septic patients.

<http://www.ncbi.nlm.nih.gov/pubmed/25983446>

Can cytokine adsorber treatment affect antibiotic concentrations? A case report

Zoller M, Döbbeler G, Maier B, Vogeser M, Frey L, Zander J.

J Antimicrob Chemother 2015; 70(7):2169-2171

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Summary

This case study reports on a patient with an excessive inflammatory response, septic shock and multi organ failure. Initial laparotomy revealed an ischemic bowel with peritonitis requiring immediate jejunum and colon segmental resection and ileotransverse colostomy. Intravenous antibiotic treatment was started with meropenem and linezolid. Due to the persistent excessive cytokine storm, four CytoSorb® adsorbers were used over 96 hours. Therapy for septic shock included surgery, antibiotic treatment and CytoSorb® which resulted in a substantial improvement in the patient's condition, including renal and liver function, and cardiorespiratory status. However, after 4 weeks and seven further repeat laparotomies, the patient died from multiple organ failure. The use of CytoSorb® in this patient proved to be effective and safe. Of note, intra-patient variability of antibiotic levels was high with substantially lower peak levels for both antibiotics when CytoSorb® was in use, pointing towards potential adsorption however, no negative impacts on the effectiveness of antibiotic therapy was detected. The authors suggest therapeutic drug monitoring wherever possible or, if not available, high loading doses or shorter intervals of administration be used to achieve adequate antibiotic levels with further studies needed.

<http://www.ncbi.nlm.nih.gov/pubmed/25786479>

First successful combination of ECMO with cytokine removal therapy in cardiogenic septic shock: A case report

Bruenger F, Kizner L, Weile J, Morshuis M, Gummert JF.

Int J Artif Organs 2015; 38(2):113-116

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Summary

This case study reports on a 39-year-old patient with fulminant Acute Respiratory Distress Syndrome and cardiogenic septic shock. After implantation of a veno-arterial ECMO for circulatory support the patient developed acute renal failure making initiation of CVVH necessary. Due to a complete cardiac arrest in both ventricles, a left ventricular assist device (LVAD) in combination with right ECMO (rECMO) was implanted despite manifest septic conditions. In the post-operative course his condition deteriorated drastically and a CytoSorb® adsorber was installed in to the CVVH circuit resulting in a decrease in IL-6, procalcitonin, and C-reactive protein concomitant with significantly reduced vasopressor support. No adverse device-related side effects were documented during or after the treatment sessions. This is the first clinical case report of a highly septic patient treated with the combined use of LVAD, rECMO, CVVH, and CytoSorb®. The combination was practical, technically feasible, and beneficial for the patient and might represent a reasonable approach for improving survival in patients with multiple organ dysfunction necessitating several organ supportive techniques.

<http://www.ncbi.nlm.nih.gov/pubmed/25656010>

Use of a novel hemoadsorption device for cytokine removal as adjuvant therapy in a patient with septic shock with multi-organ dysfunction: A case study

Basu R, Pathak S, Goyal J, Chaudhry R, Goel RB, Barwal A.

Indian J Crit Care Med 2014; 18:822-824

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Summary

This case study reports on a 36-year-old female diagnosed with urosepsis and multi-organ dysfunction (Acute Respiratory Distress Syndrome, Acute Kidney Injury, and arterial hypotension). SOFA score was 15, MODS score

10 and APACHE II score 30. CytoSorb® was added along with CRRT. The patient received three consecutive treatments with CytoSorb® over the following three days. After initiation of therapy the patient improved hemodynamically. During the further course urine output increased with improvement in ventilator parameters. SOFA score at the end of treatment was 4, MODS score was 5 and APACHE II score was 7. There were no adverse events and laboratory parameters before and after CytoSorb® therapy were within normal range. CytoSorb® therapy in septic shock patients with multi-organ failure might be an option as a rescue therapy.

<http://www.ncbi.nlm.nih.gov/pubmed/25538418>

Effects of a novel cytokine haemoadsorbition system on inflammatory response in septic shock after cephalic pancreatectomy – a case report

Tomescu D, Dima SO, Tănăsescu S, Tănase CP, Năstase A, Popescu M.

Romanian Journal of Anaesthesia and Intensive Care 2014; 21(2):134-138

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Summary

This case study reports on a 50 year old man with postoperative septic shock after undergoing cephalic pancreatectomy for a pancreatic cystic tumor. In total, two consecutive CVVH sessions with CytoSorb® were performed over a period of 64 hours (24 hours each). The clinical effects associated with CytoSorb® correlated with a rebalance in cytokine levels and translated into a more stable hemodynamic profile with a stable cardiac output and normalization of systemic vascular resistance index and decreased vasopressor requirements. The technology was simple to use, well tolerated with no adverse events, and could be easily added into conventional CVVH machines.

<https://pubmed.ncbi.nlm.nih.gov/28913446/>

Septic shock secondary to β-hemolytic streptococcus-induced necrotizing fasciitis treated with a novel cytokine adsorption therapy

Hetz H, Berger R, Recknagel P, Steltzer H.

Int J Artif Organs 2014; 37(5):422-426

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Summary

This case study reports on a 60-year-old female who was admitted to hospital due to a radial fracture. After surgical wound care by osteosynthesis the patient developed surgical wound infection progressing to necrotizing fasciitis with additional proven infection from β-hemolytic streptococcus. The patient went into septic shock exhibiting a full picture of a MODS. Therefore, the patient was treated with CytoSorb® therapy over a period of four days, resulting in a significant reduction of IL-6 and an overall improvement of the patient's condition. In this case, CytoSorb® seems to be an interesting and safe extracorporeal therapy to stabilize and bridge septic patients to surgery or recovery.

<http://www.ncbi.nlm.nih.gov/pubmed/24811308>

Pattern of cytokine removal using an adsorption column CytoSorb during severe Candida albicans induced septic shock

Bracht H, Schneider EM, Weiß M, Hohmann H, Georgieff M, Barth E.

Infection 2013;41(Suppl 1:S1–S90); Abstract No. 133

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Summary

This case study reports on a 46 old female with hypodynamic septic shock and documented candidemia infection. CRRT was started in combination with CytoSorb® therapy. Within 24 h of hemoadsorption, vasopressor and inotropic support could be withdrawn. Several inflammatory mediators (e.g. IL-6, 8, 10) could be reduced significantly. Interestingly, the authors also found an almost perfect immunological reconstitution of a variety of immune parameters including HLA-DR.

<https://www.ncbi.nlm.nih.gov/pubmed/23949887>

Improvement of hemodynamic and inflammatory parameters by combined hemoadsorption and hemodiafiltration in septic shock: a case report

Mitzner SR, Gloger M, Henschel J, Koball S.

Blood Purif 2013; 35(4):314-315

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Summary

This case study reports on an 80 year old male diagnosed with pneumogenic septic shock. The patient was in clinical need for renal replacement therapy and was therefore started on citrate-anticoagulated CVVHD in combination with a CytoSorb® adsorber for 24 hours. Over time IL-6 and other markers of inflammation as well as need for vasopressors could be drastically reduced while treatment was safe and well tolerated.

<http://www.ncbi.nlm.nih.gov/pubmed/23920222>

1.3.2 Cardiac

Hedinger syndrome – lessons learnt: a single-centre experience

El Gabry M, Arends S, Shehada S-E, Lahner H, Kamler M, Wendt D, Spetsotaki K.

J Cardiovascular Development and Disease 2023; 10:413

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Summary

Hedinger syndrome (HS), also known as carcinoid heart disease (CD), is a rare and challenging manifestation of malignant neuroendocrine tumors (NETs), which involves the heart. It has a high mortality rate due to the severity of the condition. This article summarizes the experience from a single centre, including surgical strategies, in 11 patients. Patients had an individualized, multidisciplinary team approach consisting of oncologists, cardiac surgeons, endocrinologists, cardiologists and anesthesiologists. All patients had severe tricuspid lesions, with dyspnea being the most common symptom. For the first time one patient had CytoSorb® combined with the TandemHeart® in order to treat right-ventricular failure, which avoided the need for venoarterial extracorporeal membrane oxygenation (va ECMO). The authors write that the adjunctive option of CytoSorb® could be potentially used as a valuable therapeutic treatment option to restore right ventricular failure and avoid the catastrophic results of carcinoid storm triggered by other circulatory devices such as ECMO. The authors conclude that surgery for HS, despite being high risk, can efficiently prolong survival and represents a safe and feasible procedure.

<https://www.ncbi.nlm.nih.gov/pubmed/37887860>

Intraoperative Immunomodulation during Left Heart Bypass in Open Thoracoabdominal Aortic Aneurysm Repair

Pascucci F, Donati T, Tinelli G, Arlotta G, Luparelli A, Tshomba Y.

J Vasc Surg Cases, Innov & Tech 2023; 9(3):101276

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Summary

This case report on a 53 yr old with hypertension, previous aortic valve replacement and acute type B aortic dissection 10 yrs previously, who presented with a dissecting type 1 thoraco-abdominal aortic aneurysm (TAAA). Management was according to standard procedures, but also included CytoSorb® in the left heart bypass circuit. Bypass time was 108 minutes. Vasopressor support was only required at a low level intraoperatively (maximum norepinephrine dose 0.2 µg/kg/min). Inflammatory markers increased as anticipated, but remained clinically not relevant. The patient was able to be extubated on post-op day 1, and transferred to the ward on day 5 without having developed acute respiratory distress syndrome, vasoplegia, coagulopathy or acidosis, despite the severity of his condition. The authors state that the use of CytoSorb® in this case may have attenuated the potential harmful effects of a hyperinflammatory response. It is noted that CytoSorb® can be integrated into every kind of extracorporeal circuit, which could be considered also in the postoperative period, if clinically indicated. Finally they note that more data regarding the inflammatory response during TAAA will help evaluate evidence based immunomodulation during such surgeries. At the end of the article there is a short video showing the integration of CytoSorb® into the circuit.

[Link to Video](#)

<https://pubmed.ncbi.nlm.nih.gov/37662566/>

Successful Extracorporeal Cytokine Hemoadsorption in a Marfan Syndrome Patient with COVID-19 undergoing Redo Bentall Procedure

Singh A, Nanda C, Mehta Y, Bhan A.

American Journal of Case Reports 2023; 24: e940383

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Summary

This report is of a 34 yr old patient with COVID-19 requiring redo replacement of the aortic valve and aorta due to aortic aneurysm of the ascending aorta (Bentall procedure) associated with Marfan syndrome. The patient was admitted with symptoms of worsening dyspnea, tachycardia, fever, and confirmed COVID-19. Given the severity of symptoms, COVID-19, echocardiography findings, and risk of aortic rupture, urgent surgery was performed. A CytoSorb® hemoadsorber was integrated into the cardiopulmonary bypass (CPB) circuit to attenuate the anticipated systemic hyperinflammation. Aortic cross clamp time was 165 min and CPB time 191 mins. Treatment with CytoSorb® was associated with marked improvements in vital parameters (mean arterial pressure) and inflammatory markers (procalcitonin and interleukin-6), so that weaning from the ventilator and inotropes (including norepinephrine and epinephrine) was possible after 48 hours. The remaining time in hospital was uneventful. So despite the severity of the patient's condition, the intra- and postoperative clinical course was good, and clinical outcomes were deemed favorable. This report supports the findings that extracorporeal cytokine hemoadsorption has a role to play in reducing the systemic effects of cytokine storm associated with complex surgery involving cardiopulmonary bypass alongside severe infections, including COVID-19.

<https://pubmed.ncbi.nlm.nih.gov/37749880/>

The use of CytoSorb® in a prasugrel-loaded patient undergoing emergent coronary artery bypass graft surgery

Moresco E, Dejaco H, Humbert V, Thoma M.

Clinical Case Reports 2023; e6990

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Summary

This is the case of a 63-year-old male patient with a positive history of arterial hypertension suffering from acute chest pain. Before undergoing cardiac catheterization, the patient was administered 250 mg acetylsalicylic acid (ASA), 5000 units of unfractionated heparin intravenously (i.v.), and 60 mg of prasugrel. Coronary angiography showed severe multi-vessel coronary artery disease so the decision was made to abort the percutaneous intervention and to convert to emergency open-heart surgery, which was started a few hours later. To reduce the risk of bleeding during and especially after open-heart surgery given the previous loading with prasugrel, a CytoSorb® adsorber was integrated into the cardiopulmonary bypass (CPB). Platelet function was monitored before, during, and on the first postoperative day. CPB and ACC (aortic cross-clamp) times were 112 and 81 minutes respectively. Intraoperative management was unremarkable, and postoperatively the patient was transferred to the intensive care unit (ICU) for further monitoring and treatment. During his postoperative stay in the ICU, only minor blood loss was recorded, although platelet function still seemed to be inhibited according to Multiplate® analyzer tests. The authors conclude that CytoSorb® use was shown to be associated with a significantly reduced need for blood cell transfusions in the intraoperative setting. Even without the presence of antithrombotic substances, the use of the adsorber might have an effect concerning reduction in bleeding which may be because of the reduction in inflammatory substances and therefore the reduction of prostaglandin synthesis, but a better understanding of the precise mechanisms behind this is needed as well as more structured investigations on the use of CytoSorb® in Prasugrel loaded patients.

<https://www.ncbi.nlm.nih.gov/pubmed/36950671>

Strategies to mitigate inflammation in management of complex congenital heart disease complicated by "multisystem inflammatory syndrome in children"

Kumar A, Joshi RK, Aggarwal N, Ray M, Joshi R.

Ann Pediatr Cardiol 2022; 15(3): 276-279

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Summary

In this case report, a 6-month-old boy with a congenital cardiac malformation (Shone's complex), presented with severe mitral stenosis and multisystem inflammatory syndrome in children (MISC) requiring urgent surgical intervention. Because of the high risk of hyperinflammation and a cytokine storm resulting from his clinical condition and the open heart surgery itself, various modalities including CytoSorb®, hemofiltration, steroids and intravenous immunoglobulin were successfully used to target the inflammation. Postoperatively, the child recovered well with decreases in the levels of inflammatory markers, vasopressors, and ventilatory requirements, and he was able to be discharged home in a healthy condition. The authors state that the use of CytoSorb® during cardiopulmonary bypass was a safe and a possibly effective strategy for such critically sick patients.

<https://pubmed.ncbi.nlm.nih.gov/36589656/>

CytoSorb hemoadsorption for removal of apixaban – a proof-of-concept pilot case for a randomized controlled trial)

Buonocore M, Rex S, Degezelle C, Meyns B.

Journal of Clinical Pharmacy and Therapeutics 2022; 47(12):2373-2375

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Summary

In this case report an 81 yr old on the non-vitamin-K antagonist oral anticoagulant (NOAC) apixaban for chronic atrial fibrillation, was referred for emergency cardiac surgery due to methicillin-sensitive staphylococcus aureus (MRSA) prosthetic aortic valve endocarditis and hemodynamic instability. Although apixaban was discontinued 24 hours prior to surgery, complete wash out of the drug could not be achieved, so a CytoSorb® adsorber was inserted into the cardiopulmonary bypass (CPB) circuit to remove circulating molecules of apixaban, and blood level measurements were taken pre and post the adsorber. The procedure was complicated by a massive bleed from a laceration of the pulmonary artery requiring multiple blood products (including 8 units of red blood cell concentrate, 2 units of platelets, 4 units of fresh frozen plasma and 3 grams of human fibrinogen) and a second cross-clamping. Total CPB time was 288 minutes. Despite this, at the end of surgery, his coagulation status (thromboelastometry) showed completely normalized values. Direct measurements of apixaban drug levels pre and post adsorber outlet showed the rapid and sustained decrease of apixaban through the adsorber, thereby confirming direct removal of the drug by CytoSorb® in a clinical setting. The authors confirm the concentration dependent manner of CytoSorb® adsorption, where highest efficacy may be expected with higher drug doses, normally present at the start of an operation. Therefore, drug removal might potentially be effective even during shorter CPB times. No device-related adverse events or device malfunctions were reported. The authors are currently enrolling patients into a randomized control trial to confirm these positive results.

<https://www.ncbi.nlm.nih.gov/pubmed/36351749>

A New Apheresis Device for Antithrombotic Drug Removal during Off-Pump Coronary Artery Bypass Surgery

Mair H, Micka N, Vogt F, Rosenzweig D, Vogel F, Baumer B, Ulrich S, Lamm P.

Medicina 2022; 58(10):1427

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Summary

In this report, the first reference case on the use of CytoSorb® with the direct hemoperfusion pump PUR-01 (Nikkiso) is reported, during urgent off-pump cardiac surgery (OPCAB) in a 74 yr old on concomitant Dual Antiplatelet Therapy (DAPT) with ticagrelor and aspirin. The hemoperfusion device ran for 221 mins to eliminate ticagrelor with a total blood volume through the CytoSorb® of 39.04 L. The patient's care postoperatively was uneventful and he made a good recovery with no cardiac symptoms at six week follow up. Since this initial case a further 3 patients on DAPT requiring OPCAB surgery have been operated on using this system. In all patients the intraoperative surgical procedure has not been complicated by any remarkably enhanced bleeding, no patient has required a reoperation, and the postoperative course has been uneventful. In summary, in this study the use of CytoSorb® with a hemoperfusion pump during OPCAB surgery for the removal of the antiplatelet drug ticagrelor has proved successful, with no device related adverse events occurring. Treatment has resulted in good control of the peri- and postoperative bleeding risk, hemodynamic stabilization, and satisfactory clinical outcome.

<https://www.ncbi.nlm.nih.gov/pubmed/32407851>

Use of CytoSorb hemoadsorption column during prolonged cardiopulmonary bypass in complex cardiac surgery patient

Alarie M, Savelberg M, Vautour D, Ribeiro IB.

J Cardiothorac Surg 2022; 17(1):172

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Summary

In this report a 61-year-old male with congestive heart failure was assessed for cardiac surgery, and was found to require mitral valve replacement, aortic valve replacement, tricuspid valve repair, single coronary artery bypass grafting and a left atrial appendage clip. Given the complexity of the surgery, the anticipated prolonged length of cardiopulmonary bypass, the associated risk of significant vasoplegia and his preoperative kidney dysfunction, the decision was made to integrate the CytoSorb® cartridge into the cardiopulmonary bypass (CPB) circuit. One CytoSorb® hemoadsorber was used intraoperatively throughout the CPB time (154 min). Despite an initial rise in vasopressor requirements, the mean arterial pressure (MAP) gradually improved during the time on by-pass whilst vasopressors could be weaned off completely. However, ten minutes post-bypass

(i.e. after discontinuation of CytoSorb®), the patient once again required multiple vasopressors to support his MAP. Despite the presence of postoperative thrombocytopenia, postoperative platelet counts did not significantly differ from baseline. Treatment was safe and feasible while integration into the cardiopulmonary bypass circuit was uncomplicated with no device-related complications. In this complex cardiac surgery patient, the authors state that the application of CytoSorb® during cardiopulmonary bypass contributed to a decreased need for vasoactive support during and after surgery as well as improved postoperative outcomes, rendering it a promising therapeutic option in critically ill patients at risk of significant postoperative vasoplegia and multiorgan injury following prolonged and complex cardiac surgery.

<https://www.ncbi.nlm.nih.gov/pubmed/35799205>

First Hemoadsorption during Cardiopulmonary Bypass in Neonate with Complex Cardiac Malformation

Christophel-Plathier E, Mendes V, Verdy F, Mauron S, Mury C.

Annals of Clinical Case Reports 2022; 7:2257

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Summary

In this case report a 5 day old full term newborn with congenital hypoplastic left heart syndrome (absent mitral valve and exceedingly small aortic annulus, ascending aorta and aortic arch) underwent a Norwood stage I palliation with interatrial septum resection, aortic reconstruction and creation of a Blalock-Taussig shunt. Cardiopulmonary bypass time was 227 minutes with CytoSorb® inserted between the oxygenator outlet and the venous line, assisted by a roller pump slave to the blood pump. Priming of the CPB circuit required 385 ml of blood, of which 120 ml were used for priming the CytoSorb®. Surgery was uneventful and successful, and the patient returned to the intensive care unit (ICU) intubated with norepinephrine, dopamine and milrinone infusions. Despite the severity of his condition, the baby had an uneventful post operative course, without complications. Hemodynamic adaptation was good, with rapid weaning off all amine infusions and definitive weaning off norepinephrine on post-operative day 5. The patient was extubated on day 6, left ICU on day 22 and discharged home on day 45. The authors describe the clinical course post operatively as remarkable with shortened ICU and hospital length of stay due to the lack of (anticipated) complications. They state that previous similar cases have required much longer support on ventilation and longer ICU stay. They also believe the expected benefits to anti-inflammatory processes are worth the greater homologous blood use. As the use of CytoSorb® was the only differentiating factor, its use likely helped to reduce the pre-operative and intra-operative inflammatory process and thereby helped with the positive clinical course and outcome. The authors conclude with stating that by reducing cytokine levels, the CytoSorb® may have significantly reduced catecholamine infusion time, intubation time, and ICU stay. Future studies should evaluate CytoSorb®'s effectiveness in selected pediatric cases.

[Link to article](#)

Use of the CytoSorb® filter for elimination of residual therapeutic argatroban concentrations during heparinized cardiopulmonary bypass for heart transplantation

Koster A, Warkentin H, von Dossow V, Morshuis M.

Perfusion 2023; 38(5):1088-1091

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Summary

This is a case report about a 34-year-old patient who, after a five week wait in hospital, was offered a donor heart that had to be transplanted within 2 hours. Because of a history of heparin-induced thrombocytopenia (HIT), the patient had been placed preoperatively on the anticoagulation drug argatroban for which there is currently no reversal agent. Despite ceasing the continuous infusion of argatroban immediately, concentration only declined from 0.60 µg/ml to 0.58 µg/ml before surgery, with the activated clotting time (ACT) value remaining very high (223 s). Microvascular bleeding was observed on chest incision, therefore a CytoSorb® column was integrated into the system of the heparin-anticoagulated cardiopulmonary bypass (CPB) circuit, with a flow of 400 mL/min provided during the 150 mins of extracorporeal circulation. The argatroban concentration after weaning from CPB was 0.04 µg/ml and satisfying hemostasis was achieved after protamine administration. Despite severe bleeding within the context of perioperative use of argatroban having been described, the 12-h postoperative blood loss was only 580 mL. The authors note that the availability of a technology for quick elimination of high therapeutic concentrations of argatroban may have a significant impact on the safety profile of this drug, and that the use of CytoSorb® might be an effective tool that has the potential to fulfil these criteria.

Comment from CytoSorbents

Argatroban is a direct thrombin inhibitor used instead of heparin for anticoagulation in cases of heparin-induced thrombocytopenia. This is the first published clinical case report that suggests a potential relevant

removal of argatroban, but there are a number of other published papers (case reports / case series) that confirm the feasibility of argatroban anticoagulation without the need for additional precautions. Relevant in-vitro removal of argatroban has been shown, however, with the exception of this case report, there has been no signal towards clinically important removal from the published literature. Based on the currently available, inconclusive data, we recommend regular monitoring of aPTT when argatroban is used as anticoagulant during CytoSorb® application.

<https://www.ncbi.nlm.nih.gov/pubmed/35619539>

Urgent Coronary Artery Bypass Grafting Complication by Systemic Inflammatory Response from Fulminant Herpes Zoster Successfully managed with Adjunct Extracorporeal Hemoadsorption: A Case Report

Haidari Z, Weißenberger W, Tyczynski B, Demircioglu E, Deliargyris E, Christ M, Thielmann M, El Gabry M, Ruhparwar A, Wendt D.

J Clinical Medicine 2022; 11:3106

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Summary

In this case report a 56 yr old man presented to hospital requiring complex cardiac surgery complicated by an outbreak of herpes zoster infection. After clinical and inflammatory improvement (requiring an 8 day stay in intensive care), he was taken for coronary artery bypass graft surgery. Immediately on induction of anesthesia, he became hemodynamically unstable requiring noradrenaline (>0.75 µg/kgbw/min). This situation worsened again once he was placed on cardiopulmonary bypass (noradrenaline 1.5 µg/kgbw/min). The patient then had a CytoSorb® adsorber added to the bypass circuit resulting in stabilization of this ongoing acute situation (noradrenaline 1.0 µg/kgbw/min). His post-operative course was complicated requiring maximum pharmacological and blood product support, as well as transfer onto veno-venous extracorporeal membrane oxygenation (vvECMO). He was also placed on renal replacement therapy, including 72 hours of CytoSorb® hemoadsorption (3 adsorbers for 24 hrs each). By post op day 2 his hemodynamic status, lactate levels and inflammatory parameters were all improving. Despite the fact that the patient then developed acute respiratory distress syndrome, he eventually went on to fully recover, and was asymptomatic at 6 month follow up. In this patient with a profound systemic inflammatory response during coronary artery bypass surgery and reactivated herpes zoster resulting in significant clinical instability, use of CytoSorb® both intra- and post-operatively helped stabilize hemodynamics and reduce inflammatory markers suggesting that hemoadsorption was an important contributor to the favourable outcome. In conclusion this case suggests that hemoadsorption may be a vital adjunct therapeutic option for the management of a profound systemic inflammatory response in a patient requiring urgent cardiac surgery.

<https://www.ncbi.nlm.nih.gov/pubmed/35683493>

CytoSorb usage in a dual antiplatelet agent treated patient during CABG and broken guidewire retrieval from right coronary artery ostium

Kumar N, Keshri K, Rhuyan RR.

IJMDAT 2022; 5: e379

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Summary

In this case report a 66-year-old male patient on doublet antiplatelet therapy (DAPT) with ticagrelor and aspirin underwent percutaneous transluminal coronary angioplasty (PTCA) for triple vessel disease (TVD). During withdrawal part of the guidewire became stuck in the right coronary artery. The patient began to deteriorate clinically (left ventricular ejection fraction reduced to 40% with akinetic walls and early pulmonary edema) so he was taken for emergency on-pump coronary artery bypass graft (CABG) surgery, despite being on DAPT. CytoSorb® was added to the cardiopulmonary bypass circuit in an effort to remove the ticagrelor and reduce the risk of bleeding. Post-operatively no bleeding was recorded. The patient demonstrated good pump function and sinus rhythm and was able to be discharged in a stable condition within 7 days of hospitalization including 3 days of intensive care unit stay. According to the authors use of intraoperative CytoSorb® – in line with earlier reports – prevented expected substantial postoperative bleeding, which led to short ICU stay and total hospitalization time. The authors conclude that intra-operative use of CytoSorb® during emergency cardiac surgery in patients treated with ticagrelor is an effective option which reduces risk of bleeding complications, thereby improving outcomes, reducing costs and minimizing morbidity and mortality.

[Link to Article](#)

Blood purification during valve surgery for endocarditis in an adolescent

Tirilomis T.

Artif Organs 2021; 45(1):95-96

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Summary

In this case report a 15 yr old with large endocarditic vegetations on the aortic valve was referred for urgent surgery. During the time on cardiopulmonary bypass - CPB (102 mins), a CytoSorb® adsorber was installed into the circuit due to the high risk of him developing septic shock postoperatively from the infective endocarditis, and also the possibility of an additional inflammatory reaction due to the operation itself. However, contrary to expectations, vasopressor support was able to be terminated 4 hours post-surgery, and inotropes 24 hours later. According to the authors this case shows that the prophylactic blood purification during CPB might have protective effects in the treatment of pediatric endocarditis.

<https://www.ncbi.nlm.nih.gov/pubmed/32686097>

The effect of hemoadsorption on rivaroxaban blood plasma concentration in emergency cardiac surgery

Krüger B, Renner T, Van Hemelrijck M, Sromicki J, Ouda A, Mestres CA.

Indian Journal of Thoracic and Cardiovascular Surgery 2021; 37(6):1-4

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Summary

CytoSorb® hemoadsorption was used in a 59-year-old patient with an acute type A aortic dissection, who was on rivaroxaban and dual antiplatelet therapy with clopidogrel and acetylsalicylic acid prior to the event, in order to expeditiously remove rivaroxaban preoperatively. After 2.5 hrs of hemoadsorption, the rivaroxaban blood plasma concentration (RBPC) decreased from 89.4 µg/l to 42.1 µg/l where it plateaued. Nineteen hours after the onset of symptoms the patient underwent successful ascending aorta replacement. A second CytoSorb® was used intraoperatively. Sixteen hours after surgery and a total of 13 h of hemoadsorption, the RBPC was 40.1 µg/l. Thereafter, the RBPC spontaneously decreased to 24.7 µg/l within 14 h. The patient survived the emergency surgery and it was possible to control bleeding after surgery. He could be discharged from hospital on day 40 and is, eighteen months after surgery, alive and active without impairing sequelae. In this patient, hemoadsorption with CytoSorb® may have enhanced rivaroxaban removal at higher RBPC (cutoff value 40–50 µg/l). So if used preoperatively, hemoadsorption may reduce the time of delay of emergency surgery.

<https://pubmed.ncbi.nlm.nih.gov/33907356/>

Cytosorb® hemoadsorption of apixaban during emergent cardio-pulmonary bypass: a case report

Mendes V, Colombier S, Verdy F, Bechtold X, Schlaepfer P, Scala E, Schneider A, Kirsch M.

Perfusion 2021; 36(8):873-875

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Summary

An 83-year-old woman treated with the new oral anticoagulant Apixaban (2.5 mg twice a day) because of a recent lower limb deep vein thrombosis underwent emergent redo mitral valve replacement for prosthetic valve endocarditis. The last dose of apixaban was taken seven hours before surgery. Due to the increased risk of bleeding complications and subsequent need for multiple transfusions, a CytoSorb® cartridge was added to the cardio-pulmonary bypass (CPB) circuit and an Apixaban-specific anti-factor Xa activity (AFXaA) was measured peri-operatively. After 100 minutes of CPB, a 50% AFXaA rate decrease was noted compared to pre-CPB values. Furthermore, the authors noticed reductions of 39% and 44% in AFXaA levels in comparison to the expected levels in patients with normal or altered renal function, respectively. The postoperative course was uneventful, there were no bleeding complications and the patient was hemodynamically stable. The patient left the intensive care unit after 2 days, and hospital on day 26. The authors conclude that insertion of CytoSorb® in the CPB was safe and was associated with the rapid correction of Apixaban-associated anticoagulation.

<https://www.ncbi.nlm.nih.gov/pubmed/33106093>

Experience of using an extracorporeal cytokine hemoadsorber (CytoSorb®) in systemic inflammatory response syndrome after heart transplantation

Krishan, K., Dutta R, Chand R, Malhotra R.

Indian Journal of Transplantation 2020; 14(2):166-169

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Summary

This is a case report of a 28 year male who had a heart transplant due to end stage heart failure. Post operatively he developed an hyperinflammatory response and renal dysfunction, so CytoSorb® was initiated together with SLED (sustained low-efficiency dialysis). In total he had 3 cycles of CytoSorb® of 6 – 12 hours each. With the use of CytoSorb® his hemodynamic picture improved, showing - in comparison to before and after CytoSorb® therapy: mean arterial pressure 90 v 100 mmHg, norepinephrine 8 v 4.7 µg/min, dobutamine 4.5 v 0 ml/hour and vasopressin 2 v 1.5 ml/hour. His inflammatory parameters also improved, procalcitonin decreased from 169 to 34 ng/dL, and C-reactive protein 13.7 to 6 mg/dL. The tacrolimus levels were regularly monitored and no modifications were needed. Generally there were no adjustments made to his immunosuppressive therapy because of the use of CytoSorb® and the patient showed no signs of rejection either clinically or with biopsy. The patient gradually recovered his renal function and was able to be discharged from intensive care and then hospital. The authors state that use of CytoSorb® prevented clinical deterioration and helped to regain control of the hyperinflammation resulting in a relatively short ICU and hospital stay, reducing the financial burden.

[Link to Article](#)

Ticagrelor and Rivaroxaban Elimination With Cytosorb Adsorber Before Urgent Off- Pump Coronary Bypass

Mair H, Jilek C, Haas B, Lamm P.

The Annals of Thoracic Surg 2020; 110(5):e369-e370

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Summary

This is a case report of a 58 year old male with severe coronary artery disease who was at high risk of bleeding due to treatment of coronary artery disease with ticagrelor and atrial fibrillation with rivaroxaban. The patient had an acute dissection of the left anterior descending artery during a percutaneous coronary intervention so was scheduled for urgent off pump coronary arterial bypass (OPCAB) operation. In order to reduce the risk of bleeding, CytoSorb® therapy was performed one hour before the operation and continued for a further 1.5 hrs during the operation in order to eliminate the coagulative active medications (ticagrelor and rivaroxaban). The CytoSorb® was inserted into an extracorporeal circuit with hemofilter and dialysate using citrate for anticoagulation. Blood flow rate was between 130-150 ml/min and no ultrafiltration was used. His intra- and postoperative course was uneventful with adequate bleeding control and good recovery of the patient. At six months follow up the patient continued to do well. This case highlights a novel approach for managing antiplatelet drugs and anticoagulants such as ticagrelor and rivaroxaban prior to OPCAB with CytoSorb® appearing to be effective for assisting bleeding control. There were no device-related adverse events or device malfunctions reported.

<https://www.ncbi.nlm.nih.gov/pubmed/32407851>

CytoSorb hemoadsorption and mechanical circulatory support in a newborn with refractory shock after congenital heart surgery

Perez MH, Maitre G, Longchamp D, Amiet V, Natterer J, Ferry T, Schneider A, Plaza Wuthrich S and Di Bernardo S.

Int J Artif Organs 2019; 42(9):521-514

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Summary

This is the case of a 4kg newborn boy with cardiogenic and vasoplegic shock secondary to cardiopulmonary bypass for atrioseptostomy, and prostaglandin treatment in the context of hypoplastic left heart syndrome performed around 24 hours post-partum. Post-operatively he required ongoing high levels of vasopressor and inotropic support so mechanical circulatory support (MCS) was added to restore adequate tissue perfusion. However, refractory vasoplegic shock continued requiring ongoing high doses of vasopressors, the patient remained anuric, and, as he also did not respond to steroids, the decision was taken to install CytoSorb® into the MCS circuit. After an initial short hypotensive episode, blood pressure stabilized, diuresis restarted and increased, lactate normalized and vasopressor support was able to be gradually weaned over the following hours. The same adsorber was used for 72h due to the low weight of the patient. During these 72hrs, antibiotics levels (piperacillin and vancomycin) were monitored when possible. The dosage of prostaglandins was also increased due to their possible removal by CytoSorb®. Once the CytoSorb® was removed there was a rebound in the vancomycin levels due to a lack of timely dose reduction, hence the authors recommend therapeutic drug monitoring also immediately after CytoSorb®. Of note, despite the initial severity of the condition, multiple organ failure did not develop. This is the first case in such a young patient (around 2 days

old), and only 4kg in weight. The authors state that the association of the CytoSorb® with mechanical circulatory support finally allowed a rapid and significant stabilization of the hemodynamic situation accompanied by weaning of catecholamine treatment and resumption of diuresis within a few hours after initiation of CytoSorb® therapy. This case shows that CytoSorb® is a feasible and easy therapy that can have a positive effect in the management of an uncontrolled inflammatory process even in a newborn.

<https://www.ncbi.nlm.nih.gov/pubmed/30968739>

Bilirubin Removal Using CytoSorb Filter in a Cardiac Surgical Patient

Singh A, Mehta Y, Trehan N.

J Cardiothorac Vasc Anesth 2019; 33:881-883

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Summary

In this case report a 63 year old woman was admitted to the Cardiac Intensive Care following mitral and tricuspid valve repair. Her postoperative course was complicated by prolonged ventilatory support, tracheostomy, very high vasopressor support (norepinephrine 3.5 µg/kg/min), sepsis and multiorgan failure involving the liver, kidneys, and brain. Continuous venovenous hemodiafiltration (CVVHDF) with CytoSorb® was initiated and continued for 3 days in total, resulting in significant decreases in interleukin-6 (from 245.5 to 53.9 pg/mL) and bilirubin (from 24.5 to 10.8 mg/dL), with reductions in vasopressor requirement (norepinephrine 0.5 µg/kg/min) and improvement in urine output (0.5 mL/kg/h). The authors describe the role of CytoSorb® as an effective means for the irreversible removal of cytokines and toxic molecules, concluding that it may act as a promising therapeutic option for critically ill patients with multiorgan failure after cardiac surgery and may help in cytokine reduction with improved organ function.

<https://www.ncbi.nlm.nih.gov/pubmed/30292390>

Continuous cytokine haemoabsorption incorporated into a venoarterial ECMO circuit for the management of postcardiotomy cardiogenic and septic shock – a case report

Nemeth E, Szigeti S, Varga T, Doroczi L, Barati Z, Merkely B, Gal J.

Perfusion 2018; 33(7):593-596

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Summary

In this case a 46-year-old male patient underwent emergency cardiac surgery because of infective endocarditis (IE). The development of postcardiotomy cardiogenic shock associated with cardiac surgery required the implantation of venoarterial (VA)-ECMO. Three days later the patient developed secondary septic shock, and, due to rapidly increasing vasopressor requirements, CytoSorb® was installed into the VA-ECMO circuit. A significant and rapid improvement in the patients hemodynamic and metabolic parameters was observed and after 24 hrs of treatment, the CytoSorb® treatment could be stopped and VA ECMO ceased after 7 days. Advanced intensive care led to an improvement in the patient's condition however the patient died from a new onset of fulminant septic shock two months after his initial cardiac surgery. This case demonstrates that VA-ECMO is suitable for direct installation of the CytoSorb® cartridge. The authors report that this novel application of CytoSorb® is safe, feasible and effective and can contribute to the optimal management of patients suffering from simultaneous postcardiotomy cardiogenic shock and septic shock.

<https://www.ncbi.nlm.nih.gov/pubmed/29779449>

ECMO and cytokine removal for bridging to surgery in a patient with ischemic ventricular septal defect - a case report

Marek S, Gamper G, Reining G, Bergmann P, Mayr H, Kliegel A.

Int J Artif Organs 2017; 40(9):526-529

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Summary

Post-infarction ventricular septal defect (VSD) remains a serious and often lethal complication of percutaneous coronary intervention. This is a case report the use of veno-arterial extracorporeal membrane oxygenation (VA ECMO) and extracorporeal blood purification therapy (CytoSorb®) in a 64-year-old patient with ischemic VSD leading to protracted cardiogenic shock and hemodynamic instability requiring large doses of catecholamines after a myocardial infarction. After a few hours with ECMO and CytoSorb® the patient began to stabilize hemodynamically. The catecholamines could be significantly reduced within the first 36 hours of treatment. After 4 days of treatment with ECMO and CytoSorb® the patient was stable enough to be taken to surgery, where repair of the VSD and bypass grafting was successfully

performed.

<https://www.ncbi.nlm.nih.gov/pubmed/28574104>

1.3.3 Liver

A rare case of acute liver failure with intrahepatic cholestasis due to dengue hemorrhagic fever: CytoSorb® and plasma exchange aided in the recovery: case report

Gunasekera AM, Eranthaka U, Priyankara D, Kalupahana R.

BMC Infect Dis 2022; 22(1): 938

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Summary

Dengue hemorrhagic fever (DHF) is a severe form of acute dengue infection characterized by circulatory insufficiency leading to shock. Despite varying degrees of liver involvement occurring in acute dengue infection, intrahepatic cholestasis is very rare. This is a case report of a 54 yr old with DHF complicated by acute liver failure, coagulopathy, acute renal failure and prolonged intrahepatic cholestasis. Despite the standard dengue management, she deteriorated clinically including severe encephalopathy necessitating elective intubation and mechanical ventilation. Continuous renal replacement therapy (CRRT) was started to try and stabilize the metabolic acidosis but to no avail, so CytoSorb® was introduced on day 7 of her intensive care stay for 2 days after which metabolic parameters returned to normal with a gradual drop in lactate with the correction of acidosis. Therapeutic plasma exchange was used on days 18 and 19. In this case, acute liver failure with a prolonged phase of intrahepatic cholestasis as a very rare complication of the acute dengue illness, was managed successfully with supportive therapy, also aided by CytoSorb® hemoadsorption.

<https://www.ncbi.nlm.nih.gov/pubmed/36514003>

The successful application of hemoadsorption for extracorporeal liver support in a child with acute liver failure

Hui WF, Cheung WL, Chung FS, Leung KKY, Ku SW.

Int J Artif Organs 2022; 45(10):878-882

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Summary

The following case report describes the use of CytoSorb® in a pediatric patient for the reduction of hyperbilirubinemia and elevated serum bile acids in acute liver failure. A 6-year-old boy was admitted to hospital due to prolonged dyskinetic movements resulting in rhabdomyolysis and acute kidney injury. Over the following 10 days he was given multiple antibiotics for various infections and five days later developed acute liver failure with hepatic coma due to drug rash with eosinophilia and systemic symptoms (DRESS). He had hyperbilirubinemia, elevated serum bile acids and hyperammonemia as well as raised liver enzymes. Despite standard therapies his condition deteriorated, and he was admitted to the Pediatric Intensive Care Unit (PICU) for ongoing management. In addition to the use of systemic steroids and other supportive therapies, he was started on continuous renal replacement therapy (CRRT), into which a CytoSorb® column was added as an extracorporeal liver support to try and reduce the bilirubin and bile acids. Three adsorbers were used for a total duration of 75 hrs (28, 22 and 25 hrs). Serum levels of total bilirubin reduced from 418 to 119 µmol/L, bile acids to from 174 to 58 µmol/L and ammonia reduced from 172 to 55 µmol/L. His conscious level gradually improved, as did his liver function. Except for mild, non-symptomatic thrombocytopenia and mild electrolyte disturbances, the therapy was well tolerated with no major complication encountered. He was finally able to be discharged from the PICU after 20 days. The authors state that hemoadsorption may have the merits of a faster initial rate of bilirubin removal and ease of set up compared to albumin dialysis. In summary this case demonstrates that hemoadsorption with CytoSorb® can be safely employed as an adjunctive extracorporeal liver support modality in children with acute liver failure as it can efficiently remove bilirubin and bile acids. The potential role and technical concerns of applying such technique in pediatric patients requires further evaluation in future studies.

<https://www.ncbi.nlm.nih.gov/pubmed/35918853>

Single-pass albumin dialysis and hemoadsorption for bilirubin and bile acids removal for a child with hyperbilirubinemia after ventricular assist device implantation

Hui WF, Lun KS, Hon KL.

J Artif Organs 2022; 25(3):270-273

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Summary

In this case report a 13 year old with dilated cardiomyopathy requiring veno arterial extracorporeal membrane oxygenation (VA-ECMO) developed acute kidney injury requiring continuous renal replacement therapy. He also developed hyperbilirubinemia (peak total bilirubin level of 786 µmol/L) after a biventricular assist device (BiVAD) was implanted. He was treated with single pass albumin dialysis (SPAD) which brought his bilirubin down to 672 µmol/L after 21 hours. In an effort to hasten the bilirubin and bile acid removal, SPAD was stopped and hemoadsorption using CytoSorb® started. This further lowered the bilirubin to 306 µmol/L in 24 hrs, and then 173 µmol/L by the end of the second treatment of 22 hrs. There were no complications associated with either device, however, the authors state that the ease of set-up, faster rate of bilirubin removal and the capability of CytoSorb® to also remove cytokines make it a favorable alternative to SPAD which they describe as being labor intensive.

<https://www.ncbi.nlm.nih.gov/pubmed/35038050>

Technical note: Novel use of CytoSorb™ haemadsorption to provide wound healing support in case of severe burn trauma via reduction of hyperbilirubinemia

Rachunek K, Krause M, Thiel JT, Kolbensschlag J, Daigeler A, Bury A.

Frontiers in Surgery 2021; 7:43571

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Summary

In this case report, a 59 yr old male suffered severe burns (48% Total Body Surface Area - TBSA) including head, upper extremities, thorax, upper abdomen and back. The patient initially had an escharotomy and a tracheotomy, and 2.5 weeks post trauma, epifascial debridement and autologous skin grafting. Around this time the patient developed renal failure, so continuous renal replacement therapy (CRRT) was started. He also then developed pneumonia and sepsis, and, in parallel, cholestasis, which was later diagnosed as secondary sclerosing cholangitis (SSC). His various skin grafts and xenografts then became infected and required multiple daily wound debridements. Forty days post injury he was found to have multiple biloma and intrahepatic cholestasis (bilirubin 17 mg/dl, alkaline phosphatase - ALP 275 U/l). CytoSorb® was then started to try and reduce the bilirubin levels and thereby support wound healing. In the first 6 days, CytoSorb® was changed daily (bilirubin reduced from 14.02 – 4.19 mg/dl) and then every 2–4 days. With a stable bilirubin level <5 mg/dl one week after CytoSorb® therapy began, debridement of the back with autologous skin grafting was performed successfully. After his wounds had healed, CytoSorb® therapy, after 57 days and 27 adsorber changes, was discontinued. In summary, CytoSorb® treatment resulted in a decrease in total bilirubin plasma concentrations enabling successful surgical treatment of the abdomen, back as well as lower and upper extremities within 4 weeks following CytoSorb® treatment. The authors note that as hyperbilirubinaemia negatively influences wound healing in severely burned patients and also ongoing hyperinflammatory processes can have a negative impact on wound healing, CytoSorb® therapy could be a promising support for wound and skin graft healing in selected patients by significantly reducing total bilirubin concentrations.

<https://www.ncbi.nlm.nih.gov/pubmed/34977137>

Hemoadsorption as Bridge to Liver Transplant in A Six-Month Old Patient with Hepatic Failure

Milella L, Raimondo P, Ficarella M, Calabrese G, Sisto M, Moliterni P, Lasorella ML, Cito F, Torres D, Santangelo L, Carbone V, Piscopo G, Giodano M.

Journal of Pediatrics and Neonatology 2021; 2(2):1017

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Summary

This is a case report of a 6 month old, 8kg patient with progressive familial intrahepatic cholestasis (PFIC) and consequent acute on chronic liver failure (AoCLF) admitted to intensive care. Coagulation factors (provertinum, not activated plasma derived Factor VII, pdFVII), along with platelets and fresh frozen plasma were started to reverse her dramatic coagulopathy status. Continuous renal replacement therapy was also initiated because of acute kidney injury with the addition of hemoadsorption (CytoSorb®), to limit the severe hyperbilirubinemia and hyperammonemia. Use of provertinum resulted in better coagulation parameters, stopped bleeding and absent thrombotic events. After 18 hours of CytoSorb® use there was a dramatic reduction in the bilirubin (22.98 – 2.91 mg/dL) and ammonia levels. The Sequential Organ Failure Assessment (SOFA) score also decreased from 13 to 7. After three days the patient was able to be transferred to the National Transplant Centre and underwent a successful liver transplantation. This is the first experience with the use of provertinum and CytoSorb® in a low weight infant as a bridge to liver transplantation. The authors report that this preliminary experience underlines the role of hemoadsorption in the management of severe hepatic failure in pediatric patients before liver transplantation. Finally, the authors conclude with their opinion that, in general, CytoSorb® application in neonate and pediatrics is very useful in many pathological conditions.

[Link to article](#)

Kinetics of Bilirubin and Ammonia Elimination during Hemadsorption Therapy in Secondary Sclerosing Cholangitis Following ECMO Therapy and Severe COVID-19

Tampe D, Korsten P, Bremer SCB, Winkler MS, Tampe B.

Biomedicines 2021; 9(12): 1841

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Summary

This case report describes a 61 yr old with COVID-19 and Acute Respiratory Distress Syndrome (ARDS), requiring prone positioning, continuous renal replacement therapy (CRRT) and finally veno venous extracorporeal membrane oxygenation (vvECMO). Her clinical condition improved so that she could be weaned from ECMO and invasive ventilation, however she still required intermittent renal replacement therapy (IRRT). During the course of the disease, the patient had developed laboratory signs of liver injury during the ECMO therapy, even before clinically detectable jaundice or elevated bilirubin levels had appeared, and a diagnosis of secondary sclerosing cholangitis in critically ill patients (SSC-CIP) was confirmed by endoscopic retrograde cholangiopancreatography (ERCP). Although the patient had stable elevations of bilirubin and ammonia levels she presented with progressive nausea, vomiting, weakness, and exhaustion. Because of this CytoSorb® hemoadsorption was combined with hemodialysis treatment (6 treatments in 7 days, 8 – 12 hours per session). CytoSorb® use resulted in the successful elimination of bilirubin (total reduction of 56%), ammonia (total reduction of 74%) and C-Reactive Protein levels, and her clinical symptoms (nausea, vomiting, weakness, and exhaustion) improved. The authors conclude that the use of hemoadsorption with CytoSorb® combined with hemodialysis resulted in successful elimination of bilirubin and ammonia in this patient with SSC-CIP following ECMO therapy and severe COVID-19. This observation is particularly relevant since it has been reported that a considerable subset of critically ill patients with COVID-19 suffer from liver dysfunction associated with high mortality.

<https://www.ncbi.nlm.nih.gov/pubmed/34944657>

Pericarditis Caused by Enterococcus faecium with Acute Liver Failure Treated by a Multifaceted Approach including Antimicrobials and Hemoadsorption

Köhler T, Pletz MW, Altmann S, Kirchner C, Schwier E, Henzler D, Winde G, Eickmeyer C, Akinci SB.

Case Reports in Critical Care 2021; 8824050

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Summary

This case report describes a 29 yr old female with Crohn's disease and cachexia who developed a complex case of peritonitis with pericarditis caused by Enterococcus faecium, and acute liver failure caused by septic shock. Potentially hepatotoxic antibiotic therapy levels were monitored using the liver maximum capacity (LiMAX) test, and standard treatment was supplemented by adjunctive hemoadsorption with CytoSorb®. Three CytoSorb® adsorbers were initially given over 73 hours resulting in rapid hemodynamic stabilization (norepinephrine reduced to 8.3% of the maximum dose), and the patient could be extubated. However, the patient's condition began to deteriorate again over time, and another 13 CytoSorb® adsorbers were used from day 22 onwards, over the following 16 days. Inflammatory parameters improved consistently over the course of the next week, the catecholamine dose was reduced, and invasive ventilation was changed to assisted ventilation. An efficient and sustained reduction in plasma bilirubin levels was also noted while maintaining liver function. After further improvement, the patient was discharged in a stable clinical condition from the ICU to the normal ward 53 days after her initial admission. This case shows how complex infectious diseases with an atypical infectious focus resulting in septic shock can be successfully treated. A combination of antimicrobial (tigecycline and caspofungin) and long-term adjunctive hemoadsorption CytoSorb® therapy was administered while hepatotoxic antibiotic medication was monitored by LiMAX liver function testing. CytoSorb® as an individual adjuvant treatment concept in both cycles allowed medical staff to gain control of the hyperinflammation and to clearly decrease vasopressor requirements.

<https://pubmed.ncbi.nlm.nih.gov/33815848/>

Hemoadsorption in isolated conjugated hyperbilirubinemia after extracorporeal membrane oxygenation support. Cholestasis of sepsis: A case report and review of the literature on differential causes of jaundice in ICU patient.

Piwowarzyk P, Kutnik P, Potrec-Studzinska B, Sysiak-Slawecka J, Pypulak E, Borys M, Czuczwar M.

Int J Artif Organs 2019;42(5):263-268

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Summary

In this case report a patient with septic shock and severe acute respiratory distress syndrome was retrieved to the authors hospital for veno venous Extracorporeal Membrane Oxygenation (VV ECMO). Three days after initiation of ECMO, the patient developed jaundice, with an increase in liver enzymes including bilirubin, Gamma-glutamyltransferase and Alkaline phosphatase, but without elevation of alanine aminotransferase and INR. Although ECMO was stopped, bilirubin serum levels continued to increase, reaching the peak of 18.41 mg/dL of total and 15.67 mg/dL of direct bilirubin. Abdominal computed tomography excluded viral hepatitis and sepsis-related cholestasis was diagnosed. Despite cessation of sedation, the patient remained unconscious. Hemoadsorption therapy with CytoSorb® was initiated with renal replacement therapy due to prolonged high levels of conjugated bilirubin. After 2 x 24 hrs of treatment, total bilirubin levels decreased to 2.4 mg/dL, the patient regained spontaneous eyes opening and could be transferred back to the regional hospital. Hyperbilirubinemia did not return in the 3 month follow up period indicating that CytoSorb® may have supported a sustained rebalance between the inflammatory process, cytokine production and bilirubin turnover. In this patient, CytoSorb® was a useful therapeutic option in sepsis induced prolonged cholestasis. <https://www.ncbi.nlm.nih.gov/pubmed/30919732>

Use of hemoadsorption in a case of severe hepatic failure and hyperbilirubinemia

Faltlhauser A, Kullmann F.
Blood Purif 2017; 44:98–99

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Summary

In this case study a 59 yr old patient with active hepatitis B, elevated liver enzymes and increased total bilirubin was given CVVHD with CytoSorb® for 7 days for acute kidney injury and to rebalance the excessive hyperbilirubinemia. Hepatic encephalopathy, bilirubin and liver enzymes all reduced daily with ammonia levels returning to normal. This is the first clinical case describing the use of CytoSorb® hemoadsorption during hyperbilirubinemic hepatic dysfunction due to active hepatitis B infection.

<https://www.ncbi.nlm.nih.gov/pubmed/28355595>

Application of Hemoadsorption in a Case of Liver Cirrhosis and Alcohol-Related Steatohepatitis with Preexisting Hepatitis C Infection

Buttner S, Patyna S, Koch B, Finkelmeier F, Geiger H, Sarrazin C, Farnik H.
Blood Purif 2017; 44(1):30-31

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Summary

This is the first case study that confirms the successful direct removal of liver toxins, including ammonia and bile acids by CytoSorb®. In this report a 36-year-old patient with chronic viral hepatitis C and chronic alcohol abuse was admitted to ICU with decompensated ethanol toxic liver cirrhosis. Despite an initial attempt to stabilize the patient using an albumin infusion and multiple paracenteses the patient developed hepatorenal syndrome and subsequent dialysis dependency. An evaluation as to whether the patient could be listed for a liver transplantation was rejected. As a „last resort“, CytoSorb® treatment was initiated with the rationale to remove inflammation-triggering factors and liver toxins (bile acids, bilirubin, ammonia) in the context of his systemic inflammatory condition as well as his acute-on-chronic liver failure. In total two treatments with CytoSorb® were carried out for 6 hours each with a treatment pause of 5 days between adsorbers due to lack of evidence of use in this kind of patient. Pre and post adsorber measurements during the second treatment confirmed efficient removal of ammonia, bilirubin and bile acids. After initially recovering well, the patient subsequently developed nosocomial pneumonia, then fulminant pneumogenic sepsis and died three weeks later. In this case report treatment with combination of CRRT and CytoSorb® worked extremely well and effectively as a liver support. As a consequence, hepatic encephalopathy improved significantly due to efficient removal of liver toxins including ammonia.

<https://www.ncbi.nlm.nih.gov/pubmed/28237980>

First report of cytokine removal using CytoSorb® in severe noninfectious inflammatory syndrome after liver transplantation

Tomescu DR, Dima SO, Ungureanu D, Popescu M, Tulbure D, Popescu I.
Int J Artif Organs 2016; 39(3):136-140

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Summary

In this report a 46-year-old man with primary graft non-function after liver transplantation who underwent emergency re-transplantation with an ABO-incompatible graft is described. A severe inflammatory response syndrome (SIRS) was noted in the perioperative period of re-transplantation. The patient was successfully treated with CytoSorb® in combination with CVVH throughout the intraoperative and early postoperative period. During and after each treatment a significant and rapid decrease of pro- and anti-inflammatory cytokines was observed (IL-6, IL-10, MCP-1). Reduction in cytokines was associated with normalization of cardiac output, systemic vascular resistance, and improved liver function. The authors believe this is the first case in which hemoadsorption in combination with CVVH has been used to manage SIRS in a patient with primary graft non-function undergoing emergency re-transplantation.

<http://www.ncbi.nlm.nih.gov/pubmed/27079418>

First description of SPAD combined with cytokine adsorption in fulminant liver failure and hemophagocytic syndrome due to generalized HSV-1 infection

Frimmel S, Schipper J, Henschel J, Yu TT, Mitzner SR, Koball S.

Liver Transpl 2014; 20(12):1523-1524

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Summary

This case study reports on a 50-year-old immunocompetent woman who was admitted to hospital for acute hepatitis with acute liver failure. After transfer to ICU the patient rapidly developed multi organ failure and was listed for highly urgent liver transplantation. Since existing liver support techniques (MARS treatment) for bridging while waiting for liver transplantation had no effect, Single Pass Albumin Dialysis (SPAD) in combination with CytoSorb® was applied resulting in a marked decrease in IL-6, bilirubin as well as a reduction of vasopressor need. Orthotopic liver transplantation could be successfully performed on the 4th day on ICU. CytoSorb® treatment was safe and well-tolerated, without any adverse events. CytoSorb® seems to be promising and new approach for patients with liver failure.

<http://www.ncbi.nlm.nih.gov/pubmed/25233991>

1.3.4 Myoglobinemia

NEW; Severe rhabdomyolysis after exertional heat stroke treated with a hemoadsorber CytoSorb: lesson for the clinical nephrologist

Mikacic M, Begovic TI, Jerkovic I, Batinic MM, Kovacic V.

J Nephrol 2024; epub

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Summary

In this case report a 27 year old was admitted to intensive care with acute kidney injury as a result of exertional heat stroke. Along with pyrexia, hypertension and tachycardia, laboratory test results showed a creatine kinase (CK) of 722,559 U/L and a myoglobin concentration > 120,000 ng/mL. He also had deranged liver function tests (aspartate aminotransferase - AST 17,274 U/L, alanine aminotransferase - ALT 3,200 U/L), raised lactate dehydrogenase (LDH) 16,534 U/L and a C-reactive protein of 83.6 mg/L. Continuous veno-venous hemodiafiltration (CVVHDF) was started, and after 24 hrs there was only a moderate clinical improvement (CK 592,292 U/L and myoglobin 96,662 ng/mL), accompanied by a moderate decrease in other parameters (AST 14,582 U/L, ALT 2781 U/L, and LDH 12,543 U/L). So as treatment appeared insufficient, CytoSorb was also started on day 2 of hospitalization. Within 24 hrs the myoglobin levels had significantly decreased (around 15,000 ng/mL) with a further improvement in other parameters (AST 5600 U/L, ALT 1885 U/L, and LDH 4367 U/L). Treatment was continued for the next two days, changing the CytoSorb adsorber every 24 h. On day five myoglobin was 6866 ng/mL, with improvements clinically so that CVVHDF could be changed to intermittent hemodialysis. By day 10 there was full renal function recovery. The authors note that this is the first published case on the use of CytoSorb in a patient with rhabdomyolysis caused by heat stroke. Use of CytoSorb with conventional hemodialysis led to a rapid and sustained decrease in myoglobin and CK averting potential damage to the kidneys and other organs. There were no observed side effects during the treatment.

<https://www.ncbi.nlm.nih.gov/pubmed/38512381>

Successful use of extracorporeal blood purification in treating severe cocaine-induced rhabdomyolysis

Madeo M, Magnoni S, Pellegrini D, Laici C, Mancini E, Ricci D, Siniscalchi A.

Italian J Emergency Med 2022; 11(1):45-48

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Summary

This study describes the case of a 35-year-old man admitted into the Intensive Care Unit (ICU) intubated and ventilated for acute cocaine intoxication with altered mental status, hyperthermia, hypotension and tachycardia. A few hours after his admission continuous veno-venous hemofiltration (CVVH) with CytoSorb® was started to try to reduce his very high myoglobin levels (>39,480 ng/ml, upper limit for the laboratory range). By the second day there were clinical signs of rhabdomyolysis followed by acute liver injury which was severe enough to consider liver transplantation. However, after 4 days all laboratory parameters started to return to normal (myoglobin day 3 - 12,844 ng/mL and 3776 ng/mL on day 5). After two weeks the patient was well enough to be discharged to the medical ward. The authors conclude that in this case report, CytoSorb® was a useful therapeutic strategy for severe cocaine intoxication associated with severe organ failure, the first time this has been reported in the published literature.

[Link to Article](#)

Rapid reduction of substantially increased myoglobin and creatine kinase levels using a hemoadsorption device (CytoSorb®)—A case report

Moresco E, Rugg C, Ströhle M, Thoma M.

Clinical Case Reports 2022; 10(1); e05272

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Summary

In this case report a previously healthy 24 yr old had surgery in a peripheral hospital after dislocating his knee whilst playing sports. During the five hour surgery he had a tourniquet applied to his thigh for 2 hours. The next day he developed brown colored urine and was found to have already impaired kidney function (estimated glomerular filtration rate [eGFR] 50 ml/min/1.73m, serum creatinine [SC] 1.68 mg/dl, creatinine kinase [CK] 89,968 U/l, myoglobin >500 µg/l) so a diagnosis of rhabdomyolysis was made. The patient was transferred to a central hospital for fasciotomy and hematoma evacuation and admitted to the intensive care care (ICU) post operatively. On ICU admission myoglobin was 15,993 µg/l and CK 79,182 U/l. Continuous veno-venous hemofiltration (CVVHF) with an AN69 ST membrane was then started purely so that the patient could be treated with a CytoSorb® adsorber. Within 24 hrs of treatment CK levels had reduced by more than 50% (34,630 U/l) and myoglobin by more than 80% (3730 µg/l). Prior to hospital discharge on day 15 he had a fully recovered renal function. In summary, the immediate use of CRRT with the addition of CytoSorb® led to the highly efficient reduction in CK and myoglobin concentrations from the blood. The authors speculate that in the future this might justify implementation of CRRT as well as a hemoadsorber such as CytoSorb®, as soon as excessive myoglobin peak levels are reached and the cause for this is known. The early use of CRRT with the addition of the adsorber could help to prevent acute kidney injury (AKI) instead of just treating the AKI typically caused by this clinical scenario afterwards.

<https://www.ncbi.nlm.nih.gov/pubmed/35079387>

Case Report: Prevention of Rhabdomyolysis-Associated Acute Kidney Injury by Extracorporeal Blood Purification With Cytosorb®)

Rauch S, Borgato A, Gruber E, Leggieri C, Bock M, Seraglio PE.

Frontiers in Pediatrics 2022; 9:801807

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Summary

In this case report a 12-year-old boy was hit by a motorcycle whilst riding his bicycle. He received an open wound to his right groin causing massive bleeding leading to hemorrhagic shock. The bleeding was compressed manually and after transfer to hospital, he was taken to the operating room for vascular surgery (repair of the right common vein and artery). A medial and lateral fasciotomy was performed in the lower leg to prevent compartment syndrome. Post-operatively the patient was admitted to intensive care, where over time he started to develop a massive rhabdomyolysis (creatinine kinase [CK] >42,670 U/l and myoglobin >12,000 µg/l, both upper limits of laboratory detection). Along with fluid resuscitation and despite still normal values of serum creatinine and urea as well as preserved diuresis, the authors decided to initiate continuous veno-venous hemodiafiltration and to add a CytoSorb® cartridge to the dialysis circuit to eliminate myoglobin and prevent acute kidney injury (AKI). After 12 hours the CK and myoglobin has substantially decreased, however, over the next 12 hours both parameters started to rise again suggesting saturation of the cartridge. Treatment was then interrupted for 16 hrs, but as both parameters continued to climb, treatment was recommenced with

a new adsorber for a further 24 hrs. CK and myoglobin again markedly decreased. The patient was able to be discharged from intensive care after 10 days. The authors conclude that the early use of extracorporeal myoglobin removal with CytoSorb® after severe rhabdomyolysis might be a useful option and should be further investigated as a tool to prevent the development of AKI.

<https://www.ncbi.nlm.nih.gov/pubmed/35141180>

Successful Reduction of Creatine Kinase and Myoglobin Levels in Severe Rhabdomyolysis Using Extracorporeal Blood Purification (CytoSorb®)

Dilken O, Ince C, van der Hoven B, Thijsse S, Ormskerk P, de Geus HRH.

Blood Purif 2020; 49(6):743-747

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Summary

This case describes a 56-year-old man with severe traumatic rhabdomyolysis of the lower extremities and abdominal wall due to a crush injury (initial myoglobin and creatinine kinase – CK levels 79,931mg/l and 15,032 U/L respectively). As he was unresponsive to high dose continuous renal replacement therapy (CRRT) with a high cut off EMiC-2 dialysis filter, a CytoSorb® adsorber was added into the circuit on the 2nd ICU day. Within 4 hours myoglobin and CK levels had reduced from 110,000 to 90,000 mg/l and 115,000 – 65,000 U/L respectively. The adsorber was changed after 12 hours due to evidence of saturation. This reduced myoglobin and creatine kinase levels further despite ongoing tissue ischemia. Treatment with CytoSorb® improved the microcirculatory perfusion despite abnormal macro-hemodynamic parameters, however, this was not enough, resulting in the eventual demise of the patient due to severity of the injury. This report indicates that myoglobin was efficiently removed with CytoSorb® following exchange with the conventional high cut-off filter in continuous venovenous hemodialysis in severe traumatic rhabdomyolysis. The authors emphasise the need to install CytoSorb® early for removal of inflammatory cytokines and myoglobin.

<https://www.ncbi.nlm.nih.gov/pubmed/32114569>

Successful treatment of a severe case of rhabdomyolysis following heart transplantation by hemoadsorption

Immohr MB, Lichtenberg A, Boeken U, Akhyari P.

J Card Surg 2020; 35(4):940-941

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Summary

This is a case reporting on a 61 yr old male patient, who post orthotopic heart transplantation developed cardiogenic shock and cardiac arrhythmias requiring support with veno-arterial extracorporeal membrane oxygenation (va-ECMO). The patient stabilized, however, 2 days later an enormous increase in plasma creatine kinase (CK) level was seen (>100,000U/L). His myoglobin concentration also increased to 380,000 mg/L and rhabdomyolysis most probably caused by the combination of statin and immunosuppressive therapies was diagnosed. Conventional therapies failed and the patient further developed acute renal failure requiring continuous veno-venous hemodialysis. A CytoSorb® adsorber was then installed into the va-ECMO circuit and continued for the next 4 days. Plasma concentrations of immunosuppressive drugs and antibiotics were closely monitored (the patient received treatment with tacrolimus, mycophenolate mofetil, prednisolone, amphotericin, levofloxacin and cotrimoxazole). As soon as the CytoSorb® adsorber was installed the patient stabilized. His CK and myoglobin rapidly and continuously decreased (at end of treatment CK 45,866U/L, myoglobin 53,700 µg/L). Plasma drug concentrations remained stable throughout the treatment period with no problems concerning pharmacokinetics seen. At six-month follow up there were no further postoperative complications, and he had full kidney function despite this episode of severe rhabdomyolysis. The authors state that CytoSorb® was a safe and feasible technique (to purify the blood to preserve kidney function).

<https://www.ncbi.nlm.nih.gov/pubmed/32101624>

Cytosorb for Management of Acute Kidney Injury due to Rhabdomyolysis in a Child

Padiyar S, Deokar A, Birajdar S, Walawalkar A, Doshi H.

Indian Pediatr 2019; 56(11):974-976

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Summary

This is a case report of a previously healthy 6-year-old girl that presented with rhabdomyolysis following a febrile illness. Diagnostics revealed positive findings for Influenza B and enterovirus with very high serum creatine kinase (CK) and myoglobin levels (around 3,000 ng/ml). She developed myoglobinuria with oliguria leading to acute kidney injury so was

put on intermittent and then continuous renal replacement therapy (CRRT) because of hemodynamic instability. A CytoSorb® adsorber was added to remove the myoglobin and CK. After three days of CytoSorb® her myoglobin had dropped to under 600 ng/ml and after two more days of CRRT she was able to be switched back to intermittent dialysis which she received until day 33. The patient was eventually discharged home. This is the first published case of the use of CytoSorb® for removal of myoglobin in a pediatric patient.

<https://www.ncbi.nlm.nih.gov/pubmed/31729332>

Hemoadsorption in Infection-Associated Rhabdomyolysis

Suefke S, Sayk F, Nitschke M.

Ther Apher Dial 2016; 20(5):531-533

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Summary

This case study reports on a 55-year-old patient with history of arterial hypertension who was admitted with complaints of dyspnea and symptoms of respiratory infection. He went on to develop fulminant pneumogenic sepsis and acute respiratory distress syndrome (ARDS) with considerable requirements for fluids and catecholamines for hemodynamic stabilization. Plasma concentrations of myoglobin and creatine kinase increased drastically on top of his inflammatory response, indicative of severe infection-associated rhabdomyolysis. For treatment of his acute kidney injury grade III (crush kidney) and to lower inflammatory mediator and myoglobin levels CytoSorb® was installed in combination with renal replacement therapy (RRT). During the course of the treatment, plasma concentrations of IL-6, procalcitonin, myoglobin and creatine kinase decreased significantly. Levels of leucocytes, thrombocytes, alanine aminotransferase, and aspartate aminotransferase normalized over the 4 consecutive treatments. The clinical situation improved considerably including improvement of the patient's respiratory situation and liver function and he was discharged on day 13 with ongoing renal failure and need for RRT. In this patient, the application of CytoSorb® resulted in a significant reduction of cytokines (i.e. IL-6) but also had an important additive effect on myoglobin removal.

<http://www.ncbi.nlm.nih.gov/pubmed/26991687>

Cytosorb™ in a patient with legionella-pneumonia associated rhabdomyolysis

Wiegele M, Krenn CG.

ASAIO J 2015; 61(3):e14-e16

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Summary

This case study reports on a 44-year-old man presenting with ongoing fever and general malaise for more than 5 days. Respiratory insufficiency led to hospitalization and admission to ICU for intubation and ventilatory support. Chest x-ray and computed tomography confirmed the clinical diagnosis of acute respiratory distress syndrome and he was found to have Legionella pneumophila. Despite administration of antibiotics, his liver enzymes and parameters of renal function deteriorated over the following days, indicating a trend toward multiple organ failure. Creatine kinase and myoglobin levels increased in combination with reduced urine excretion. Therefore CytoSorb® was run in stand-alone mode on day 6 after admission. Within 8 hours, myoglobin levels decreased from 18,390 to 10,020 ng/ml and with a second cycle it again declined from 13,400 to 8,359 ng/ml. The patient's condition improved subsequently. Renal function completely recovered and hemodialysis was not necessary at any time of hospitalization. No side effects of therapy were observed. This is the first time that a decrease in myoglobin levels following application of CytoSorb® have been demonstrated in vivo.

<http://www.ncbi.nlm.nih.gov/pubmed/25635933>

1.3.5 Other indications

Case Report: The management of hemorrhagic shock of different origins by target-controlled coagulation and extracorporeal organ support (continuous renal replacement therapy)

Pertich Á, Lovas A.

Frontiers in Anesthesiology 2024 2:1323180

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Summary

This short case series included two patients, one with poly-trauma-related severe bleeding and one with peripartum hemorrhage complicated by shock. Management steps included damage control surgery, maintenance of optimal

clotting preconditions, point-of-care and targeted supplementation of coagulation factors. Extensive tissue damage and surgical management of bleeding activates the proinflammatory process, leading to a dysregulated immune response. The originating systemic inflammation produces further damage, harmfully altering clot formation through the activation of immunothrombosis. Along with the above, continuous renal replacement therapy (CRRT) and hemoadsorption with CytoSorb was added to regulate the large-scale tissue injury-mediated immune over-response and restore homeostasis. In both cases, CytoSorb was applied for 24 hrs, using citrate anticoagulation. The authors note that by regaining balance over the shock state and controlling the dysregulated immune response - including the disproportionate coagulation, there was a significant reduction in vasopressor requirements and normalization in lactate levels over the 24 hrs of CytoSorb use. The authors also note that by introducing CytoSorb early in the patients treatment plan the adverse effects of hemorrhagic shock, including systemic inflammation, could be potentially mitigated.

[Link to Article](#)

The use of CytoSorb in acute oral mercuric chloride poisoning at a potentially lethal dose

Krakowiak A, Janasik B, Sadowski L, Szwabe K, Wisniewski T, Anna Rak M, Machala W.

Int J Artif Organs 2024; 47(1):67-72

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Summary

The study presents the case of acute mercuric chloride poisoning in a 21 yr old patient following a suicide attempt. She was admitted to the intensive care unit due to multiple organ damage. The performed laboratory tests confirmed high levels of mercury in the blood (1051 µg/L) which rose to a peak of 2354 µg/L around 65 hours post admission. Due to acute renal failure, continuous renal replacement therapy (first CVVHD then changed to CVVHDF) was initiated and CytoSorb was added on day 3 along with a specific antidote therapy (DMPS) which had been started after admission to the ICU. CytoSorb was used for 6 hours and serum mercury levels were taken pre, during and post treatment to monitor effects. The ongoing treatment resulted in a reduction in subjective complaints, a decrease in blood mercury levels to 580 µg/L, and an improvement in organ function. The authors conclude that despite the potentially fatal levels of the inorganic mercury compounds (mercuric chloride), continuous renal replacement therapy using CytoSorb as an extracorporeal blood purification method considerably shortened the toxin elimination time (by almost four times), which proves the significant impact that CytoSorb had on the decontamination process.

<https://www.ncbi.nlm.nih.gov/pubmed/38142295>

Effective Treatment of Acute Tricyclic Antidepressant Poisoning with Cardiogenic Shock and Severe Rhabdomyolysis Using ECMO and CytoSorb® Adsorber

Zitoun Z, Kugener L, Jonckheer J, Lanckmans K, Hantson P, Devriendt J, Honore PM.

Am J Case Rep 2023; 24:e939884

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Summary

This is a case of a 55-year-old woman admitted to the Intensive Care Unit (ICU) with acute imipramine (tricyclic antidepressant) self-poisoning. She arrived at the emergency department 7 hours after imipramine ingestion already with severe rhabdomyolysis (creatin phosphokinase levels around 52, 500 IU/L, normal <200 IU/L). She quickly developed cardiogenic shock with malign arrhythmias requiring veno-arterial extra corporeal membrane oxygenation (VA-ECMO). Continuous renal replacement therapy (CRRT) with CytoSorb® was started 19 hours after admission. Serial blood measurements of imipramine and its active metabolite desipramine were taken 6 hourly. Three CytoSorb® adsorbers were used for 24 hrs each. On average, post adsorber levels of imipramine were 45% lower than pre-adsorber levels. Cardiac function improved and ECMO was able to be explanted after 4 days. She had severe acute respiratory distress syndrome which resolved spontaneously. The patient regained full consciousness on the fifth day despite having been in a coma without sedation. She was discharged home several weeks later. This is the first published case on the efficacy of the CytoSorb® adsorber for removing imipramine from a patient's bloodstream.

<https://www.ncbi.nlm.nih.gov/pubmed/37542369>

Severe clozapine poisoning treated by extracorporeal blood purification therapy

Hartjes A, Machnik M, Kubasta C, Schratlbauer K.

Case Reps Neph & Dialysis 2023; 13(1):84-89

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Summary

This case involves a 56 yr old who was admitted with generalized seizures and arrhythmias following ingestion of 5000mg clozapine in a suicide attempt (toxic dose 500mg). The patient had to be intubated and ventilated. Despite standard treatment (including insertion of a gastric tube and administration of activated charcoal) the arrhythmias continued. To accelerate drug removal, continuous veno-venous hemodiafiltration (CVVHDF) including CytoSorb® was started around 6 hours after the suspected clozapine ingestion. Systemic clozapine levels before the start of CVVHDF and CytoSorb® were 4779 ng/ml, and serial measurements pre and post adsorber showed direct removal of clozapine and its metabolite by the adsorber and confirmed the rapid reduction in systemic levels. The patient remained hemodynamically stable throughout and no further arrhythmias were detected. Levels fell to around 2,000 ng/ml after two adsorbers were used for 12 hrs each. Eventually it was possible to extubate the patient on day 3 fully vigilant and with no residual neurological abnormalities. The authors conclude that the use of CytoSorb® hemoabsorption in this severe clozapine intoxication helped quickly and efficiently reduce clozapine levels to nontoxic serum levels while preserving organ function. They note that, although currently off label use, the use of CytoSorb® might therefore represent an alternative treatment modality to be considered for potentially lethal clozapine intoxications.

<https://pubmed.ncbi.nlm.nih.gov/37900923/>

Extracorporeal hemoabsorption therapy as a potential therapeutic option for rapid removal of Apixaban in high risk-surgical patients: a case report

Dalmastri V, Angelini A, Minerva V, Ballarini M, Grammatico F, Todeschini P, Pizzini AP, Silingardi M, La Manna G. *J Medical Case Reports* 2023; 17(1):283

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Summary

This case reports on an 82-year-old patient who was admitted with post-renal acute renal failure and nausea from severe bilateral hydronephrosis, and locally advanced prostate adenocarcinoma. The patient was also on apixaban for atrial fibrillation. Due to renal failure, continuous renal replacement therapy (CRRT) was initiated, and the patient scheduled for a bilateral nephrostomy. However, the next day an apixaban blood assay confirmed still elevated drug values (180 ng/mL) so that the operation was postponed. The following day, due to ongoing high levels of apixaban (139 ng/mL), CytoSorb® was installed into the running CRRT circuit to enable prompt surgical intervention, without waiting for physiological drug clearance of the apixaban. CytoSorb® was run for 2 hours 30 min and within this time the apixaban level decreased from 139 ng/ml to 72 ng/ml (reduction rate of 48.2%). The reduced apixaban level finally allowed for surgery to be performed, with the successful placement of bilateral nephrostomies without complications. The authors note that combined treatment with CRRT and CytoSorb® hemoabsorption therapy was associated with a rapid and effective reduction in apixaban plasma levels allowing for prompt and urgent surgery while simultaneously ensuring a low risk of bleeding as well as an uneventful post-operative period.

<https://www.ncbi.nlm.nih.gov/pubmed/37415195>

Comparison of two treatments for verapamil overdose

Eijsink JFH, Grol BJH, Naber HR, van Egmond PS.

Clin Toxicol (Phila) 2023; 61(4): 315-316

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Summary

This is a letter to the editor describing a case report where the same patient presented twice to the emergency department (ED) following multi-drug overdose including the drugs verapamil, quetiapine and lorazepam. During the first episode she was treated in the intensive care unit (ICU) with insulin, glucose and isoprenaline, epinephrine and fluids and was noted to have two episodes of asystole. After acute recovery she was discharged to the psychiatric unit and then home. The following day she again presented the ED with a multiple drug overdose (verapamil, omeprazole, topiramate, quetiapine, lorazepam and escitalopram). Electrocardiography again showed cardiac involvement. Treatment was the same as the previous overdose with the addition of intravenous (IV) lipid emulsion therapy followed by continuous veno-venous hemofiltration (CVVH) combined with CytoSorb® for 12 h. During treatment in the ICU the patient was alert and cooperative. There were no side effects and she was able to be discharged from the ICU to medical psychiatric unit within 48 hrs. The authors note that the addition of IV lipids and CVVH plus CytoSorb® appeared to produce faster drug clearance and faster resolution of verapamil toxicity when added to standard care (serial measurements of the verapamil concentrations at regular time points showed an apparent half-life of 9.7–22.7 h in the first overdose compared to only 4.1–10.3 h in the 2nd).

<https://www.ncbi.nlm.nih.gov/pubmed/37129224>

Successful use of extracorporeal life support and hemadsorption in the context of venlafaxine intoxication requiring cardiopulmonary resuscitation: a case report

Hoffmann M, Akbas S, Kindler R, Bettex D.

J Artif Organs 2023; epub

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In this case report, a 17 yr old took a life threatening amount (presumed 24 g) of the antidepressant, venlafaxine plus a range of other medications including opioids and betablockers. The patient had to be admitted to intensive care, intubated and ventilated due to recurrent seizures, hemodynamic deterioration and arrhythmias, eventually leading to cardiac arrest. She then required extracorporeal life support (ECLS) for cardiovascular collapse (cardiogenic shock). Along with gastric lavage and use of activated charcoal, CytoSorb® was initiated 6 h after admission and changed three times over 72 h, integrated into the ECLS circuit. Serial serum blood concentrations of venlafaxine were measured on admission (approx. 24 h after ingestion) and subsequently 6 h and 18 h thereafter, and on days 2 and 4. The initial blood concentration of venlafaxine was 53.52 µmol/l. After 12 h of hemadsorption, the blood level decreased to 9.6 µmol/l. On day 2, it was 7.17 µmol/l and decreased further to 3.74 µmol/l. Additional continuous renal replacement therapy was only implemented on day 5 due to anuria, so didn't contribute to the observed detoxification process. The combination of hemadsorption with CytoSorb® with ECLS, along with traditional decontamination strategies, resulted in the intact neurological survival of the highest venlafaxine intoxication reported in the literature to date. The authors state this case supports the evidence that that hemadsorption with CytoSorb® might help to reduce blood serum levels of venlafaxine, and that swift clearance of toxic blood levels may support cardiovascular recovery after life-threatening intoxications.

<https://www.ncbi.nlm.nih.gov/pubmed/37115336>

Hemadsorption: A New Therapeutic Option for Selected Cases of Bromazepam Intoxication

Mekeirele M, Verheyen S, Van Lancker R, Wuyts S, Balthazar T.

Case Reports in Nephrology and Dialysis 2022; 12(3):163-166

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Summary

Benzodiazepine ingestion can account for around 21% of all intoxications requiring admission to Intensive Care (IC). Management is normally with a supportive approach and with the use of flumazenil, an antidote for benzodiazepines, however, flumazenil does not influence elimination. In this case report, a 67 yr old patient with impaired liver function (CHILD-C cirrhosis) was admitted after intoxication with the benzodiazepine, bromazepam. The initial plasma concentration was very high (874 µg/L, upper limit of normal 170 µg/L). She became increasingly drowsy with respiratory insufficiency so a flumazenil infusion was started resulting in her becoming more alert, however, the infusion rate could not be decreased due to her repeatedly relapsing into stupor. Due to her liver failure (and consequent slow metabolism), it was calculated that the half-life of bromazepam would be 10 days rather than 10 hrs, requiring a stay of 23 days on the ICU, so CytoSorb® hemoadsorption was initiated using continuous venovenous hemofiltration (CVVHF). Pre and post CytoSorb® adsorber blood levels were taken. Results showed that elimination of bromazepam by CytoSorb® was quick and efficient (-31% after 1 h, -56% after 11 h). After the first 11 hrs there was a quick decline in adsorbing capacity suggesting saturation, however, by this time the patient was in the upper limit of normal for bromazepam, so no second hemoadsorber was needed and the flumazenil infusion could be quickly tapered off within 1 day. The authors conclude that hemoadsorption is a viable option to reduce length of ICU stay or need for intubation in slow metabolizers. They state that the cost of a prolonged stay in the intensive care unit is significantly higher than the cost of an adsorber.

<https://www.ncbi.nlm.nih.gov/pubmed/36518360>

Case report: Cytokine hemoadsorption in a case of hemophagocytic lymphohistiocytosis secondary to extranodal NK/T-cell lymphoma

Ruiz-Rodriguez JC, Chiscano-Camon L, Ruiz-Sanmartin A, Palmada C, Bajana I, Iacoboni G, Bonilla C, Garcia-Roche A, Paola Plata-Menchaca E, Maldonado C, Perez-Carrasco M, Martinez-Gallo M, Franco-Jarava C, Hernandez-Gonzalez M, Ferrer R.

Front Med (Lausanne) 2022; 9: 925751

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Summary

This case report includes a 50 yr old patient with hemophagocytic lymphohistiocytosis (HLH) due to NK-type non-Hodgkin lymphoma and Epstein-Barr virus reactivation with multiorgan dysfunction and distributive shock. Despite receiving the recommended treatment for HLH (including dexamethasone and etoposide), the patient rapidly deteriorated with distributive shock and multi-organ failure (renal, neurological, hemodynamic, respiratory and hepatic), requiring high doses of vasopressors, continuous veno-venous hemodiafiltration (CVVHDF), and invasive mechanical ventilation. Due to hypercytokinemia (i.e. interleukin – IL-6 233 pg/ml, IL-10 5643 pg/ml) and the refractory shock, CytoSorb® was added on the 2nd day of admission to intensive care, inserted into the CVVHDF circuit. After starting the procedure, there was rapid hemodynamic control with a significant reduction in norepinephrine levels (1.5 – 0.1 mcg/kg/min). Vasopressor support could be stopped within 37 hrs of the CytoSorb® start. The authors report that there were no adverse effects and that CytoSorb® was a safe procedure. In conclusion this case report highlights that cytokine hemoadsorption can be an effective and safe rescue therapy in patients with HLH and multiorgan dysfunction, complementary to standard protocol treatments. It was associated with a rapid decrease in IL-10 levels and a significant hemodynamic improvement. The authors suggest real-time monitoring of plasma cytokine concentrations as a tool to monitor the biological effect of cytokine hemoadsorption, optimizing the duration of this procedure.

<https://www.ncbi.nlm.nih.gov/pubmed/36045925>

Successful treatment of severe quetiapine intoxication with CytoSorb hemoadsorption

Reuchsel C, Gonnert FA.

J Clin Pharm Ther 2022; 47(9):1471-1474

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Summary

In this case report a 64 yr old woman who had attempted suicide by ingesting an unknown amount of the tricyclic antidepressant, quetiapine, was admitted to intensive care in a deeply somnolent state. CytoSorb® hemoadsorption was started on the second day of admission due to her not improving clinically, and potentially lethal levels of quetiapine being found in her blood and urine. Pre and post CytoSorb® adsorber blood samples confirmed direct removal and there was a clear and rapid decrease in plasma levels of the drug over the following few hours. The following day the patient could be extubated and was alert and cooperative. CytoSorb® was discontinued after 2 days, whereby the patient was discharged into the care of psychiatry. The authors describe CytoSorb® as an alternative novel therapeutic option for life threatening complications of quetiapine intoxication. In order to maintain optimal removal capacity it is recommended that the adsorber be changed after 8 – 12 hrs.

<https://pubmed.ncbi.nlm.nih.gov/35537706/>

Successful Treatment of Severe Lamotrigine Intoxication with CytoSorb Hemoadsorption

Reuchsel C, Gonnert FA.

Blood Purif 2022; 51(8):679-682

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Summary

In this case report a deeply comatose 60 yr old woman was treated in intensive care for severe lamotrigine intoxication for which there is no antidote. As other conventional therapeutic measures including lipid infusion failed to have any effect on the lamotrigine levels, a CytoSorb® adsorber was started on day 8, together with continuous veno-venous hemodialysis, and continued for 44 hours (3 adsorbers used). Within the first 24 hrs of CytoSorb® use the patient began to try to open her eyes to command. This was accompanied by a rapid and sustained decrease in lamotrigine plasma concentrations and concomitant further clinical improvement in regard to vigilance. The patient was able to be discharged two days after CytoSorb® cessation. The authors conclude that comparison of pre- and post-adsorber levels suggested the direct adsorption of the drug by the adsorber and state that its use could represent a viable treatment option for patients with severe lamotrigine intoxication.

<https://www.ncbi.nlm.nih.gov/pubmed/34736249>

Hemoadsorption Treatment with CytoSorb in Probable Hemophagocytic Lymphohistiocytosis: A Role as Adjunctive Therapy?

Ceruti S, Glotta A, Adamson H, Mauri R, Molnar Z.

Case Reports in Hematology 2021: 5539126

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Summary

In this case report a 76-year-old man with abdominal septic shock due to a perforated colon received an emergency laparotomy. The septic shock initially resolved following a hemicolectomy, however, several days later he became critically unwell and severe Hemophagocytic Lymphohistiocytosis (HLH) was strongly suspected (serum ferritin 14,299 ng/mL). As intravenous immunoglobulin therapy failed to show any benefit, continuous venovenous hemodiafiltration therapy plus CytoSorb® was started on day 7 for a total of 48 hours (2 x 24 hrs). From the start of hemoadsorption therapy, his clinical and biochemical parameters improved (including several inflammatory markers, norepinephrine levels and level of consciousness). However, once the therapy was discontinued the biological and clinical condition reverted, and unfortunately the patient died 4 days later.

<https://pubmed.ncbi.nlm.nih.gov/34462671/>

Novel Use of Extracorporeal Blood Purification for Treatment of Severe, Refractory Neurotoxicity After Chimeric Antigen Receptor T-Cell Therapy-A Case Report

Singbartl K, Rosenthal A, Leis J, Patel B, Sen A.

Crit Care Explor 2021; 3(7):e0472

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Summary

In this case reports on a 53-year-old patient with primary refractory high-grade B-cell lymphoma who developed severe, refractory neurotoxicity following chimeric antigen receptor (CAR) T-cell therapy. Six days after CAR T-cell therapy, the patient developed severe cytokine release syndrome (CRS), prompting administration of dexamethasone and tocilizumab. His C-reactive protein levels started to decrease with tocilizumab and dexamethasone treatments. However, his ferritin levels continued to rise, and his interleukin (IL)-6 levels were above the upper detection threshold. Thirty-six hours later, the patient showed improved cytokine release syndrome but developed severe immune effector cell-associated neurotoxicity syndrome (ICANS) with predominant encephalopathy (grade 3) despite ongoing treatment with dexamethasone/methylprednisolone, tocilizumab, and anakinra. Following emergency use authorization, extracorporeal blood purification with CytoSorb® was inserted into his renal replacement therapy circuit. As selective blockade of single mediators might not be sufficient to attenuate the overall response, the authors sought a rescue strategy that allowed for broad-spectrum, continuous cytokine elimination. Four-days later, including 6 CytoSorb® adsorbers for 12-24 hrs each, used in conjunction with standard CRRT, there was complete resolution of the immune effector cell-associated neurotoxicity syndrome with greater than 95% reduction in IL-6 levels without side effects. The patient was discharged home 10 days later with no signs of neurotoxicity or other secondary end-organ dysfunction. This case represents the first reported, successful application of extracorporeal blood purification with CytoSorb® to treat severe, refractory neurotoxicity following CAR T-cell therapy.

<https://www.ncbi.nlm.nih.gov/pubmed/34235458>

Novel diagnostic and therapeutic techniques reveal changed metabolic profiles in recurrent focal segmental glomerulosclerosis

Muller-Deile J, Sarau G, Kotb AM, Jaremenko C, Rolle-Kampczyk UE, Daniel C, Kalkhof S, Christiansen SH, Schiffer M.

Sci Rep 2020; 11(1):4577

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Summary

Idiopathic forms of the condition Focal Segmental Glomerulosclerosis (FSGS) are most likely caused by circulating permeability factors, which can lead to early recurrence of FSGS and kidney failure after kidney transplantation. In this case report a 24 yr old woman was given a kidney transplant from her mother after a three-year history of progressive renal failure resulting in end stage renal disease and regular hemodialysis. Initially the patient did well, but after a month her condition rapidly deteriorated. The patient received intravenous corticoid treatment and two doses of rituximab (1 g) within 2 weeks, but proteinuria did not improve. Interestingly, the classically published circulating factors were all in normal range in this patient, but due to the early recurrence of the primary disease, and the severity of the original disease it was decided to start CytoSorb® apheresis as a compassionate use approach for the potential removal of circulating factors that might cause FSGS. CytoSorb® was given daily for four days with good response so the frequency of CytoSorb® was reduced to once per week. However, her proteinuria rapidly relapsed (327 mg/g – 4235 mg/g) so CytoSorb® was given daily again until the patient went into clinical remission. After a period of stabilization, the patient's condition started to deteriorate once more so she was given CytoSorb® daily again. Over time treatment

was able to be tapered to once per week, with the patient currently receiving CytoSorb® 2nd weekly for, what is now two years post-transplant with excellent transplant function. Weaning from CytoSorb® apheresis, however, is still not possible and also attempts to increase the time between treatment cycles have failed so far. The authors performed additional cell-based ex-vivo models to detect morphological changes in podocytes caused by FSGS serum. Further novel innovative analysis revealed changed lipid metabolome profiles associated with idiopathic FSGS that might reflect a new subtype of the disease. This is the first case of acute and chronic use of CytoSorb® in a post renal translation patient for the successful ongoing management of their kidney disease.

<https://www.ncbi.nlm.nih.gov/pubmed/33633212>

Hemoadsorption to treat severe iatrogenic intoxication to Patent Blue: A Case Report

Taccone FS, Gardette M, Creteur J, Brasseur A, Lorent S, Grimaldi D.

Journal of Medical Case Reports 2021; 15:63

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Summary

This is a case report concerning a 27 yr old female admitted with ecstasy (MDMA) intoxication resulting in multi-organ failure (acute respiratory distress syndrome – ARDS; metabolic acidosis; capillary leakage syndrome; renal failure; and shock refractory to standard resuscitation). She was started on continuous renal replacement therapy (CRRT) and veno-venous (V-V) extracorporeal membrane oxygenation (ECMO) and it was decided to also prescribe Methylene blue to reverse the vasoplegia and high norepinephrine requirements. Instead of Methylene Blue, Patent Blue V was erroneously administered, resulting in a severe clinical picture of methemoglobinemia and tissue hypoxia. CytoSorb® hemoadsorption was initiated into the CRRT circuit resulting in a rapid and significant reduction in plasma methemoglobin, accompanied by an improvement in hemodynamics and normalization in plasma lactate levels. Two adsorbers were used (15 hours and 20 hours). After a prolonged recovery period the patient was eventually discharged home on day 75. According to the authors there is a potential role for CytoSorb® in wider drug intoxications, which, however, needs to be verified in larger series.

<https://www.ncbi.nlm.nih.gov/pubmed/33557948>

Cytokine adsorption therapy in lymphoma-associated hemophagocytic lymphohistiocytosis and allogeneic stem cell transplantation

Rademacher J-G, Wulf G, Koziolok, MJ, Zeisberg M, Wallbach M.

J Artif Organs 2021; 24(3):402-406

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Summary

This is a report of a 57 yr old female patient with aggressive lymphoma secondary to chronic lymphocytic leukemia with rapidly progressive Hemophagocytic lymphohistiocytosis (HLH) upon conditioning chemotherapy prior to allogeneic stem cell transplantation (ASCT). Continuous hemodiafiltration (CHDF) was initiated for the treatment of shock with acute renal failure, lactacidosis and need for high-dose catecholamine therapy. A CytoSorb® adsorber was added to reduce cytokine levels for a total of 7 x 24 hr sessions. This was followed by a scheduled allogeneic stem cell transplantation on day 3 of CHDF and CytoSorb®. A marked decrease in interleukin-6 plasma levels was observed (peak 622 pg/ml to 54.8 pg/ml) which was associated with a reduced need for vasopressor therapy and organ function stabilization. Hematopoietic engraftment was present at day 14 post-ASCT, leading to disease-free discharge at day 100 post-transplantation. The authors conclude that cytokine adsorption may serve as a safe adjunct to HLH/sepsis treatment during allogeneic stem cell transplantation. In summary, cytokine adsorption may have contributed to the mitigation of lymphoma-associated HLH under conditioning therapy, allowing successful ASCT.

<https://pubmed.ncbi.nlm.nih.gov/33459910/>

Case Report: Successful Use of Extracorporeal Therapies After ECMO Resuscitation in a Pediatric Kidney Transplant Recipient

Rybalko AS, Pytal AV, Kaabak M, Rappoport N, Bidzhiev A, Lastovka V.

Frontiers in Pediatrics 2020; 8:593123

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Summary

In this case report a 30-month old, 6.4 kg child, resuscitated with extracorporeal membrane oxygenation (ECMO), after a cardiac arrest during kidney transplantation surgery was additionally treated with a number of

extracorporeal blood purification methods (plasma exchange - PE, CytoSorb®, and lipopolysaccharide – LPS/endotoxin - adsorption), in the setting of immunosuppression therapy. Following three PE sessions, and, as the therapeutic effect was not as hoped (slight decrease in liver enzymes, and rise in inflammatory parameters), CytoSorb® was started for a total of 21 hours. Use of CytoSorb® resulted in a decrease in inflammatory parameters but, due to an occult and untreated infection, the inotropic requirements still increased. Once the infection was treated properly hemodynamics quickly stabilized and the patient gradually recovered and was able to be discharged from intensive care and then the hospital 116 days after his initial admission. This case report shows the successful use of multimodal extracorporeal therapies with a good patient outcome. As the authors note, the lack of response to CytoSorb® therapy from a hemodynamic perspective could be seen as an indication for the need for ongoing investigation for an (as yet) unidentified infection and is not necessarily failure of treatment.

<https://pubmed.ncbi.nlm.nih.gov/33384974/>

Successful treatment of a severe digitoxin intoxication with CytoSorb® hemoadsorption

Breuer TGK, Quast DR, Wiciok S, Labedi A, Ellrichmann G.

Blood Purification 2021; 50(1):137-140

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Summary

In this case report an 81 year old female was admitted to intensive care with severe digitoxin intoxication, acute renal failure and a urinary tract infection (UTI). Continuous renal replacement therapy (CRRT) was started combined with a CytoSorb® hemoadsorption. The patient stabilized hemodynamically within the first 4 hours of treatment and all catecholamines could be stopped within 24 hrs. Pre- and post CytoSorb® adsorber drug level measurements showed a rapid elimination of digitoxin. Antibiotic treatment with piperacillin/tazobactam was initiated and the UTI successfully treated without dose adaptations. After three days of CytoSorb® treatment, digitoxin plasma levels were stable and almost normalized with no clinical signs of intoxication present. Five days after presentation, the patient was transferred from ICU in a stable condition. The authors describe CytoSorb® hemoadsorption as maybe a more cost efficient and easily available option than treatment with the Fab fragment, which is the currently recommended therapy for digitalis intoxications. Therefore, the use of CytoSorb® might represent an alternative treatment for life-threatening complications of digitoxin intoxications.

<https://pubmed.ncbi.nlm.nih.gov/32937619/>

Use of the CytoSorb adsorption device in MDMA intoxication: a first-in-man application and in vitro study

Lang CN, Sommer M, Neukamm M, Staudacher DL, Supady A, Bode C, Duerschmied D, Lother A.

Intensive Care Med Exp 2020; 8(1):21

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Summary

MDMA (3,4-Methylenedioxymethamphetamine, "ecstasy") abuse and overdose has been known to cause severe and eventually lethal multi-organ failure in some cases. To date, there is no treatment for MDMA intoxication or removal. This case presents the first-in-man experience and in-vitro data that supports the potential role of CytoSorb® in severe MDMA overdose. A 21 yr old male presented with severe MDMA intoxication and multi-organ failure, including neurological impairment, hyperpyrexia, rhabdomyolysis, oliguric renal failure, liver failure, and coagulopathy with disseminated gastrointestinal and intramuscular bleeding. Use of CytoSorb® integrated into the hemodialysis circuit was associated with a decline in MDMA concentrations in serum from 540 to 140 ng/ml within the first 24 h, a decrease of interleukin 6 (48,129 to 4991 pg/ml) and myoglobin levels (75,420 to 18,400 ng/ml), and subsequent clinical improvement. Effective elimination of MDMA by CytoSorb® was then confirmed in vitro, where the device lowered MDMA concentrations measured distal of the adsorber, to non-detectable levels indicating full removal. The authors conclude that early integration of CytoSorb® use may enhance the management of severe MDMA intoxication, although it is not proven whether clinical improvement in this case was directly related to elimination of MDMA or the beneficial effects on rhabdomyolysis, hyperinflammation, or liver failure by the CytoSorb® adsorber.

<https://www.ncbi.nlm.nih.gov/pubmed/32542550>

Paediatric patient with dengue fever and associated multi-organ dysfunction syndrome (MODS) receiving hemoadsorption using Cytosorb®; A case report on clinical experience

Kumar S, Damera S.

IJMDAT 2020; 3:e233

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Summary

In this case report a 10 year old patient with dengue haemorrhagic fever and systemic inflammatory response syndrome was admitted to hospital. He also had acute fulminant hepatic failure, with encephalopathy and oliguria. Despite liver protective measures (N-Acetyl Cystine infusion), his liver function and other organs became increasingly worse so CytoSorb® was initiated on day 3 of admission. The adsorber was inserted in a post dialyser position in hemodiafiltration mode with a blood flow of 40 ml/min without anticoagulation for a total of 18 hours. After this time his liver function including bilirubin levels improved (7.2 – 4.8 mg/dL). Over five days his platelet count increased from 17,000 to 108,000 (per µL). His condition continued to improve, and he was eventually discharged in a stable condition. CytoSorb® along with standard care is described as a safe and advantageous extracorporeal therapy option for paediatric dengue patients with multiple organ dysfunction.

[Link to Article](#)

Extracorporeal cytokine adsorption for treating severe refractory cytokine release syndrome (CRS)

Wallet F, Bachy E, Vassal O, Friggeri A, Bohe J, Garnier L, Salles G, Allaouchiche B.

Bone Marrow Transplant 2020; 55(10):2052-2055

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Summary

In this case report a 79 year old otherwise well patient from the hematology ward with aggressive large B-cell lymphoma refractory to several lines of therapy. He was treated with a T-cell-engaging bispecific antibody linking CD3+ T cells to CD20+ malignant B cells. After several hours he developed a reaction to the treatment (Cytokine Release Syndrome - CRS, initially grade 2 then grade 4), and had to be admitted to intensive care for management. Despite receiving tocilizumab, steroids and aggressive fluid management during the next 24 hrs his condition continued to deteriorate, his cytokine levels remained unchanged and he required rapidly increasing doses of norepinephrine (up to 1.5 µg/kg/min), intubation and mechanical ventilation and continuous venovenous hemodialysis (CVVHD). After two days on ICU, CytoSorb® therapy was added to the dialysis circuit. Within 6 hours of commencement the noradrenaline could be reduced and stopped after the second 24 hr treatment. No more fluid expansion was needed after the initiation of CytoSorb® epuration. Interleukin (IL)-6 was reduced by 75% two hours after CytoSorb® was initiated (11813 to 2941 pg/mL), and IL-10 by 63% (170 to 63 pg/mL). After 24 hours, IL-6 had reduced further to 841 pg/mL and IL-10 to 15 pg/mL. The patient received two 24 hour treatments with CytoSorb®, and after another 48 hours his condition had improved enough for him to be extubated. Unfortunately, a few days later the patient went on to develop an invasive fungal infection with septic shock and multi-organ failure, and treatment was withdrawn in accordance with the families wishes. After CytoSorb® treatment, his cytokine levels did not massively rebound indicating that the CRS was under control. During his CytoSorb® treatment some of the levels of antimicrobials used were measured. Piperacillin trough concentrations ranged from 70 to 123 (mean ± standard deviation [SD] 89.36 mg/L ± 20.24), and caspofungin trough concentrations ranged from 0.54 to 0.93 (0.74 mg/L ± 0.19), all within the expected range indicating there was no need to adjust levels because of the CytoSorb® adsorber. There were no serious adverse effects associated with CytoSorb® use.

<https://www.ncbi.nlm.nih.gov/pubmed/32277144>

Extracorporeal cytokine removal in severe CAR-T cell associated cytokine release syndrome

Stahl K, Schmidt BMW, Hoepfer MM, Skripuletz T, Mohn N, Beutel G, Eder M, Welte T, Ganser A, Falk CS, Koenecke C, David S.

J Crit Care 2020; 57:124-129

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Summary

In this case report a 65 yr old male with relapsed diffuse large B-cell lymphoma was admitted to ICU after he was treated with CD-19 Chimeric antigen receptor - T (CAR-T) cells and then developed grade 4 cytokine release syndrome (CRS) with refractory shock and severe capillary leakage. He was treated with IL-6 blockade (tocilizumab), methylprednisolone and additionally CytoSorb®. During the next 24 hrs, the patient became more hemodynamically unstable, so the CytoSorb® was then changed 8 hrly. Within hours the shock completely reversed, vasopressor dose could be decreased to 10% of the peak dose, and inotropic support stopped completely. Plasma was obtained before and 8 hrly following the start of CytoSorb® treatment. While multiple soluble inflammatory factors were elevated and most of them decreased by more than 50% following

CytoSorb®, markers of endothelial injury increased steadily (e.g. Angpt-2/Angpt-1) leading to profound endothelial activation and leakage in ex vivo assays. This is the first reported use of cytokine adsorption for CRS showing efficacy in absorption of various cytokines but not endothelial growth factors. Findings suggest the possibility that removal of excessive circulating cytokines rather than pharmacological blockage of a single key cytokine alone might be a more effective treatment strategy for CRS. The authors are currently recruiting to a randomized controlled trial to evaluate additional CytoSorb® treatment in CRS.

<https://www.ncbi.nlm.nih.gov/pubmed/32113143>

Multimodal Therapeutic Approach of Cytokine Release Syndrome Developing in a Child Given Chimeric Antigen Receptor-Modified T Cell Infusion

Bottari G, Merli P, Guzzo I, Stoppa F, Ruggeri A, Di Nardo M, Del Bufalo F, Galaverna F, Corrado C, Locatelli F. *Critical Care Explorations* 2020; 2(1):e0071

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Summary

In this case report a 14-year-old boy with refractory B cell precursor acute lymphoblastic leukemia who was treated with chimeric antigen receptor (CAR) cells then developed severe (grade 4) cytokine release syndrome 7 days after the drug infusion, with progressive respiratory failure. He was admitted to the pediatric intensive care unit (PICU) with acute respiratory distress syndrome (ARDS) requiring mechanical ventilation, hemodynamic instability requiring vasopressors, and also secondary hemophagocytic lymphohistiocytosis (HLH) with extremely high ferritin levels. The patient was treated with five CytoSorb® adsorbers (first two changed 12 hrly, then 24 hrly) in combination with continuous renal replacement therapy (CRRT). Tocilizumab was given 6 hours before admission to PICU and on the 3rd and 4th days after start of CytoSorb®. This treatment resulted in a decrease of the inflammatory biomarkers over the first 96 hours (e.g. ferritin from 146,095 to 6,934 ng/mL and interleukin-6 from 4,048 – 247 pg/mL,) which was associated with progressive improvement in his ARDS (Pao2/Fio2 ratio). The patient was able to be discharged from PICU after 19 days. This case suggests that CytoSorb® treatment with CRRT and tocilizumab is safe and potentially effective in pediatric patients with severe cytokine release syndrome.

<https://www.ncbi.nlm.nih.gov/pubmed/32166291>

A case report to highlight the impact of extracorporeal cytokine elimination therapy in viper snakebite induced septic shock with acute kidney injury

Parikh K, Patel H, Kothari M, Maheshwari L, Shetty V, Khadke SS.

IJMDAT 2020; 3:e222

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Summary

In this case a 40-year-old male patient developed hypotensive and circulatory shock post viper snakebite. He went on to develop septic shock and multi organ failure, with acute respiratory distress syndrome followed by acute kidney injury despite full standard care. Due to high inflammatory markers indicative of a cytokine storm, CytoSorb® was initiated along with hemodialysis for 8 hours. Post CytoSorb®, noradrenaline dose could be reduced and eventually terminated, mean arterial pressure improved, and ventilatory support could be weaned. Circulatory shock was resolved, alongside normalization of hemoglobin, platelet and leukocyte counts. Procalcitonin dropped from 3 pre to 0.6 ng/ml post adsorber use. Sequential Organ Failure Assessment (SOFA) score reduced significantly from 12 pre-adsorber to 1 so that twelve hours after CytoSorb® was stopped he was discharged to the normal ward, and from the hospital 3 days later completely recovered.

[Link to Article](#)

Cardiogenic shock in a hemodialyzed patient on flecainide: treatment with intravenous fat emulsion, extracorporeal cardiac life support and CytoSorb hemoadsorption

De Schryver N, Hantson N, Haufroid V, Dechamps M.

Case Reports in Cardiology 2019; 1905871

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Summary

A 67-year-old woman on chronic hemodialysis for end stage renal disease who had received a therapeutic dose of the anti-arrhythmia drug flecainide for three weeks was admitted to the Emergency Department for malaise, dizziness and ventricular tachycardia. Her hemodynamic condition remained stable so toxicity from the flecainide was not suspected until she developed cardiogenic shock requiring vasopressors 8 hours later. The

patient then received sodium bicarbonate and dobutamine but two hours later went into cardiac arrest. She was given intravenous fat emulsion (IFE) which was associated with a return of spontaneous circulation, but as there was a relapse in the cardiovascular shock at the end of the IFE infusion, she was placed on extracorporeal cardiac life support (ECLS), and continuous hemofiltration with hemoadsorption using CytoSorb®. Serial determinations of serum flecainide concentrations (initially > 9000 ng/ml, normal range 200 – 1000 ng/ml), were obtained pre and post the CytoSorb® so that the clearance rate of flecainide could be calculated. Within 4 hours the flecainide levels had reduced to around 2000 ng/ml. The authors calculated that a mean plasma clearance of 40.3 ml/min was observed using CytoSorb®. Although the impact of CytoSorb® on the clinical course has to be understood in the context of the other therapeutic interventions including ECLS, this patient was eventually discharged home with no apparent side effects. This is the first case reporting the removal of flecainide with the CytoSorb® adsorber.

<https://www.ncbi.nlm.nih.gov/pubmed/31428479>

Cytokine adsorption is a promising tool in the therapy of hemophagocytic lymphohistiocytosis

Frimmel S, Hinz M, Schipper J, Bogdanow S, Mitzner S, Koball S.

Int J Artif Organs 2019; 42(11):658-664

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Summary

This is a case series of two patients with hemophagocytic lymphohistiocytosis (HLH), a life-threatening clinical syndrome caused by severe hyper-cytokemia brought on by a highly stimulated but ineffective immune response. In the first patient with the herpes virus, despite being put on the Molecular Adsorption Recirculation system (MARS) as a bridge to liver transplant, her condition continued to deteriorate (increasing hemodynamic instability) so she was also placed on single-pass albumin dialysis (SPAD®) and then continuous venovenous hemodialysis (CVVHD) into which the CytoSorb® was inserted. This resulted in a dramatic decrease in interleukin-6 (IL-6) plasma levels and norepinephrine requirements, and successful liver transplant 20 hours later. The second patient had two episodes of HLH two months apart, most likely triggered by refractory septic shock and then an acute Epstein–Barr virus infection. A CytoSorb® adsorber was inserted into his CVVHD circuit, on both occasions for 48 hrs total (2 adsorbers for 24 hours each). With both CytoSorb® treatment episodes, his clinical condition stabilized with a marked decrease in his IL-6 and a stabilization or decrease in his norepinephrine requirements. Importantly, the treatment in both patients was safe and well-tolerated, without any adverse events.

<https://www.ncbi.nlm.nih.gov/pubmed/31238776>

Severe quetiapine voluntary overdose successfully treated with a new hemoperfusion sorbent

Giuntoli L, Dalmastri V, Cilloni N, Orsi C, Stalteri L, Demelas V, Giuliani G, Gordini G, De Ponti F, La Manna G.

Int J Artif Organs 2019; 42(9):516-520

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Summary

Overdose on quetiapine (a psychiatric medication), although rare, is linked to heart arrhythmias, somnolence, coma, hyperglycemia, and eventually hepatotoxicity and myocarditis. Use of extracorporeal techniques for quetiapine removal has been only rarely reported in the literature. In this case report, a 27-year-old healthy woman, admitted to Intensive Care Unit after deliberate quetiapine overdose is described. After 24 hrs of standard treatment including charcoal, diuretics and laxatives, her quetiapine levels were still very high (1850 µg/L, normal range of 70–170 µg/L) so she was treated with CytoSorb® hemoperfusion in combination with continuous renal replacement therapy (CRRT), for 48 hrs (2 adsorbers used for 24 hrs each) in order to accelerate quetiapine elimination. After only 12 hrs the level of quetiapine had already reduced by 65% to 648 µg/L. After 96 hrs she was able to be extubated, and eventually discharged to a step down unit after 7 days. This is the first published experience of the application of hemoadsorption therapy (CytoSorb®), after a large overdose of quetiapine. Use of CytoSorb® resulted in the fast and efficient elimination of quetiapine from the blood and stabilization of a critical situation.

<https://www.ncbi.nlm.nih.gov/pubmed/31006356>

Snake bite induced sepsis with multi organ failure successfully treated with Extracorporeal Cytokine Adsorption Device (ECAD) therapy along with standard of care - a case series

Sathe P, Sakhavalkar P, Borse R, Parathody A, Huparikar A, Rayte N.

IJMDAT 2018; 1(2):e158

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Summary

This publication reports on two snake bite patients and describes the use of CytoSorb® because of local pain and swelling, disseminated intravascular coagulation (DIC) and Acute Kidney Injury (AKI) caused by the venom from the snake bite. In both patients two CytoSorb®s were used and associated with a decrease in IL6 and good overall clinical stabilization. Both patients were able to be discharged from hospital and the authors describe the use of CytoSorb® along with standard of care to be a promising and safe treatment modality in order to stabilize and decrease envenomation induced complications, potentially leading to shorter ICU stays and better survival.

[Link to Article](#)

Hemoadsorption in cardiac shock with biventricular failure and giant cell myocarditis: A case report

Dogan G, Hanke J, Puntigam J, Haverich A, Schmitto J.

Int J Artif Organs 2018; 41(8):474-479

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Summary

In this case a 57-year-old patient with the autoimmune disorder giant cell myocarditis, developed fulminant right heart failure, respiratory insufficiency, hemodynamic instability and oliguric-anuric renal failure. Extracorporeal life support (ECLS) with an Impella was applied for circulatory support along with continuous veno-venous hemodialysis (CVVHD). Since adequate hemodynamic stabilization could not be achieved despite high catecholamine support and due to increasing inflammatory mediators and bilirubin levels, the decision was made to additionally integrate CytoSorb® into the CVVHD system. The following day the patient had a left ventricular assist device (LVAD) inserted, and veno-pulmonary-arterial (VPA) Extra Corporeal Membrane Oxygenation (ECMO) was started. CytoSorb® was then inserted into the VPA ECMO circuit. In total 9 CytoSorb® treatments were performed over 23 days with a 7-day pause (due to a secondary septic surge). With the last CytoSorb® treatment the right ventricular bypass could be explanted and the patient was discharged to a high care program. The combined ECLS treatment including CytoSorb® resulted in a clear and steady improvement in hemodynamics and the inflammatory condition with marked reductions in all measured parameters throughout the treatment period. Metabolic acidosis resolved and liver function also improved. The authors describe the combination of all techniques applied as practical, technically feasible, and highly beneficial for the patient.

<https://www.ncbi.nlm.nih.gov/pubmed/29779449>

A rare case of septic shock due to Neisseria meningitidis serogroup B infection despite prior vaccination in a young adult with paroxysmal nocturnal haemoglobinuria receiving eculizumab

Reher D, Fuhrmann V, Kluge S, Nierhaus A.

Vaccination 2018; 36(19):2507-2509

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Summary

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare acquired haematopoietic stem cell disease which causes defects in complement inhibiting proteins. Following approval of eculizumab, a humanized antibody for PNH treatment, several cases of invasive meningococcal disease (IMD) have been reported in eculizumab-treated patients. This is a report of a rare case of septic shock due to infection with Neisseria meningitidis serogroup B despite prior vaccination in a young PNH patient treated with eculizumab where CytoSorb® was used for treatment of excessive hypercytokinemia along with IgM-enriched IgGAM for three days.

<https://www.ncbi.nlm.nih.gov/pubmed/29631884>

Successfully treated necrotizing fasciitis using ECLS combined with hemoadsorption device and continuous renal replacement therapy

Eid M, Fouquet O, Pierrot M, Kouatchet A, Mercat A, Baufreton C.

Int J Artif Organs 2018; 41(3):178-182

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Summary

In this case a 41 yr old patient presented with necrotizing fasciitis and multi organ failure. Extracorporeal life support (ECLS – veno-arterial) was implemented to compensate for his heart failure (ejection fraction 15%) requiring high doses of catecholamines. Due to acute renal failure continuous renal replacement therapy

(CRRT) was also started. Despite these treatments the patient continued to deteriorate, so a CytoSorb® adsorber was added to the CRRT circuit, in parallel to the ECLS. Two consecutive treatments were run for 24 hrs each. After the two sessions catecholamines could be decreased dramatically, and hemodynamic stabilization was observed, along with normalization of lactic acidosis and other blood parameters. This case describes the successful use of Cytosorb with CRRT and ECLS used in combination to overcome a critical phase of septic shock in a young adult patient with necrotizing fasciitis.

<https://www.ncbi.nlm.nih.gov/pubmed/29546811>

First-in-Man Fully Percutaneous Complete Bypass of Heart and Lung

Napp LC, Vogel-Claussen J, Schäfer A, Haverich A, Bauersachs J, Kühn C, Tongers J.
JACC Cardiovasc Interv 2017; 10(24):e231-e233

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Summary

This case reports on a 24-year-old man admitted to a regional hospital after an attempted suicide by taking 9 g of the antidepressant venlafaxine. After initial seizures, he developed progressive cardiogenic shock resulting in cardiac arrest from electromechanical dissociation 12 h after ingestion. Emergency femoral venoarterial extracorporeal membrane oxygenation (ECMO) was inserted under continued cardiopulmonary resuscitation and the patient was then transferred to a tertiary hospital. In an attempt to restore pulmonary gas exchange a novel form of mechanical support was initiated by a triple cannulated ECMO and the Impella, resulting in a complete takeover of upper and lower body gas exchange and circulation by the devices. In addition, CytoSorb® hemoadsorption was connected to the circuit due to post cardiac arrest syndrome, high demand of catecholamines and venlafaxine intoxication. The result was hemodynamic stabilization accompanied by a significant decrease in catecholamines. Over time the patient could be weaned from mechanical ventilation and was transferred to rehabilitation 28 days after admission.

<https://www.ncbi.nlm.nih.gov/pubmed/29198456>

First application of CVVHDF, plasmapheresis and "CytoSorb adsorber" to solve a pediatric haemophagocytic Histiocytosis case

Milella L, Ficarella MT.

Res Pediatr Neonatal 2017; 1(2):1-6

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Summary

This is the case of a 4 yr old girl (body weight 19 kg) with secondary hemophagocytic lymphohistiocytosis (HLH) due to a bacterial infection. She developed septic shock and sepsis with multi-organ failure so was put on mechanical ventilation, high dose catecholamines and fluids to support her cardiovascular system, and dialysis (continuous veno-venous hemodiafiltration CVVHDF) for 20 hrs per day and intermittent plasmapheresis for 4 hrs per day. As she was so critically ill, a CytoSorb® adsorber was added to the CVVHDF circuit. After the first 2 hrs of CVVHDF plus CytoSorb®, the patient rapidly improved her cardiovascular and respiratory status with complete stabilization after 24 hrs. There was a swift decrease in the hyperammonemia, improvement in renal and hepatic function and a rapid decrease in inflammatory markers. The patient went on to make a full recovery. The authors state that CytoSorb® in this pediatric case seemed to be very helpful in resolving the patient's clinical complications including respiratory, cardiovascular, liver (ascites), renal function and laboratory tests that had confirmed the presence of multi-organ failure in a short time period.

[Link to Article](#)

Pediatric patient with dengue fever and associated multiorgan dysfunction syndrome (MODS) receiving haemoadsorption using CytoSorb - a case report on clinical experience

Mekala N, Damera S.

Nephrol Dial Transplant 2017; 32(Suppl 3):iii746

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Summary

In this case report a 10- year old boy with dengue hemorrhagic fever and multi organ dysfunction (including thrombocytopenia, coagulopathy, systemic inflammatory response syndrome, acute fulminant hepatic failure with encephalopathy and oliguria) was treated successfully and safely with a combination of standard care and hemoadsorption with CytoSorb® for an 18 hour period. The patient was eventually discharged alive and well.

[Link to Article](#)

Cytokine adsorption is a promising tool for therapy of hemophagocytic lymphohistiocytosis (HLH)

Frimmel S, Bogdenow S, Schipper J, Hinz M, Mitzner S, Koball S.

Nephrol Dial Transplant 2017; 32(Suppl 3):SP247

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Summary

In this case series 2 patients with 3 episodes of severe hemophagocytic lymphohistiocytosis (HLH) were treated with CytoSorb®. In the first case a 50 yr old woman with acute necrotizing hepatitis caused by Herpes simplex and HLH, CytoSorb® was used to help bridge the time to liver transplant. In the second case a 42-year-old male patient with respiratory and circulatory failure, septic shock and acute renal failure was treated for 48 hours with 2 CytoSorb® adsorbers. After a second relapse he was again treated with CytoSorb® and went on to make a full recovery. In both cases a marked decrease in IL-6 plasma levels, and vasopressor needs were the major results. Importantly, treatment was safe and well-tolerated, without any adverse events.

[Link to Article](#)

Venlafaxine intoxication with development of takotsubo cardiomyopathy: successful use of extracorporeal life support, intravenous lipid emulsion and CytoSorb

Schroeder I, Zoller M, Angstwurm M, Kur F, Frey L.

Int J Artif Organs 2017; 40(7):358-360

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Summary

This case report describes a 19 yr old female who ingested 18g of the antidepressant venlafaxine (240 times the daily therapeutic dose) who went on to develop severe takotsubo cardiomyopathy and multi-organ dysfunction syndrome. As there is minimal clearance of the drug with hemodialysis, and there is no specific antidote available, she was treated with intravenous lipid emulsion (ILE) and CytoSorb® to enhance detoxification of the drug, and extracorporeal life support (ECLS) as a bridge to support the cardiac failure. Despite the relatively short use of CytoSorb® (9 hours), a massive reduction in venlafaxine and its metabolites was observed under the combined therapy with ILE. Over time other therapies including the ECLS, ventilation, and dialysis could be withdrawn and the patient went on to make a full recovery.

<https://www.ncbi.nlm.nih.gov/pubmed/28574114>

Removal of focal segmental glomerulosclerosis (FSGS) factor suPAR using CytoSorb

Schenk H, Müller-Deile J, Schmitt R, Hinrich Bräsen J, Haller H, Schiffer M.

Journal of Clinical Apheresis 2017; 32(6):444-452

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Summary

This case looked at the potential effect of suPAR elimination (a circulating factor that causes renal failure) in a 32 yr old woman who developed severe post-partum nephrotic syndrome who went on to develop FSGS (focal segmental glomerulosclerosis). After three treatments with total plasma exchange (TPE - the normal method used to remove suPAR) she was given one 8 hour treatment with CytoSorb® and the efficiency of both was compared. CytoSorb® hemoadsorption caused a 27.33% reduction in the suPAR level in a single treatment, whereas 3 sessions with TPE caused a reduction of 25.12% (P<0.01). The authors conclude that compared to TPE, plasmapheresis, and immunoabsorption, CytoSorb® hemoadsorption is an effective novel treatment alternative for removing circulating factors in patients with idiopathic FSGS or for patients with a recurrence of primary FSGS in the transplanted kidney.

<https://www.ncbi.nlm.nih.gov/pubmed/28370393>

Rescue of cytokine storm due to HLH by hemoadsorption in a CTLA4-deficient patient

Greil C, Roether F, La Rosée P, Grimbacher B, Duerschmied D, Warnatz K.

Journal of Clinical Immunology 2017; 37(3):273-276

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Summary

In this letter to the editor the authors describe the use of a CytoSorb® in a patient with secondary hemophagocytic lymphohistiocytosis (HLH) caused by CTLA-4 deficiency (caused by a heterozygous germ line mutation of the cytotoxic T lymphocyte antigen-4 (CTLA-4) gene leading to a syndrome with prominent features of immune dysregulation). HLH is characterized by fever, splenomegaly, bicytopenia, highly elevated

serum levels of ferritin and soluble interleukin-2 receptor (sIL2-R), decreased natural killer (NK) cell activity, hypertriglyceridemia and detection of hemophagocytosis in bone marrow or other tissue. To date, HLH has never been described in a patient with CTLA-4 deficiency. A 50 yr old patient was admitted to ICU with systemic inflammatory response syndrome and multi-organ failure. Despite aggressive intervention his clinical condition rapidly worsened so a CytoSorb® adsorber was added into the circuit of the hemodiafiltration. In total 4 adsorbers were used, with columns being changed every 24 hrs. Cytokine adsorption resulted in an immediate decrease in inflammatory parameters, the clinical condition improved in parallel. This suggests the CytoSorb® was the decisive therapeutic intervention in this case. The patient was discharged to the regular ward nine days after CytoSorb® initiation.

<https://www.ncbi.nlm.nih.gov/pubmed/28265964>

(The Use of a Cytokine Adsorber (CytoSorb) in a Patient with Septic Shock and Multi-Organ Dysfunction (MODS) after a Severe Burn Injury)

Houschyar KS, Nietzsche I, Siemers F.

Handchir Mikrochir Plast Chir 2017; 49(2):123-126

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Article in German only

Summary

This case report reports on a 21-year-old patient admitted to hospital immediately following an explosion at home with 2b-3-degree burns to a total of 60% of the body surface area. On admission, he was immediately given bath therapy while he was still hemodynamically stable, with surgical wound treatment of the burned areas. Because of the burn severity, multiple operations were performed, with transplants on his lower abdomen, both upper arms, the upper thorax and both forearms. Further therapy consisted of epifascial debridements, keratinocyte deposits and automatic prone / supine positioning. With sustained elevation of the inflammatory parameters (leukocytes, C-reactive protein and procalcitonin) and renal function, positive blood cultures and wound smears for *Acinetobacter baumannii*, the decision was made to start hemofiltration therapy with additional CytoSorb® adsorbers. The CytoSorb® adsorber was used daily from the 9th - 17th treatment days and from days 32 - 52. The interleukins IL-6 and IL-10 were significantly reduced during the treatment, catecholamine requirement was significantly reduced and circulatory stabilization could be achieved. However, due to cardiopulmonary insufficiency in the context of a multiorgan failure, the patient died on the 52nd postoperative day.

<https://www.ncbi.nlm.nih.gov/pubmed/27931049>

A clinical experience of using extracorporeal cytokine adsorption device (CytoSorb) in a case of Dengue fever

Khan ZA.

J Evid Based Med Healthcare 2016; 3(87):4779-4781

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Summary

This case study reports on a patient with Dengue fever, septic shock and multiple organ failure (MOF). Dengue is a mosquito-borne viral disease where it is thought that elevated cytokines (tumour necrosis factor alpha - TNF- α , interleukins and interferon gamma - IFN- γ) cause damage to the endothelial cells of the capillaries that results in fluid leakage. Here a 32 year old male patient was admitted to the intensive care unit and because of multiple organ failure, he was mechanically ventilated and put on renal replacement therapy. CytoSorb® was used as an adjuvant supportive therapy on days 2, 4 and 6 of admission. The patient also received multiple transfusions to address thrombocytopenia and coagulopathy. The patient showed gradual improvement with a normalization of the central nervous system, improved oxygenation status, adequate renal function and normal platelet count (APACHE score 27 before and 12 at the end of CytoSorb® treatment). Liver function also improved significantly. Serum Glutamic Oxaloacetic Transaminase – GOT (AST) fell from 15,690 U/L to 156 U/L, and Serum Glutamic Pyretic Transaminase - GPT (ALT) fell from 3910 to 84 after CytoSorb® treatment). The patient was discharged from ICU on day 13 and subsequently discharged home. The authors note that CytoSorb® seems to be a useful and safe extracorporeal therapy option to stabilize and help dengue shock patients with MODS to recover.

[Link to Article](#)

1.3.6 COVID-19

Treating Complications of Extracorporeal Life Support in a Patient with COVID-19 (Case Report)

Rybalko AS, Galkina SN, Saryglar AS, Kolerov VA, Voronin AV, Perekhodov SN, Karpun NA.

General Reanimatology 2022; 18(6): 30-36

Original Article in Russian

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Summary

This is a case of mechanical hemolysis as a complication of extracorporeal membrane oxygenation (ECMO) occurring in a 49 year old COVID-19 patient as a result of pump head thrombosis. After emergency extracorporeal circuit replacement, hemoadsorption with CytoSorb® was initiated via a renal replacement machine to try and correct the negative hemolysis effects and the rise in plasma free hemoglobin in the setting of rapid clinical deterioration and impaired renal function. Three consecutive hemoadsorption sessions of 24 hrs each were performed. During therapy hemolysis severity reduced, lactate dehydrogenase (LDH) levels decreased, and respiratory function improved (P/F ratio increased two-fold). Bilirubin also reduced, while the patient's clinical condition remained stable throughout with no adverse events. The authors conclude that the timely, properly chosen, and clinically relevant use of hemoadsorption with CytoSorb® combined with advanced high-technology therapeutic procedures can have a positive impact on the patient's outcome.

https://www.reanimatology.com/rmt/article/view/2207/1681?locale=en_US

CytoSorb® in the Treatment of Severely-Ill Patient with Post-COVID-19 Complications: A Case Report

Paul P, Ma A, Gorla N, Mohammed Z, Maitra S.

Clinical Case Reports: Open Access 2022; 5(4): 238

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Summary

In this case report a 42-year-old man, with post-COVID-19 pneumonia was admitted to hospital with complaints of headache, vomiting, and abdominal discomfort associated with generalized weakness. He had pre-existing comorbidities of diabetes, hypertension, and acute kidney injury. Blood parameters showed increased levels of inflammatory biomarkers which indicated the presence of a cytokine storm and sepsis, hence CytoSorb® therapy was started 7 days after admission to the intensive care unit. He received two sessions of 18 and 20 hours incorporated into his sustained low-efficiency dialysis (SLED) dialysis treatment. After the treatment there was a remarkable decrease in C-reactive protein (CRP) values (39%), creatinine (6.52%), lactate (54%), leucocytes (44%) and procalcitonin (PCT) (33%) observed. There was also a reduction in interleukin (IL)-6 levels noted from 5975 to 3171 pg/ml, 46.9% and in the norepinephrine dose (from 0.8 to 0.2 mcg/kg/hr). The patient was discharged from hospital after 54 days in a stable condition. The authors note that CytoSorb® therapy was effective in providing hemodynamic stability, improving organ dysfunction, and modulating the cytokine storm.

[Link to Article](#)

The Sequential Use of Extracorporeal Cytokine Removal Devices in an Adolescent With COVID-19 Receiving Continuous Renal Replacement Therapy

Hui WF, Chan RWY, Wong CK, Kwok KHA, Cheung WL, Chung FS, Leung KKY, Hon KL, Ku SW.

ASAIO J 2022; 68(12):e230-e234

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Summary

A 14-year-old male (43kg) developed multisystem inflammatory syndrome in children (MIS-C) after acquiring the SARS-CoV-2 infection. He deteriorated rapidly requiring inotropic and ventilatory support as well as continuous renal replacement therapy (CRRT) due to rhabdomyolysis-associated acute kidney injury. CytoSorb® was first incorporated into the post-CRRT filter circuit for myoglobin and cytokine removal (hour 18 – 40), which was followed by sequential use of oXiris® (hour 40 – 80), followed by another CytoSorb® adsorber (hour 85 – 110), giving a total of 100 hours of extracorporeal blood purification [EBP] therapy. There were no major complications related to the EBP therapy including hemodynamic compromise. Cytokine profile revealed a marked reduction of levels of several cytokines including tumor necrosis factor-alpha (TNFα), interleukin (IL)-6, IL-8, and IL-10 after the EBP therapy. It was noted that both pro-inflammatory and anti-inflammatory cytokines were removed, and the removal efficacy varied between different devices. The authors note that the two devices appeared to complement each other's adsorption capacity. His condition improved and the serum ferritin, C-reactive protein, and procalcitonin levels also dropped gradually, which correlated well with his clinical progress and the trend of cytokine levels. The authors conclude that this case demonstrates that extracorporeal cytokine removal can be safely applied in children with MIS-C and can be considered as adjunctive therapy in selected patients with critically ill conditions.

<https://www.ncbi.nlm.nih.gov/pubmed/36318755>

Hemoadsorption for severe MIS-C in critically ill children, should we consider it as a therapeutic opportunity?

Bottari G, Severini F, Markowich AH, Lorenzetti G, Ruiz Rodriguez JC, Ferrer R, Francalanci P, Ammirati A, Palma P, Cecchetti C.

Int J Artif Organs 2022; 45(10):871-877

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Summary

Multisystem inflammatory syndrome (MIS-C) is a new severe clinical condition that has emerged during the COVID-19 pandemic and affects children and the young usually after a mild or asymptomatic COVID-19 infection. Symptoms commonly include cardiovascular dysfunction for which support is required in the majority of cases. In the case report a 13 yr old boy with refractory shock secondary to left ventricular dysfunction (LVD) in the context of MIS-C, the use of hemoadsorption with CytoSorb® is described. The therapeutic strategy resulted in hemodynamic and clinical stabilization (reduction then cessation of vasopressors) as well as control of the hyperinflammatory response (including C-Reactive Protein, interleukin – IL-6 and IL-10). The patient received in total 5 adsorbers over 72 hrs. with the first 2 adsorbers for 12 hours each, and a further 3 adsorbers for 24 hours each inserted into the continuous renal replacement circuit. Treatment appeared to be safe and feasible. The authors then compare this case with two more published cases where CytoSorb® has been used as an adjuvant therapy in similarly critically ill children with severe forms of MIS-C. All three patients responded with a prompt improvement in their myocardial function (within the first 24 h) following the start of hemoadsorption. The authors state that using this blood purification strategy could be a therapeutic opportunity in severe LVD due to MIS-C, sparing the need for extracorporeal membrane oxygenation (ECMO) and other mechanical cardiocirculatory supports, with the advantage of it being less invasive. They also state that CytoSorb® does not appear to interfere with most common immunomodulatory therapies although further evidence is required.

<https://www.ncbi.nlm.nih.gov/pubmed/35822878>

Corona, Acute Ischemic Stroke, Malignant Cerebral Edema, and Hemo-adsorption: A Case Report

Shah MK, Kaidawala Z, Shah A, Desphande R.

Indian J Crit Care Med 2022; 26(2): 235 - 238

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Summary

This case includes a young patient with malignant cerebral edema due to an acute cerebrovascular accident, with COVID-19. Due to the massively elevated intra-cranial pressure, he was taken up for life-saving decompression craniotomy amidst a cytokine storm and multiorgan failure. Post operatively he was treated with steroids, antibiotics, and CytoSorb® therapy in combination with renal replacement therapy (RRT) for 4 days. During this time his markers of hyperinflammation (interleukin - IL-6 and procalcitonin- PCT) reduced by 99.5 and 98.6%, respectively. Vasopressors were stopped on day 4 and he was successfully weaned off ventilator support after 2 weeks. He was de-cannulated and discharged neurologically stable on day 32. According to the authors CytoSorb® therapy with dialysis may have played a significant role in reducing the cytokine storm in the presented case. They conclude that timely detection of COVID-19 and anti-inflammatory and hemoadsorption measures may be helpful in modulating cytokine storm, thereby reducing morbidity and mortality.

<https://pubmed.ncbi.nlm.nih.gov/35712732/>

Cytokine hemoadsorption in the treatment of a critically ill postpartum woman with COVID-19 pneumonia

Pavlis G, Mihaljevic S, Premuzic V.

Ther Apher Dial 2022; 26(4):858-859

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Summary

This case reports on a 35 yr old pregnant woman with severe COVID-19 pneumonia who was initially given standard treatment including dexamethasone and antibiotics. Due to a deterioration in her respiratory status, she had to be invasively ventilated and a decision was made to terminate the 32 week pregnancy delivering a healthy, premature infant. Over the following 4 days, and despite maximum therapy she continued to deteriorate so that extracorporeal blood therapy (EBT) with CytoSorb® inserted into a continuous veno-venous hemodiafiltration circuit was started. The procedure was discontinued after 12 hrs due to respiratory conditions required proning. The day after the use of CytoSorb®, a reduction in inflammatory parameters and

an initial improvement in respiratory status were observed (PaO₂/FiO₂ 71 – 103). However, she then went on to develop a right-sided pneumothorax and pneumomediastinum, which complicated the course. On day 14 it was decided to restart CytoSorb® for another 24 hours. This resulted in substantial respiratory recovery (PaO₂/FiO₂ 235 - 310) and reduction in inflammatory parameters including interleukin 6 and C Reactive Protein. Two days after CytoSorb® use the chest CT-scan showed a significant regression in the pulmonary infiltrates and pneumomediastinum. On the 20th treatment day the patient was successfully weaned from mechanical ventilation and subsequently fully recovered. The authors conclude that acute respiratory distress syndrome is one of the most serious complications of COVID-19 disease which is primarily a consequence of excessive production of various proinflammatory cytokines. Non-selective cytokine removal using the EBP technique may have advantages over treatment approaches targeting a single cytokine.

<https://www.ncbi.nlm.nih.gov/pubmed/34859960>

CytoSorb® Hemoadsorption as a Promising Tool to Handle COVID-19-Induced Cytokine Storm

Acevedo AC, Zoller M, Scharf C, Liebchen U, Irlbeck M, Schroeder I, Nin N.

Case Reports in Critical Care 2021;2021;9937499

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Summary

In this case report a 59 yr old with chronic lymphocytic leukemia (CLL) was admitted with SARS-CoV-2 induced acute respiratory distress syndrome (ARDS). Despite maximum standard therapy, including broad anti-infective therapy and prone positioning, his inflammatory markers continued to increase, accompanied by fever and norepinephrine requirements. Continuous renal replacement therapy was started and CytoSorb® was inserted into the circuit over the next 9 hours. Within 30 mins, his interleukin-IL 6 levels had decreased significantly (4302 – 2495 pg/mL), and within 24 hours his hemodynamic situation had stabilized. An improvement was also seen in his respiratory function (PaO₂/FiO₂ 90 – 165 mmHg). The application of CytoSorb® in this case was feasible and safe with no adverse or any device-related side effects documented during or after the treatment. The authors conclude that they are convinced that CytoSorb® showed a clear benefit within the framework of a multimodal therapy concept, and that despite the clinical picture of severe ARDS, a good outcome could be achieved.

<https://www.ncbi.nlm.nih.gov/pubmed/34650819>

Fatal COVID-19 in a Child with Persistence of SARS-CoV Despite Extensive Multidisciplinary Treatment: A Case Report

Apostolidou S, Harbauer T, Lasch P, Biermann D, Hempel M, Lutgehetmann M, Pfeifferle S, Herrmann J, Ruffer A, Reinshagen K, Kozlik-Feldmann R, Gieras A, Kniep I, Oh J, Singer D, Ebenebe CU, Kobbe R.

Children (Basel) 2021; 8(7):564

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Summary

This case report describes how critical Coronavirus disease 2019 (COVID-19) developed in a 7-year-old girl with a history of dystrophy, microcephaly, and central hypothyroidism. Starting with gastrointestinal symptoms, she then developed severe myocarditis followed by progressive multiple organ failure complicated by *Pseudomonas aeruginosa* bloodstream infection. Intensive care treatment initially consisted of invasive ventilation and drainage of the pleural effusion. High catecholamine therapy could not prevent the progression of heart failure, leading to the implantation of venoarterial extracorporeal life support (VA-ECLS) and an additional left ventricle support catheter (Impella pump). Continuous venovenous hemofiltration (CVVH) and extracorporeal hemadsorption therapy (CytoSorb®) were also initiated. CytoSorb® was initiated a few days after her transfer from the regional hospital to university medical centre and was noted to temporarily improve the clinical picture, and reduce serum levels of interleukin 6, C-Reactive Protein and Ferritin. However, COVID-19 specific antiviral and immunomodulatory treatment did not lead to viral clearance or control of hyperinflammation resulting in the patient's death on extracorporeal life support-(ECLS) after 39 days of illness. This fatal case illustrates the potential severity of pediatric COVID-19 and suggests further evaluation of antiviral treatment strategies and vaccination programs for children.

<https://www.ncbi.nlm.nih.gov/pubmed/34208887>

Efficacy of CytoSorb in a Pediatric Case of Severe Multisystem Inflammatory Syndrome (MIS-C): A Clinical Case Report

Bottari G, Confalone V, Cotugno N, Guzzo I, Perdichizzi S, Manno EC, Stoppa F, Cecchetti C.

Frontiers in Pediatrics 2021; 9:676298

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Summary

In this case report a 14-year-old girl was admitted to the pediatric intensive care unit (PICU) with COVID-19 induced severe MIS-C (multisystem inflammatory syndrome in children). Her symptoms included confusion, tachypnea and hypotension with oliguria. Due to a low cardiac output syndrome, she was intubated and mechanically ventilated and vasopressors started. Continuous venovenous hemodiafiltration (CVVHD) along with an ANST69 filter was initiated due to metabolic acidosis and hyperlactatemia and a CytoSorb® hemoadsorption also added due to the hyperinflammation. In total 4 CytoSorb® adsorbers were used (the first 2 for 12 hours each, and the second 2 for 24 hrs each). Blood purification was able to control the hyperlactatemia, reaching normal lactate blood levels 3 h after the start of the blood purification. The D-dimer, CRP, and ferritin all decreased as the ejection fraction improved, and vasopressors were weaned off. The same time course was observed for IL-6 and IL-10 blood levels. The patient was able to be discharged home 32 days post PICU admission. In summary the authors observed a rapid recovery in the myocardial dysfunction associated with a progressive reduction in pro- BNP, lactate, and other inflammatory biomarkers. This clinical experience shows that maybe “intensive” hemoperfusion could be an advantageous adjuvant therapy in patients with refractory shock and multiple organ dysfunction in MIS-C, potentially avoiding the need for ECMO and without interfering with the most common immunomodulatory therapies. Through analysis of the sublingual microcirculation the authors also showed a lack of hemodynamic coherence between macro- and microcirculation in MIS-C, with late restoration of the microcirculation despite the more rapid improvement in the (macro-)hemodynamic parameters. In conclusion, patients with severe multisystem involvement, particularly those with shock, should receive prompt immunomodulatory treatment. In this scenario, CytoSorb® could also represent a valid adjuvant therapeutic option.

<https://pubmed.ncbi.nlm.nih.gov/34178891/>

Successful Treatment of Suspected Donor-derived Human Herpesvirus-8 Infection in a Liver Transplant Patient With Coronavirus Disease-19

Peri AM, Magro B, van den Bogaart L, Dalla Pria A, Giuffrida P, Gianatti A, Fabretti F, Maria Barbui A, Tebaldi A, Rizzi M, Fagioli AS.

Transplantation 2021; 105(6):e65-e67

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Summary

This letter to the editor describes the case of a 62 yr old liver transplant recipient infected with the coronavirus (COVID-19), who developed life threatening organ dysfunction due to the onset of human herpes virus-8 (HHV8) and who was successfully treated with rituximab and CytoSorb®. The patient was admitted two months after the initial liver transplant with COVID-19 associated pneumonia. Despite maximum therapy his condition rapidly deteriorated so rituximab (an anti-lymphocyte (CD20) monoclonal antibody) and continuous venovenous hemodialysis (CVVHD) plus CytoSorb® were started. The patient responded quickly with a significant clinical improvement over the following days. He soon regained full consciousness, and his acute kidney injury and thrombocytopenia resolved. The patient was discharged after a full recovery and was found to be doing well with no adverse events observed at 1 year follow-up. Finally, the authors discuss extracorporeal cytokine adsorption as a promising alternative to pharmacological inhibition of IL-6 in severe cases of COVID-19. They describe as an advantage the fact that CytoSorb® non-selectively blocks the immune cascade, and in particular that it is possible to terminate CytoSorb® at any time without long term effects that might harm immunocompromised hosts.

<https://www.ncbi.nlm.nih.gov/pubmed/34048423>

Hemadsorption as a Treatment Option for Multisystem Inflammatory Syndrome in Children Associated With COVID-19. A Case Report

Ruiz-Rodríguez JC, Chiscano-Camón L, Palmada C, Ruiz-Sanmartin A, García-de-Acilu M, Plata-Menchaca E, Perurena-Prieto J, Hernandez-Gonzalez M, Pérez-Carrasco M Soler-Palacin P, Ferrer R.

Frontiers in Immunology 2021; 12:665824

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Summary

In this case report a 17 year old with a history of COVID-19 was admitted to intensive care unit (ICU) eventually diagnosed with acute myocarditis secondary to multisystem inflammatory syndrome in children (MIS-C). On the first day in ICU he was started on standard pharmacological treatments along with CytoSorb® (for 24 hours). Pre and post CytoSorb® use showed inflammatory parameters such as interleukin (IL)-6 and IL-10 decreased from 3457 – 47.8 pg/mL and 90.3 – 9.24 pg/mL respectively. His respiratory function improved with

an increase in the PaO₂/FiO₂ ratio from 60 – 400 mmHg. With CytoSorb® use the amount of noradrenaline required also decreased by more than 80% (0.8 – 0.08 µg/kg/min). Despite the severity of his condition, the patient was able to be discharged from ICU on day 5 and from hospital on day 20 with no chronic sequelae detected. The authors consider hemoadsorption responsible for the rapid improvement in respiratory, hemodynamic, and organ dysfunction and therefore is a potential adjunctive therapy in patients with MIS-C severe multiorgan dysfunction.

<https://www.ncbi.nlm.nih.gov/pubmed/34140949>

Successful use of CytoSorb in a Covid-19 patient with secondary septic shock due to a sacral decubitus infection

Pancani F, Pavani R, Quacquarelli A, Feri M.

Int J Artif Organs 2021; 44(12):1034-1038

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Summary

This is a case of a 75-year-old man with respiratory failure due to Sars-CoV-2 infection and secondary septic shock due to a sacral decubitus ulcer. He was admitted to the Intensive Care Unit five days after his initial admission to hospital with a Glasgow Coma Scale of 5, hypotension (systolic pressure 65 mmHg), and dyspnoeic (35 breaths per min). The patient presented with a clinical picture of mixed acidosis with high levels of lactate (7.57 mmol/L) and inflammatory indexes (procalcitonin – PCT 10.23 ng/ml, C-Reactive Protein – CRP 14.3 mg/L). Along with intubation and protective mechanical ventilation, and antibiotic therapy, a norepinephrine infusion was started (0.6 – 1.4 µg/kg/min) along with terlipressin in the later course. After 24 hrs, the inflammatory parameters remained high (interleukin – IL-6 6768 pg/mL) so hemoadsorption treatment with CytoSorb® was started for the septic clinical picture, first in hemoperfusion mode and later in combination with continuous venous-venous hemodiafiltration (CVVHDF). Three consecutive cycles of 24 hrs each were performed. After the three days of treatment, PCT decreased to 1.1 ng/ml, CRP 9.4 mg/L, lactate 1.91 mmol/L and IL-6 to 1731 pg/mL. Norepinephrine and Terlipressin doses were progressively decreased as the hemodynamics stabilized. Due to an obvious deterioration in the decubitus lesion, curettage and vacuum assisted therapy (VAC) was performed. At the end of the treatment the patient had recovered his vital functions and the infection was successfully treated. Use of the CytoSorb® device in this COVID-19 positive patient was safe and well-tolerated. Early use of CytoSorb® within 24h from ICU admission decreased IL-6 plasma levels and inflammatory indexes, resulting in earlier stabilization of homeostasis. The authors conclude that this case suggests that the use of CytoSorb® could be a possible adjuvant therapy in patients with septic shock even when affected by COVID-19.

<https://pubmed.ncbi.nlm.nih.gov/33998306/>

Cytosorb treatment in severe COVID-19 cardiac and pulmonary disease

Ciabatti M, Martinese L, Quacquarelli A, Pieroni M, Feri M, Bolognese L.

Eur Heart J Case Rep 2021; 5(4):ytab123

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Summary

A 75-year-old man was admitted for COVID-19-related pulmonary disease. He was initially treated with intravenous dexamethasone, enoxaparin and non-invasive ventilation. Levels of cardiac damage and inflammatory biomarkers were significantly elevated (including interleukin-IL-6 6768 ng/L). He received two cycles of tocilizumab therapy over the following 2 days, but over the next 3 days his clinical condition deteriorated with severe respiratory failure, severe hypoxaemia, hypotension, and hypoperfusion. He was intubated and mechanically ventilated before being transferred to the COVID-19 intensive care unit. Computed tomography showed bilateral ground-glass lesions, sub-pleural consolidations, pleural effusions, and subsegmental pulmonary embolism. Despite treatment with high-dose vasoactive drugs, unfractionated heparin and antibiotics, he developed refractory shock with anuria so was started on continuous renal replacement therapy (CRRT) with CytoSorb® on day 6. After 72 hrs, a significant hemodynamic improvement together with an important decline in inflammatory (IL-6 decreased from 7100 to 2500 ng/L, Ferritin from 1250 µg/l to 450 µg/l), and cardiac damage markers levels (e.g. high sensitivity troponin T reduced from 55 – 35 pg/mL during treatment) was observed, and, due to the presence of spontaneous diuresis with negative fluid balance, CRRT and CytoSorb® therapy were stopped. The patient was extubated 3 days later and on day 14 transferred to a respiratory rehabilitation centre with stable hemodynamics and no need for CRRT. After 6 months, the patient has completely recovered with normal right ventricular function.

<https://www.ncbi.nlm.nih.gov/pubmed/33870079>

The Combined Use of Tocilizumab and Hemoadsorption in a Patient with SARS-COV-2-19-Associated Pneumonia: A Case Report

Berlot G, Tomasini A, Roman Pognuz E, Randino A, Chiella F, La Fata C, Piva M, Amato P, di Maso V, Bianco F, Gerini U, Tomietto P, Trenti T.

Nephron 2020; 144(9):459-462

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Summary

In this case report a 40 year old previously well man was admitted to Intensive Care with severe respiratory failure caused by SARS-CoV-2 (COVID-19). Due to the high interleukin (IL)-6 and C-Reactive Protein (CRP) levels the anti-IL-6 drug, tocilizumab plus hemoperfusion with CytoSorb® was started. Tocilizumab was given for 2 days, and CytoSorb®, given in hemoperfusion mode - due to the lack of a need for renal replacement therapy (RRT) - for 3 days (exchanged every 24 hrs). Notably, tocilizumab was not removed by the CytoSorb® due to its elevated molecular weight. Levels of IL-6 decreased from 1,040 to 415 pg/mL and CRP from 229 to 59 mg/L, respectively. The gas exchange and the chest imaging rapidly improved (PaO₂/FiO₂ ratio from 132 – 220), and the patient was extubated 10 days later, and eventually discharged home. The authors suggest considering the use of the combined approach of CytoSorb® and tocilizumab in patients with SARS-CoV-2 induced pneumonia, Acute Respiratory Distress Syndrome (ARDS), and/or multiple organ dysfunction syndrome with elevated levels of CRP.

<https://pubmed.ncbi.nlm.nih.gov/32694244>

COVID-19 presenting as acute abdomen and sepsis: a rare case-report

Alharthy A, Balhamar A, Faqihi F, Nasim N, Noor A, Alqahtani SA, Memish ZA, Karakitsos D.

New Microbes and New Infections 2020; 38:100818

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Summary

In this case report a 45 year old man with severe COVID-19 pneumonia with associated pulmonary embolism, presented with an acute abdomen (bowel ischemia). He underwent emergency laparotomy, where he was found to have a small intestinal perforation with peritonitis, so he underwent resection of an ischemic area of the jejunum. Postoperatively, he had septic shock, acute-respiratory-distress syndrome, and acute kidney injury (AKI) necessitating continuous-renal-replacement-therapy (CRRT). He was given therapeutic anticoagulation along with two sessions of hemoadsorption by CytoSorb® (24 hrs each), in conjunction with the CRRT. After 2 days his inflammatory biomarkers and lactate levels normalised, and vasopressors could be weaned off by day 3 of ICU stay. His renal function and oxygenation progressively improved, too and he was able to be extubated on day 7 of his ICU stay. The authors conclude that extracorporeal blood purification may be useful in managing perioperative sepsis, AKI and cytokine storm which are all poor prognostic factors in critically ill patients with COVID-19. Presumably, the early application of hemoadsorption mitigated a full blown picture of COVID-19 related hyperinflammation and/or the development of refractory septic shock.

<https://pubmed.ncbi.nlm.nih.gov/33224507/>

SARS-CoV-2 infection in kidney transplant recipients: experience of the Italian Marche region

Maritati F, Cerutti E., Zuccatosta L, Fiorentini A, Finale C, Ficosecco M, Cristiano F, Capestro A, Balestra E, Taruscia D, Vivarelli M, Donati A, Perna GP, Giacometti A, Tavio M, Onesta M, Di Sante L, Ranghino A.

Transpl Infect Dis 2020; 22(5):e13377

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Summary

This case series included 5 patients who were kidney transplant recipients (KTR) and also SARS-CoV-2 (COVID-19) positive. One of the patients developed acute kidney injury with the need for continuous renal replacement therapy (CRRT) where CytoSorb® was also used for 3 x 24hr treatments. The authors speculate that use of CytoSorb® in this patient for removal of the initially very high interleukin 6 levels, could potentiate the effect of tocilizumab, an IL6 receptor agonist. Indeed, during CRRT treatment plus CytoSorb®, the patient's hemodynamic and hypoxemic conditions improved. Finally, it is suggested that the use of CytoSorb® in combination with tocilizumab might be considered in patients with severe SARS-CoV-2 with need of CRRT.

<https://www.ncbi.nlm.nih.gov/pubmed/32573895>

Cytosorb filter: An adjunct for survival in the COVID-19 patient in cytokine storm? a case report.

Rizvi S, Danic M, Silver M, LaBond V.

Heart & Lung 2021; 50(1):44-50

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Summary

This report describes the case of a 51 yr old male patient with COVID-19 admitted to hospital with dyspnea, lethargy, myalgias and fever. He initially responded well to treatment on the respiratory ward, but on day 4 he had to be intubated and ventilated due to his hypoxemia and developing acute respiratory distress syndrome (ARDS) so was transferred to intensive care. Here he continued to deteriorate however, and so on day 6 his antibiotics and ventilator settings were reviewed and adjusted accordingly (including prone positioning). After an initial positive response, it was noted that his creatinine was starting to increase and his oxygenation to worsen again so it was decided to start continuous renal replacement therapy (CRRT). After having received IRB approval for compassionate use the decision was then made to insert the CytoSorb® adsorber into the CRRT before his developing cytokine storm became insurmountable. The adsorber was changed 12hrly for the first 48 hrs, and thereafter every 24 hrs. Eight adsorbers were used over a 12 day period with a temporary halt of four days into the treatment. Once the CytoSorb® adsorber was placed in the pre-filter position his hemodynamic status improved and stabilized. Having survived the cytokine storm and sepsis associated COVID-19, the patient was able to tolerate further novel treatments including tocilizumab and convalescent plasma. The patient's clinical course was then complicated further by a hypoxic cardiopulmonary arrest, upper GI bleed and severe depression and anxiety, before he was finally discharged to subacute rehab after 60 days in hospital. The authors believe that in this severely ill patient the use of CytoSorb® seemed to stabilize the patient (better oxygen requirements, pressor support and inflammatory markers), and that the use of CytoSorb® successfully completed the goal of prolonging the patient's life to bridge to definitive therapies during the cytokine storm.

<https://pubmed.ncbi.nlm.nih.gov/33041058/>

Hemoadsorption cartridge and coronavirus disease 2019 infections: A case report and brief literature review

Melegari G, Bertellini E, Melegari A, Trenti T, Malaguti S, Barbieri A.

Artif Organs 2021; 45(5):E130-E135

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Summary

In this case report a 71 year old man with COVID-19 was admitted after a 5 day history of high temperature, general weakness and difficulties breathing. He was admitted to intensive care with severe acute respiratory syndrome in COVID-19 and acute renal failure - for intubation and mechanical ventilation, and renal replacement therapy (RRT). Despite maximum therapeutic interventions, his clinical condition continued to deteriorate so hemoadsorption with CytoSorb® was added to his renal circuit in order to reduce the cytokine release syndrome. RRT plus CytoSorb® was continued for 5 days and two treatments with CytoSorb® were performed for 48 hrs. each. During this time the interleukin (IL) 6 was reduced from 123.53pg/ml to between 18.51 and 22.64 pg/ml and the patient's respiratory function improved allowing him to be weaned from the ventilator. He was discharged home after 2 months in the hospital with normal respiratory function but chronic renal failure. The authors conclude that CytoSorb® is compatible with the concomitant use of antiviral drugs, chloroquine, or antirheumatic drugs, with a possible synergistic relationship. The safety and versatility of adsorption treatments highlight their interesting features and potential applications in critically ill patients, including COVID-19 patients, especially with the concomitant use of ECMO or RRT, in order to reduce cytokine hyperproduction and their related life-threatening effects.

<https://www.ncbi.nlm.nih.gov/pubmed/33084021>

Cytokine adsorption in a patient with severe coronavirus disease 2019 related acute respiratory distress syndrome requiring extracorporeal membrane oxygenation therapy: A case report

Rieder M, Zahn T, Benk C, Lothar A, Bode C, Staudacher D, Duerschmied D, Supady A.

Artif Organs 2021; 45(2):191-194

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Summary

In this letter to the editor the case of a 59 year old female with COVID-19 related ARDS is described. After 8 days of various symptoms she was finally admitted to hospital with severe respiratory insufficiency requiring immediate non-invasive ventilation. Over the following days, and despite maximum therapeutic measures including progression to invasive ventilation and prone positioning, her hypoxemia deteriorated further so that the decision was made to put her on veno-venous extracorporeal membrane oxygenation (vv ECMO) on day 5 of her hospital stay. Because of her elevated inflammatory parameters (interleukin – IL 6 540 pg/ml, C-Reactive Protein – CRP 482.3 mg/L) a CytoSorb® adsorber was included directly into the ECMO circuit. CytoSorb®

therapy was continued for 72 hours. No adjustments to the antibiotic doses appeared to be necessary during this time. Very quickly after the start of ECMO / CytoSorb®, the patient stabilized clinically allowing lung protective ventilation strategies according to the ARDS treatment guidelines. The need for vasopressors also decreased significantly as did the CRP and IL-6 levels. The authors noted abnormal clotting of the ECMO circuit despite PTT monitored anticoagulation (D-dimers increased while platelets decreased) which they attributed to the effects of the hypercoagulability with COVID-19 infection. During the further course of treatment the patient developed a septic shock with multi-organ failure, most likely due to bacterial superinfection of the lung and, based on the presumed will of the patient, the therapy was therefore terminated 17 days after the initial hospital admission. According to the authors this case suggests that cytokine adsorption may help with the initial stabilization of patients with severe COVID-19 disease requiring vv ECMO support.

<https://www.ncbi.nlm.nih.gov/pubmed/32929761>

Cytokine Hemoadsorption in the Management of a Pregnant Woman with COVID-19 Pneumonia: Case Report

Karabulut Keklik ES, Dal H, Bozok Ş.

SN Comprehensive Clinical Medicine 2020; 2(11):2376-2380

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Summary

This case report describes a 22-year-old pregnant woman (gestational age: 32 weeks) infected with COVID-19 who presented with fever (39.1 °C) and respiratory symptoms. The patient was admitted for supportive care and anti-viral and anti-inflammatory agents, however, her general health status deteriorated and she had to be transferred to the intensive care unit (ICU) on day 3 of her hospital admission. In ICU she deteriorated further with the development of respiratory failure and acute respiratory distress syndrome (ARDS). Thus, extracorporeal cytokine hemoadsorption with CytoSorb® was performed every other day (3 sessions in total) in order to remove inflammatory cytokines from the circulation and to relieve the systemic inflammatory response. On day 7 of ICU admission, it was decided to terminate her pregnancy due to worsening hypoxemia and a healthy, premature infant was born. On day 2 after the cesarean section, the patient needed to be intubated and mechanical ventilation was initiated due to a worsening of her respiratory system. She continued to show an increasingly complicated clinical course (including acinetobacter sepsis and deep vein thrombosis) and died on day 22 after ICU admission. The authors describe the use of CytoSorb® in this patient for controlling fever, improving hypoxemia and reducing the inflammatory status (reduction in C-Reactive Protein levels) and buying extra time for hemodynamic and metabolic stabilization. According to the authors there may be a “window of opportunity” for patients with severe COVID-19, where early application of blood purification therapies should be considered.

<https://pubmed.ncbi.nlm.nih.gov/32954212/>

2 Pre-Clinical data

2.1. Animal models

Pharmacokinetics of immunosuppressive agents during hemoperfusion in a sheep model

Leber B, Liebchen U, Rohrhofer L, Weber J, Klaus T, Scheier J, Sucher R, Stiegler P.

Frontiers in Medicine 2023; 10:1258661

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Summary

In this interventional study, CytoSorb® hemoperfusion was tested in healthy sheep (n = 5) against a sham extracorporeal circuit (n = 3). Seven different immunosuppressant drugs (ID) (tacrolimus (TAC), cyclosporin A (CYA), mycophenolate mofetil (MMF), everolimus (EVER), basiliximab (BAS), methylprednisolone (MP) and prednisolone (PRED)) were administered in clinically relevant doses and combinations to the sheep and levels of the ID were measured repeatedly in blood samples from the extracorporeal circulation for 6 h following administration. Results showed that there was negligible clearance was observed for PRED and BAS. For all other substances, a saturable adsorption sub-model with linear decrease of the adsorption effect over the adsorbed amount best described the measured concentrations. The maximum absolute adsorbed amounts for TAC, CYA, MMF, EVER, and MP indicated an adsorption of less than 5% of the daily administered dose for all investigated substances. This is the first, standardised model testing the possible influence of CytoSorb® on a range of immunosuppressant drugs, showing negligible, or a limited effect on removal. Despite the limitations

of an animal model, this represents important safety information for the use of CytoSorb® in patients on immunosuppressants, both in the context of organ transplantation and long-term treatment for other reasons. However, as noted by the authors, clinical decision-making should always be supported by therapeutic drug monitoring whenever available.

<https://www.ncbi.nlm.nih.gov/pubmed/37928476>

Proteomic changes to immune and inflammatory processes underlie lung preservation using ex vivo cytokine adsorption

Niroomand A, Hirdman G, Pierre L, Ghaidan H, Kjellström S, Stenlo M, Hyllén S, Olm F, Lindstedt S.
Frontiers in Cardiovasc Med 2023; 10:127444

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Summary

The field of graft preservation has made considerable progress in recent years improving outcomes related to solid organ restoration and regeneration. In lungs, the use of ex vivo lung perfusion (EVLP) in line with devices and treatments has shown promising results in preclinical and clinical studies with the potential to improve graft quality thereby increasing the pool of organs able to be transplanted. Cytokine adsorption with CytoSorb® has been demonstrated as a potentially safe and effective therapy when applied to the EVLP circuit and post transplantation. The current study investigated in a pig model (variables and outcome of this model already published by Ghaidan et al.*) the molecular mechanisms and signalling pathways of how cytokine adsorption impacts on lung function when used during EVLP and post transplantation (as hemoperfusion). Lung tissue from EVLP and post lung transplantation were analyzed for their proteomic profile using mass spectrometry. Through gene set enrichment analysis (GSEA) it was found that inflammatory, immune process, and coagulation pathways were significantly affected by cytokine treatment both following EVLP and transplantation. This demonstrates the important effects of the therapy on processes that extend beyond the examination of individual cytokine levels. The authors conclude that the findings of this study augment the clinical and histopathological improvements previously seen within studies on cytokine adsorption in line with EVLP and demonstrate the efficacy of using the treatment in graft preservation.

*Ghaidan et al., Reduction of primary graft dysfunction using cytokine adsorption during organ preservation and after lung transplantation. *Nat Commun* 2022; 13(1):4173

<https://www.ncbi.nlm.nih.gov/pubmed/37849943>

Extracorporeal cytokine adsorption reduces systemic cytokine storm and improves graft function in lung transplantation

Ehsam JP, Arni S, Weisskopf M, Nowack M, Inci I.

Journal of Thoracic and Cardiovascular Surgery Open 2023; 15:497-507

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Summary

In this lung perfusion study, the effect of *in vivo* extracorporeal cytokine adsorption with CytoSorb® was investigated in a pig model. Left lung transplantation was performed following 24h of cold ischemic storage. In the treatment group (6 lungs), CytoSorb® was started after 30 mins before reperfusion and continued for 6 hrs. The control group (3 lungs) did not receive CytoSorb®. In the CytoSorb® treated lungs there was a significant decrease in plasma pro-inflammatory cytokines (including interleukin – IL 2, Tumor Necrosis Factor alpha (TNFα) and IL-1α). There was also significantly improved lung function, including CO₂ removal, better PO₂/FiO₂ ratio and less acidosis in the CytoSorb® treated group when evaluating the left lung allograft independently after 24 hrs. of observation. Autopsy findings then revealed less neutrophil invasion into the alveolar space in the treated group. The authors conclude that cytokine adsorption during and after reperfusion is a viable approach to reduce post-transplant inflammation following lung transplantation, and may increase the acceptance of extended criteria donor lungs, which are more susceptible to ischemia-reperfusion injury.

<https://www.ncbi.nlm.nih.gov/pubmed/37808017>

Pumpless Extracorporeal Hemadsorption Technique (pEHAT): A Proof-of-Concept Animal Study

Fiedler MO, Muellenbach RM, Rolfes C, Lotz C, Nickel F, Muller-Stich BP, Supady A, Lepper PM, Weigand MA, Meybohm P, Kalenka A, Reyher C.

J Clin Med 2022; 11(22): 6815

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Summary

In this second article on this topic from this group of authors, the use of CytoSorb® (and oXiris®) was tested in a pumpless set up (off label use) over a wide range (45 – 85 mmHg) of mean arterial pressures (MAP). The hemoadsorption devices were inserted into the (femorofemoral arteriovenous) shunt circulation; four pigs received CytoSorb® and four oXiris®. Extracorporeal blood flow was measured in a range between mean arterial pressures of 45-85 mmHg preset with intravenous infusions of noradrenaline, urapidil, or increased sedatives. Results showed that extracorporeal blood flows through CytoSorb® and oXiris® linearly increased with increasing mean blood pressures and remained well above the minimum flows recommended by the manufacturers throughout all MAP steps for both devices. Maximum blood flows were achieved at a MAP of 85 mmHg with 360.7 ± 39.9 mL/min for CytoSorb® and 326.6 ± 14.1 mL/min for oXiris®. The authors conclude that arteriovenous pumpless extracorporeal hemoadsorption resulted in sufficient blood flows through the devices even at low blood pressures mimicking septic shock, therefore is likely an intriguing therapeutic option in the early phases of septic shock or hyperinflammatory syndromes.

NB: This set up is not covered by the current IFU of CytoSorb®.

<https://www.ncbi.nlm.nih.gov/pubmed/36431292>

Cytokine Adsorber Use during DCD Heart Perfusion Counteracts Coronary Microvascular Dysfunction

Saemann L, Hoorn F, Georgevici A, Pohl S, Korkmaz-Icöz S, Veres G, Guo Y, Karck M, Simm A, Wenzel F, Szabó G. *Antioxidants* 2022; 11(11):2280

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Summary

In this animal (pig) study, the impact of cytokine adsorption during ex-vivo blood perfusion (BP) to prevent coronary microvascular dysfunction (CMVD) in hearts donated after circulatory death (DCD) was studied. DCD hearts were maintained for four hours by normothermic blood perfusion through the ascending aorta with (DCD-BP^{CytoS}, n = 5) or without (DCD-BP, n = 5) cytokine adsorption (CytoSorb®). Microvascular autoregulation was assessed by increasing the coronary perfusion pressure, while myocardial microcirculation was measured by Laser-Doppler-Perfusion (LDP). Finally, the hearts of all groups underwent 60 min of perfusion with fresh blood to mimic the reperfusion effects after transplantation. The concentration of 13 cytokines were assessed in the perfusate and the expression of 84 genes was determined and analyzed using machine learning and decision trees. A further 5 non-DCD hearts served as a control for the gene expression analysis. Compared to DCD-BP, relative perfusion improved in the CytoSorb® treated group (1.51 ± 0.17 vs. 1.08 ± 0.17), and several pro- and anti-inflammatory cytokines were reduced. The authors also demonstrated a reduced level of oxidative stress and an alleviated microvascular endothelial ischemia reperfusion injury in this group (DCD-BP^{CytoS}). Regarding gene analysis, the expression of eNOS significantly increased, and the expression of nitrotyrosine, HNE, CD54, CD106, and CD31, all markers of endothelial injury, majorly decreased in the CytoSorb® group. Three genes allowed exact differentiation between groups. The authors conclude that the use of cytokine adsorption during ex-vivo blood purification counteracts preload dependent microvascular dysfunction and preserves the microvascular endothelium by preventing oxidative stress and ischemic reperfusion injury of the coronary arterioles in circulatory death hearts. The findings suggest that the use of CytoSorb® in DCD hearts could be beneficial in the clinical setting.

<https://www.ncbi.nlm.nih.gov/pubmed/36421466>

Can We Attenuate Ischemia-Reperfusion Injury of Allografts in a Porcine Left Lung Transplant Models by Adsorption of Cytokines?

Frick AE, Orlitova M, Bleeser T, Vanstapel A, Claes S, Schols D, Mathysen C, Ceulemans LJ, Vos R, Verleden GM, Vanaudenaerde BM, Verleden SE, Van Raemdonck DE, Neyrinck AP.

Eur J Cardiothorac Surg 2022; 63(1):ezac483

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Summary

In this experimental animal study, left porcine lung transplantation was performed with allografts preserved for 24 hours at 4 degrees C. In the treatment group [T] (n = 7), a veno-venous shunt was created to insert the CytoSorb®. In the sham group [S] (n = 4) the shunt was created without the cytokine filter. Hemodynamic parameters, lung mechanics, blood gases and plasma cytokines were assessed during the 6-hours in vivo reperfusion. During this time there were significant differences in the plasma pro-inflammatory cytokines (IFN-alpha, IFN-gamma, and Interleukin - IL-6) between [T] and [S], but with higher plasma levels in the [T] group. Plasma concentrations of other pro-inflammatory cytokines (IL-1beta, IL-12p40, IL-4, IL-6, IL-8, IFN-alpha, IFN-gamma, and TNF-alpha) and anti-inflammatory cytokines (IL-10) did not find any evidence of a difference. Furthermore, there were no differences in hemodynamics and blood gases between the two groups, nor with biopsies or wet-to-dry ratio at the end of the experiment. The authors note, that the

severity of injury in their model was not severe enough. They conclude that use of CytoSorb® did not achieve the intended effect, with no significant impact on the allograft, which is in contrast to previous studies with CytoSorb® use during ex vivo lung perfusion as a surrogate LTx model.

<https://www.ncbi.nlm.nih.gov/pubmed/36214633>

Reduction of primary graft dysfunction using cytokine adsorption during organ preservation and after lung transplantation

Ghaidan H, Stenli M, Niroomand A, Mittendorfer M, Hirdman G, Gvazava N, Edström D, Silva IAN, Broberg E, Hallgren O, Olm F, Wagner DE, Pierre L, Hyllén S, Lindstedt S.

Nature Communications 2022; 13:4173

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Summary

Despite improvements, lung transplantation for end-stage disease remains hampered by both a scarcity of donor organs and by mortality following primary graft dysfunction (PGD). Since acute respiratory distress syndrome (ARDS) limits donor lung utilization, this study investigated the use of CytoSorb® cytokine adsorption as a means of treating ARDS donor lungs. Ex-vivo lung perfusion (EVLV) was used to assess the donor lungs. Mild to moderate ARDS was induced via lipopolysaccharide (LPS) in 16 donor pigs. The non-treated group received EVLP and underwent transplantation without cytokine adsorption. The treated groups were subdivided between a 'two step' group (lungs were treated with CytoSorb® both during EVLP (4 hours) and for 12 hours post transplantation) and a 'one step' group (use of CytoSorb® only for 12 hrs postop). The primary endpoint of lung function was the PaO₂/FiO₂ ratio. Results showed that treatment with CytoSorb® significantly decreased cytokine levels during EVLP and decreased levels of immune cells post-transplantation. Histology demonstrated fewer signs of lung injury across both treatment periods and the incidence of PGD was significantly reduced among treated animals. The effects of CytoSorb® seemed to increase when used at two times points. In summary, CytoSorb® cytokine adsorption in the context of ARDS injured lungs (i) reduced inflammation and restored pulmonary function during EVLP, (ii) restored pulmonary function and decreased inflammation following transplantation, and (iii) reduced the incidence of PGD in transplanted recipients. The authors suggest this treatment will increase the availability of donor lungs and increase the tolerability of donor lungs in the recipient.

<https://pubmed.ncbi.nlm.nih.gov/35882835/>

A new ex-situ machine perfusion device. A preliminary evaluation using a model of donors after circulatory death pig livers

Ghinolfi D, Melandro F, Patrono D, Lai Q, De Carlis R, Camagni S, Gambella A, Ruberto F, De Simone P.

Artif Organs 2022; 46(12):2493-2499

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Summary

Ischemia–reperfusion injury (IRI) during liver transplantation is associated with a high incidence of graft dysfunction and ischemic cholangiopathy. Machine perfusion (MP) has been introduced to overcome limitations of traditional methods of preserving grafts from extended criteria donors. In this animal study, the use of a new ex-situ perfusion device, PerLife®, is described using liver grafts procured after circulatory death from slaughterhouse pigs. Fourteen pig liver grafts were included procured by 5 different transplant teams in Italy. The PerLife® device has been designed for both kidney and liver perfusion providing oxygenated pressure-controlled pulsatile perfusion of the hepatic artery and smoothed flow perfusion of the portal vein. A thermoregulator enables hypothermic, sub-normothermic and normothermic perfusion with slow re-warming and re-cooling options. CytoSorb® can be added in parallel to the circuit using a dedicated roller pump to remove inflammatory mediators such as cytokines. Results showed that the perfusion device allowed stable perfusion in both hypothermic (HMP, n = 6) and normothermic (NMP, n = 8) conditions and no technical failures were observed. During perfusion, perfusate and bile samples were collected to assess liver metabolism and viability, with no signs of injury. The 3 grafts treated by NMP plus CytoSorb® showed lower ALT, improved lactate clearance, and produced bile with higher pH. CytoSorb® also appeared to effectively remove inflammatory cytokines from the perfusate. This preliminary experience represents the starting point for further investigations on the potential clinical benefits of cytokine and other inflammatory mediator adsorption during machine perfusion of organs retrieved for transplantation. The authors conclude that the potential advantage of this new perfusion technology with cytokine adsorption during MP should now be evaluated in the setting of well-designed clinical trials.

<https://pubmed.ncbi.nlm.nih.gov/36136037/>

Use of extracorporeal therapy in a dog with heatstroke

Tracy A, Lynch A, Messenger K, Vaden S, Vigani A.

J Vet Emerg Crit Care (San Antonio) 2022; 32(4):512-519

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Summary

In this case review a three year old Rhodesian Ridgeback dog presented with heat-related illness following strenuous exercise. Despite intensive supportive care, the dog developed progressive and refractory hyperkalemia, hypoglycemia, neurologic dysfunction, acute kidney injury (AKI), and pulmonary dysfunction. Four extracorporeal therapy (ECT) sessions were performed consisting of 4 intermittent hemodialysis (HD) sessions, the first 2 of which concurrently utilized hemoperfusion with a cytokine adsorption filter (VetResQ, made by CytoSorbents Inc). Even though major extraction of cytokines (IL-6, IL-8, IL-10 and MCP-1) could not be demonstrated, from a clinical point of view rapid and sustained glycemic and electrolyte control were achieved after the first ECT session. The dog survived to discharge and was nonazotemic 3 months following initial management. This represents the first clinical use of ECT consisting of HD and cytokine adsorption in the management of severe heat-related illness in a dog and warrants further investigation.

<https://www.ncbi.nlm.nih.gov/pubmed/34904781>

Pharmacokinetics of anti-infective agents during CytoSorb hemoadsorption

Schneider AG, Andre P, Scheier J, Schmitt M, Ziervogel H, Buclin T, Kindgen-Milles D.

Scientific Reports 2021; 11(1):10493

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Summary

In this experimental study, 24 pigs were randomly allocated to either CytoSorb® hemoadsorption or sham extracorporeal circuits (controls) and to different drug combinations. Seventeen different drugs were evaluated including; clindamycin, fluconazole, linezolid, meropenem, piperacillin, anidulafungin, ganciclovir, clarithromycin, posaconazole, teicoplanin, tobramycin, ceftriaxone, ciprofloxacin, metronidazole, liposomal amphotericin B, flucloxacillin and cefepime. Repeated blood measurements were taken from the extracorporeal circulation (pre and post adsorber) over six hours and total - and adsorber specific - clearance computed. Hemoadsorption was associated with increased clearance of all study drugs, except ganciclovir. However, CytoSorb® impact on total body clearance was considered as moderate for fluconazole (282%) and linezolid (115%), mild for liposomal amphotericin B (75%), Posaconazole (32%) and teicoplanin (31%) and negligible for all other drugs. This classification is based on the classification proposed by the WHO Committee for Proprietary Medicinal Products (CPMP) for drug inhibitors and inducers according to potency. Hemoadsorber clearance declined over time, with even delayed desorption for beta-lactams. In conclusion, hemoadsorption with CytoSorb® appears to have a limited effect on the pharmacokinetics of the majority of drugs tested. However, the clearance of fluconazole, linezolid and liposomal amphotericin B appears to be increased by the procedure. Studies in humans are required to confirm the need for dosage adjustments for these agents.

<https://www.ncbi.nlm.nih.gov/pubmed/34006946>

Pumpless Extracorporeal Hemoadsorption Technique: A New Method for Early Cytokine Elimination?

Fiedler MO, Reyher C, Kalenka A, Rolfes C, Lotz C, Muellenbach RM.

Blood Purif 2021; 50(6):968-970

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Summary

In this proof of principle experimental study on two pigs, a femoral arteriovenous shunt was established with a CytoSorb® adsorber inserted into the shunt circulation. A small 10 Fr arterial cannula was placed as the arterial line and a 14 French venous cannula was utilized as the venous re- turn. As a major determinant for flow through the adsorber, the mean arterial pressure (MAP) was varied between 45 and 85 mmHg using norepinephrine or urapidil. Pre and post adsorber pressures, cardiac output and shunt blood flows were continuously recorded. Blood flows were observed between 206 and 393 mL/min through the CytoSorb® adsorber, thus ranging between 3 and 6% of the cardiac output. This is the first experimental study to show the feasibility of using CytoSorb® without the need for an additional pump (such as a renal replacement machine). Knowing that treatment with CytoSorb® seems to be most effective when started within the first 24 hrs, this pumpless technique might be a valuable option in order to expedite the commencement of cytokine elimination in critically ill patients. Potential ischemia of the arterially cannulated limb is noted as one of the

possible main complications which would need continuous monitoring, as would monitoring of flow. At the present time this remains an experimental application.

<https://www.ncbi.nlm.nih.gov/pubmed/33503608>

Perfusate-adsorption during *ex vivo* lung perfusion improves early post-transplant lung function

Iskender I, Arni S, Maeyashiki T, Citak N, Sauer M, Monné Rodriguez J, Frauenfelder T, Opitz I, Weder W, Inci I. *Journal of Thoracic and Cardiovascular Surgery* 2021; 161(2):e109-e121

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Summary

In this *ex vivo* lung perfusion study (EVLP), the effect of ischemia-reperfusion injury after lung transplantation was studied in donor pig lungs. In the treatment group, the perfusate was also adsorbed through a CytoSorb® adsorber, whereas the control lungs were perfused according to the standard protocol (n = 5, each). Variables of EVLP physiology and biochemistry were monitored. Cytokine concentrations in the perfusate were markedly lower with CytoSorb®, resulting in improved EVLP physiology and biochemistry during the 6-hour *ex-vivo* perfusion period. After the subsequent transplant, dynamic lung compliance was markedly better during the 4-hour reperfusion period in the treatment group, as was isolated allograft oxygenation function and dynamic compliance at the end of reperfusion which was accompanied by a markedly decreased local inflammatory response. The authors conclude that the implementation of CytoSorb® has refined the standard EVLP protocol. Furthermore, cytokine removal during EVLP improved immediate post-transplant graft function together with a less intense inflammatory response as a consequence of reperfusion in this pig model.

<https://www.ncbi.nlm.nih.gov/pubmed/32201002>

Hemoadsorption Improves Survival of Rats Exposed to an Acutely Lethal Dose of Aflatoxin B1

Ruggeberg KG, O'Sullivan P, Kovacs TJ, Dawson K, Capponi VJ, Chan PP, Golobish TD, Gruda MC. *Scientific Reports* 2020; 10(1):799

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Summary

Mycotoxins, including aflatoxin B1 (AFB1), are highly toxic, causing a severe inflammatory reaction, and pose a serious threat as biological weapons due to their easy accessibility and lack of effective therapeutics. This study investigated whether CytoSorb® (CS) could improve survival in rats after a lethal aflatoxin dose. The rats received a lethal dose of AFB1 intravenously and hemoperfusion with CytoSorb® or a control device was initiated immediately, or after 30, 90, or 240-minute delays, and then conducted for 4 hours. It was found that CytoSorb® removes AFB1 from the circulation and significantly improves survival when initiated within 90 minutes of toxin administration. It is known that CytoSorb® also removes damage associated molecular patterns (DAMPs), which, together with the reduction in inflammatory mediators, may be an additional aspect that helps to explain the reduction of associated tissue damage, and the observed survival benefit. The authors suggest that CytoSorb® could be a viable countermeasure against acute mycotoxin exposure.

<https://www.ncbi.nlm.nih.gov/pubmed/31964964>

Midkine Is Elevated After Multiple Trauma and Acts Directly on Human Cardiomyocytes by Altering Their Functionality and Metabolism

Lackner I, Weber B, Baur M, Haffner-Luntzer M, Eiseler T, Fois G, Gebhard F, Relja B, Marzi I, Pfeifer R, Halvachizadeh S, Lipiski M, Cesarovic N, Pape H-C, Kalbitz M.

Frontiers in Immunology 2019; 10:1910

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Summary

Midkine is an inflammatory marker which is elevated in humans after fractures, burns and traumatic spinal cord injuries and appears to be associated with cardiac pathologies in these patients. In this experimental model, midkine levels were investigated in the blood plasma of 11 multiply injured humans admitted to an Emergency Dept, and 20 pigs treated according to a trauma model. Human cardiomyocytes were also cultured in the presence/absence of midkine and analysed. Finally, the ability of CytoSorb® to adsorb midkine was tested with recombinant midkine or plasma from these multiply injured patients. Results showed that midkine levels were significantly increased in the blood plasma of multiply injured humans and pigs, and that it acted on human cardiomyocytes by altering their mitochondrial respiration and calcium metabolism *in vitro*, affecting both the function and metabolism of the cardiomyocytes, depressing cardiac function. Adsorption with CytoSorb® reduced midkine concentrations both *ex vivo* and *in vitro* in a concentration dependent manner (by

up to 95% when the midkine levels were 10,000 pg/ml). The use of CytoSorb® may be a very promising therapeutic approach for the treatment and prevention of post-traumatic cardiac dysfunction. As noted, one huge benefit of using CytoSorb® is that it is able to adsorb a high amount of many miscellaneous damage-associated and inflammatory molecules after trauma. Furthermore, adsorption of midkine by CytoSorb® might limit other negative effects of midkine in polytrauma patients, as it has been previously shown that midkine inhibits fracture healing and is associated with poor outcome in septic patients.

<https://www.ncbi.nlm.nih.gov/pubmed/31552013>

Blood Purification by Non-Selective Hemoadsorption Prevents Death after Traumatic Brain Injury and Hemorrhagic Shock in Rats

McKinley TO, Lei Z, Kalbas Y, White FA, Shi Z, Wu F, Xu ZC, Rodgers RB.

J Trauma Acute Care Surg; 85(6):1063-1071

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Summary

Patients who sustain traumatic brain injury (TBI) and concomitant hemorrhagic shock (HS) are at high risk of inflammation which can lead to poor outcomes and death. To investigate the influence of hemoadsorption (HA) on outcome after TBI and HS, rats were subjected to a combined injury of a controlled cortical impact to their brain and hemorrhagic shock. The rats were then instrumented with an extracorporeal blood circuit and treated with either therapeutic hemoadsorption with a 2 ml cartridge filled with CytoSorb® beads (HA-group, 14 rats) or sham intervention (19 rats) for 180 minutes. CytoSorb® beads improved survival from 47% in sham treated rats to 86% in HA treated rats. HA resulted in decreases in circulating concentrations in several biomarkers compared to sham treatment, but the majority of cytokines were not affected by HA treatment. In conclusion blood purification by non-selective HA is an effective intervention to prevent death in a combined TBI/HS rat model.

<https://www.ncbi.nlm.nih.gov/pubmed/30211852>

Haemoadsorption reduces the inflammatory response and improves blood flow during ex vivo renal perfusion in an experimental model

Hosgood SA, Moore T, Kleverlaan T, Adams T, Nicholson ML.

J Transl Med 2017; 15(1):216

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Summary

Ex-vivo normothermic perfusion strategies are a promising new instrument in organ transplantation and whilst they are designed to be protective, the artificial environment can induce a local inflammatory response. The aim of this study was to determine the effect of incorporating a CytoSorb® adsorber into an isolated kidney perfusion system. Porcine kidneys were subjected to 22 h of cold ischaemia then reperfused for 6 h in an ex vivo reperfusion circuit. Pairs of kidneys were randomised to either control (n = 5) or reperfusion with a CytoSorb® adsorber (n = 5) integrated into the circuit. Baseline levels of cytokines were similar between groups. Levels of IL-6 and IL-8 in the perfusate significantly increased during reperfusion in the control group but not in the CytoSorb® group. Levels of other cytokines were numerically lower in the CytoSorb® group. The mean renal blood flow (RBF) was significantly higher in the CytoSorb® group. Perfusate levels of prostaglandin E2 and thromboxane were significantly lower in the CytoSorb® group. While no effect of hemoadsorption on creatinine clearance or renal function could be shown in this model, it can reduce the inflammatory response and improve renal blood flow during perfusion.

<https://www.ncbi.nlm.nih.gov/pubmed/29070045>

Cytokine filtration modulates pulmonary metabolism and edema formation during ex vivo lung perfusion

Iskender I, Cosgun T, Arni S, Trinkwitz M, Fehlings S, Yamada Y, Cesarovic N, Yu K, Frauenfelder T, Jungraithmayr W, Weder W, Inci I.

J Heart Lung Transplant 2018; 37(2):283-291

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Summary

This study tested the safety and efficacy of cytokine adsorption during ex vivo lung perfusion (EVLP) in an animal model. Pig donor lungs were preserved for 24 hours at 4°C (to induce lung injury) and then randomly divided into 2 groups, the treatment and control groups (n=5 each), for a 12 hour EVLP procedure. In the treatment group, the perfusate ran continuously through CytoSorb® via a veno-venous shunt from the reservoir, whereas perfusions were run without additional filtering in the control group. Cytokine filtration with CytoSorb® significantly improved airway pressure and

dynamic compliance during the perfusion period. Electrolyte imbalance, glucose consumption and lactate production were markedly worse in the control group while cytokine expression profile, tissue myeloperoxidase activity and microscopic lung injury were significantly reduced in the CytoSorb® treatment group. Continuous perfusate filtration through CytoSorb® was found to be effective and safe during prolonged EVLP and cytokine removal decreased the development of pulmonary edema and modulated pulmonary metabolism through the suppression of anaerobic glycolysis and neutrophil activation.

<https://www.ncbi.nlm.nih.gov/pubmed/28587802>

Evaluation of the CytoSorb hemoadsorbent column in a pig model of severe smoke and burn injury

Linden K, Scaravilli V, Kreyer SF, Belenkiy SM, Stewart JJ, Chung KK, Cancio LC, Batchinsky AI.

Shock 2015; 44(5):487-495

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Summary

The aim of this in vivo study in a porcine model of smoke inhalation and burn injury was to investigate the feasibility, technical safety and efficacy of cytokine and myoglobin removal by early use of CytoSorb®. Female Yorkshire pigs (n = 15) were injured by wood bark smoke inhalation and deep burn to 40% total body surface area, and observed for 72 hours or death. The animals were randomized to hemoadsorption treatment (n = 9) or sham treatment (n = 6) before injury and underwent a six hour hemoadsorption or sham session on days one, two and three. Serum cytokines (IL-1b, IL-6, IL-8, IL-10, TNF-alpha) and myoglobin were measured systemically, locally in broncho-alveolar lavage fluid and also in circulating blood before and after the adsorbing column. Use of CytoSorb® resulted in a significant removal of IL-1b, IL-6, IL-10 and myoglobin mainly during the first run, while systemic cytokine and myoglobin serum concentrations did not change. The authors conclude that further investigations are needed to optimize the efficiency of mediator clearance to impact on both circulating levels and clinically relevant outcomes.

<http://www.ncbi.nlm.nih.gov/pubmed/26368927>

Modulation of chemokine gradients by apheresis redirects leukocyte trafficking to different compartments during sepsis, studies in a rat model

Peng ZY, Bishop JV, Wen XY, Elder MM, Zhou F, Chuasuwan A, Carter MJ, Devlin JE, Kaynar AM, Singbartl K, Pike F, Parker RS, Clermont G, Federspiel WJ, Kellum JA.

Crit Care 2014; 18(4):R141

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Summary

In this in vivo rat study of polymicrobial abdominal sepsis the authors investigated whether the removal of chemokines from the plasma changed chemokine gradients and subsequently enhanced leukocyte localization into the infected compartment, and away from healthy tissues. The results demonstrated the efficacy of CytoSorb® to target leukocyte trafficking control by influencing chemokine gradients and thereby reducing leukocyte infiltration into remote organs.

<http://www.ncbi.nlm.nih.gov/pubmed/24992991>

Role of cytokine hemoadsorption in cardiopulmonary bypass-induced ventricular dysfunction in a porcine model

Vocelka CR, Jones KM, Mikhova KM, Ebisu RM, Shar A, Kellum JA, Verrier ED, Rabkin DG.

J Extra Corpor Technol 2013; 45(4):220-227

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Summary

This in vivo study in a porcine model undergoing cardiopulmonary bypass investigated the role of hemoadsorption using CytoSorb® on left ventricular function, cytokine removal, hemodynamics and non-cardiac organ functions.

<http://www.ncbi.nlm.nih.gov/pubmed/24649569>

Effect of cytokine hemoadsorption on brain death-induced ventricular dysfunction in a porcine model

Mikhova KM, Don CW, Laflamme M, Kellum JA, Mulligan MS, Verrier ED, Rabkin DG.

J Thorac Cardiovasc Surg 2013; 145(1):215-224

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Summary

This in vivo study investigated the effect of CytoSorb® on cytokine levels (TNF, IL-6), cell injury (liver, kidney) and heart function (cardiac output, ventricular function) in a brain-dead porcine model.

<http://www.ncbi.nlm.nih.gov/pubmed/23127374>

Hemoadsorption Reprograms Inflammation in Experimental Gram-Negative Septic Peritonitis: Insights from In Vivo and In Silico Studies

Namas RA, Namas R, Lagoa C, Barclay D, Mi Q, Zamora R, Peng Z, Wen X, Fedorchak MV, Valenti IE, Federspiel WJ, Kellum JA, Vodovotz Y.

Mol Med 2012; 20(18):1366-1374

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Summary

This combined in vivo/in silico study in a rat model of E.coli-induced peritonitis investigated whether CytoSorb® hemoadsorption was able to reduce, re-localize and reprogram sepsis-induced acute inflammation (determined by analysis of 14 different cytokines and bacterial count in peritoneal fluid).

<http://www.ncbi.nlm.nih.gov/pubmed/22751621>

Acute removal of common sepsis mediators does not explain the effects of extracorporeal blood purification in experimental sepsis

Peng ZY, Wang HZ, Carter MJ, Dileo MV, Bishop JV, Zhou FH, Wen XY, Rimmelé T, Singbartl K, Federspiel WJ, Clermont G, Kellum JA.

Kidney Int 2012; 81(4):363-369

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Summary

This in vivo study in a subacute rat model of intraabdominal sepsis (cecal ligation puncture) investigated the effect of CytoSorb® hemoadsorption that did not exert its positive effect as a direct reduction of cytokine plasma concentrations. Levels of cytokines in this model were low, resulting in low removal by CytoSorb® (a concentration-dependent technology). However, 7-day survival was significantly improved in the treatment group, with a reduction in latent organ injury. Cytokine removal (TNF α , IL-1 β , IL-6 und IL-10), organ injury/dysfunction (HMGB-1, ALT, and creatinine), production of cytokines (via NF κ B binding in neutrophils) and 7-day survival was analyzed. The effect of exchange blood transfusions (between CytoSorb®-treated and sham animals) on IL-6 levels and 7-day mortality was also analyzed.

<http://www.ncbi.nlm.nih.gov/pubmed/21918497>

Effects of hemoadsorption on cytokine removal and short-term survival in septic rats

Peng ZY, Carter MJ, Kellum JA.

Crit Care Med 2008; 36(5):1573-1577

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Summary

In this in vivo study in a rat model of intraabdominal sepsis (cecal ligation and puncture) the authors explored the effect of hemoadsorption (using CytoSorb®) on cytokine adsorption (TNF α , IL-1 β , IL-6 and IL-10), on mean arterial pressure (MAP) and short-term survival.

<http://www.ncbi.nlm.nih.gov/pubmed/18434884>

Hemoadsorption removes tumor necrosis factor, interleukin-6, and interleukin-10, reduces nuclear factor- κ B DNA binding, and improves short-term survival in lethal endotoxemia

Kellum JA, Song M, Venkataraman R.

Crit Care Med 2004; 32(3):801-805

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Summary

This in vivo study in a lethal endotoxemic rat model (in septic shock) investigated the effect of hemoadsorption (using CytoSorb®) on cytokine adsorption, inflammation and short-term survival.

<http://www.ncbi.nlm.nih.gov/pubmed/15090965>

Cytokine removal with a novel adsorbent polymer

Song M, Winchester J, Albright RL, Capponi VJ, Choquette MD, Kellum JA.

Blood Purif 2004; 22(5):428-434

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Summary

This study characterized the CytoSorb® adsorbent polymer in terms of cytokine removal in 50 LPS challenged rats by measuring TNF alpha, interleukin 10 and interleukin 6 concentrations under a variety of conditions to evaluate adsorption kinetics. The authors found that all three cytokines were rapidly removed from the blood with less than 50% of the initial concentrations present after 1 h of circulation through the cartridge pointing towards a high efficiency, while binding was relatively unaffected by a variety of physical conditions.

<http://www.ncbi.nlm.nih.gov/pubmed/15316198>

2.2 In-Vitro Data

In-vitro removal of protein-bound retention solutes by extracorporeal blood purification procedures

Schildböck C, Harm S, Hartmann J.

Blood Purif 2024; 53(4):231-242

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Summary

The aim of this in-vitro study was to determine whether hemoperfusion adsorbers are suitable for removing protein-bound retention solutes (produced by failing organs and causing cardiovascular and neurotoxic complications) from human plasma and whole blood as well as to compare the removal to conventional hemodialysis. For in-vitro testing whole blood and plasma were spiked with the uremic retention solutes (homocysteine, hippuric acid, indoxyl sulfate, 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid) and the toxins of liver failure (bilirubin, cholic acid, tryptophan, phenol) and the protein binding of each retention solute determined. The adsorption characteristics of the Jafron HA330, Biosky MG and CytoSorb were tested by incubating them in spiked whole blood or plasma for one hour. Subsequently, adsorption characteristics of the adsorbers were also tested in a dynamic system. Results showed that hippuric acid, homocysteine, Indoxyl Sulfate and Tryptophan were most effectively removed by hemodialysis and that bilirubin and cholic acid were removed best by CytoSorb. Bilirubin, the most protein-bound toxin of the liver failure, was reduced by 43 % by hemoperfusion treatment with CytoSorb. Treatment with Jafron HA, Biosky MG and hemodialysis could not reduce the bilirubin concentration. β 2-microglobulin was removed fastest by CytoSorb. HA330 and Biosky MG showed similar results for the adsorption of the tested retention solutes and were best for removing phenol. 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid could not be removed with any treatment method. In conclusion, a combination of hemodialysis with hemoperfusion appears promising for improving the removal of some toxic metabolites in extracorporeal therapies. However, some very strongly protein-bound metabolites cannot be removed adequately with the adsorbers tested. The results of this study confirm that the use of CytoSorb in liver failure is justified.

<https://www.ncbi.nlm.nih.gov/pubmed/38262384>

Proteins Adsorbed during Intraoperative Hemoadsorption and Their In Vitro Effects on Endothelium

Piskovatska V, Navarrete Santos A, Kalies K, Korca E, Stiller M, Szabó G, Simm A, Wächter K.

Healthcare 2023; 11(3): 310

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Summary

Intraoperative hemoadsorption has the potential to remove substances that may have an unfavorable effect on the endothelium, thus preventing endothelial damage. In this experimental study the authors aimed to identify the spectrum of blood proteins adsorbed onto the polymer matrix of the CytoSorb® hemoadsorption system to investigate their influence on cultured endothelial cells, in vitro. The authors obtained adsorbers from patients who had undergone intraoperative hemoadsorption for infective endocarditis surgery. Over 125 different proteins were extracted from the adsorbers, purified, identified with mass-spectrometry and applied to cultured human aortic endothelial cells (EC). A broad range of blood proteins were identified in the material collected from the CytoSorb® adsorber. Proteins retained on the polymer matrix generally possess molecular weights below 60 kDa and are mainly annotated as residential plasma proteins. When added to cultured ECs, these protein extracts caused severe reductions in cell viability and migration. After 24 h exposure, transcriptional changes with up-regulation of multiple metabolic regulators were observed and verified on the protein level. Genes responsible for control of mitosis were significantly down-regulated. In summary, this data shows that intraoperative hemoadsorption allows broad spectrum removal of a wide range of molecules which may cause endothelial damage.

<https://pubmed.ncbi.nlm.nih.gov/36766885/>

Comparison of the CytoSorb 300mL and Jafron HA380 hemoadsorption devices: an *in vitro* study

Nierhaus A, Morales J, Wendt D, Scheier D, Gutzler D, Jarczak D, Born F, Hagl C, Deliargyris E, Mehta Y.
Min Invasive Ther & Allied Tech 2022; 31(7):1058-1065

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Summary

In this *in vitro* study, the ability of CytoSorb® and Jafron HA380 to remove interleukin – IL 6, & IL 10, tumor necrosis factor (TNF) and monocyte chemoattractant protein (MCP)1 from the blood was compared. Using a hemoperfusion blood recirculation benchtop circuit, both devices were primed in accordance with the manufacturers instructions for use and multiplex cytokine kits were used for determining cytokine concentrations as each time point (pre-spike, 0, 15, 30, 60, 120, 180, 240, 300, 360, 540 and 720 mins). At the end of 12 hrs, both devices had reduced cytokine levels, however, the rate of removal varied between the two devices with CytoSorb® removing 62 – 99% of all cytokines within 2 hrs, and Jafron HA380 removing 34 – 86% of cytokines. Also, the overall amount of cytokines removed during the observational period as measured by the help of the area under the curve (AUC) was significantly higher with the CytoSorb® device. The authors conclude that the measured dynamics and efficiency seem to be in favor of the CytoSorb® device. It may therefore be the preferred device in severe septic states where rapid cytokine clearance is desired.

<https://www.ncbi.nlm.nih.gov/pubmed/35913784>

Antithrombotic Drug Removal from Whole Blood Using Haemoadsorption with a Porous Polymer Bead Sorbent

Tripathi R, Morales J, Lee V, Gibson CM, Mack MJ, Schneider DJ, Douketis J, Sellke FW, Ohman EM, Thourani VH, Storey RF, Deliargyris EN.

European Heart Journal - Cardiovascular Pharmacotherapy 2022; 8(8):847-856

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Summary

This experimental in-vitro study evaluated the removal of the antithrombotic drugs apixaban, rivaroxaban, and ticagrelor by the DrugSorb-ATR hemoadsorption device in a benchtop clinical scale model using bovine whole blood. Blood containing clinically relevant concentrations of the antithrombotic agents was continuously circulated through a 300-mL DrugSorb-ATR hemoadsorption device at a flow rate of 300 mL/min. Drug concentration was monitored over 6 hours to evaluate drug removal. Results were compared to a control circuit without the hemoadsorption device. Removal rates at 30, 60, 120 and 360 minutes were: apixaban: 81.5%, 96.3%, 99.3% >99.8%; rivaroxaban: 80.7%, 95.1%, 98.9%, >99.5%; ticagrelor: 62.5%; 75%, 86.6%, >95% (all p<0.0001 compared to control). Blood pH and hematological parameters were not significantly affected by DrugSorb-ATR when compared with the control circuit. In conclusion, DrugSorb-ATR efficiently removes apixaban, rivaroxaban, and ticagrelor in a clinical-scale benchtop recirculation circuit with the highest removal rate occurring in the first 60 minutes. The clinical implications of these findings (fewer bleeding events in patients undergoing urgent cardiac surgery) are currently investigated in patients undergoing on-pump cardiothoracic surgery in two U.S trials (STAR-T and STAR-D, ClinicalTrials.gov Identifiers: NCT04976530 and NCT05093504).

N.B. DrugSorb-ATR is based on the CytoSorb® technology.

<https://pubmed.ncbi.nlm.nih.gov/35657375/>

In-Vitro Apixaban Removal by Cytosorb® Whole Blood Adsorber. An Experimental Study

Røed-Undlien H, Haagenrud Schultz N, Lunnan A, Husebråten IM, Malene Wollmann B, Molden E, Lagethon Bjørnstad J.

Journal of Cardiothoracic and Vascular Anesthesia 2022; 36(6):1636-1644

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Summary

In this experimental study, reconstituted whole blood was spiked with the oral anticoagulant, apixaban, circulated in an in-vitro circuit with the CytoSorb® device connected. A total of 3100 mls blood were pumped through the circuit at a flow rate of 300ml/min. Blood samples were drawn immediately before adding apixaban, then after 0, 5, 15, 30, 60 and 120 minutes of adsorption. Six experiments with the CytoSorb® adsorber column and four control experiments without the adsorber were performed. The apixaban concentration was measured by an anti-Xa activity method calibrated for apixaban, as well as by an ultraperformance liquid chromatography (UPLC-MS), which is considered gold standard for the quantification of NOAC levels in blood. After 30 minutes of adsorption, mean apixaban concentration was reduced

from 414.3 ng/ml to 33 ng/ml (anti-Xa activity method) or 839 ng/mL to 73 ng/mL (UPLC-MS). After the total circuit time of 120 mins, mean apixaban concentration was <2% of the added concentration (for both measurement techniques). Thrombin generation showed a maximum effect of adsorption after 60 mins and clotting time (thromboelastometry) was found to be close to normal after 120 minutes. In the control experiment without CytoSorb®, the apixaban levels remained unchanged throughout. In conclusion, apixaban concentrations were effectively reduced and clotting time and thrombin generation assays normalized by the use of CytoSorb®. The study, as noted by the authors, indicates that CytoSorb® may represent a promising intraoperative reversal strategy in apixaban treated patients undergoing acute cardiothoracic surgery. However, clinical in vivo studies are warranted.

<https://www.ncbi.nlm.nih.gov/pubmed/35272914>

Hemoadsorption eliminates remdesivir from the circulation: Implications for the treatment of COVID-19

Biever P, Staudacher D, Sommer M, Triebel H, Neukamm MA, Bode C, Supady A, Lother A.

Pharmacol Res Perspect 2021; 9(2):e00743

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Summary

This in-vitro study tested whether the antiviral drug, remdesivir - and its main active metabolite GS-441524, was adsorbed by CytoSorb®, as both can be used for the treatment of severe COVID-19 patients. Fetal calf serum containing remdesivir or GS-441524 was circulated in a custom-made system containing a CytoSorb® device. Concentrations of remdesivir and GS-441524 before and after the adsorber were analyzed. Measurements of remdesivir post adsorber indicated almost complete removal by the device, with concentrations showing an exponential decay which were no longer detectable after 60 mins. GS-441524 showed a similar exponential decay but reached an adsorption-desorption equilibrium at ~48 microg/L. In conclusion, remdesivir and GS-441524 are rapidly eliminated from the perfusate by the CytoSorb® adsorber device in vitro. This should be considered in patients for whom both therapies are indicated, and so simultaneous application should maybe avoided. While benefit from the use of remdesivir in later stages of the COVID-19 disease remains questionable at this time, hemoadsorption therapy may be limited to critical cases of COVID-19 that are associated with a significant increase in cytokine levels. In general, however, and as also recommended by the company, plasma levels of therapeutic drugs should be closely monitored in patients who are also on concurrent CytoSorb® therapy.

<https://www.ncbi.nlm.nih.gov/pubmed/33710753>

Cytokine adsorption during human kidney perfusion reduces delayed graft function-associated inflammatory gene signature

Ferdinand, JR, Hosgood SA, Moore T, Ferro A, Ward CJ, Castro-Dopico T, Nicholson ML, Clatworthy MR.

Am J Transplant 2021; 21(6):2188-2199

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Summary

Transplantation is the optimal treatment for most patients with end stage kidney disease but organ shortage is a major challenge. A new technique, normothermic machine perfusion (NMP) has been used to re-condition marginal organs however mechanisms by which NMP might benefit organs are not well understood. Using pairs of human kidneys obtained from the same donor, the authors compared the effect of NMP with that of cold storage on global kidney transcriptome. Cold storage led to the global reduction in gene expression, including inflammatory pathway genes. In contrast NMP, led to upregulation of the OXPHOS genes (required for energy generation processes), but also of a number of immune and inflammatory pathway genes. Using biopsies from kidneys undergoing NMP that were subsequently transplanted, the authors found that higher inflammatory gene expression occurred in organs with prolonged delayed graft function (DGF). Therefore, CytoSorb® was used to remove pro-inflammatory cytokines for a period of 4 hours. Use of CytoSorb® attenuated the negative effects of immune gene induction, and increased OXPHOS pathway genes. There were no effects on renal blood flow, urine output or composition, oxygen consumption or acid-base homeostasis. The authors suggest that their data shows that adsorption of pro-inflammatory mediators from the perfusate represents a potential intervention which may improve organ viability, including also liver and lung transplantation.

<https://www.ncbi.nlm.nih.gov/pubmed/33098231>

Similarities, Differences, and Potential Synergies in the Mechanism of Action of Albumin Dialysis Using the MARS Albumin Dialysis Device and the CytoSorb Hemoperfusion Device in the Treatment of Liver Failure

Dominik A, Stange J.

Blood Purif 2021; 50(1):119-128

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Summary

In this *in vitro* two-compartment model the molecular adsorption recirculating system (MARS) albumin dialysis was compared to CytoSorb® for effects on marker molecule removal. Ammonia removal was increased using CytoSorb®. CytoSorb® also led to a statistically significant reduction of albumin-bound toxins, total bilirubin and subfractions. Bile acid removal was comparable. MARS did not appear to remove the cytokines interleukin (IL)-6 and tumor necrosis factor-alpha (TNF-alpha), whereas CytoSorb® allowed for near complete removal. Notably, CytoSorb® displayed 50% of lipophilic substance and cytokine removal during the first hour of treatment. Compared to MARS, CytoSorb® hemoperfusion led to an initially fast removal of cytokines, TNF-alpha and IL-6, as well as reduction of albumin-bound toxins such as indirect bilirubin and bile acids in this model. Whether the observed reduction of albumin is specific for more oxidized forms of albumin should be investigated in further studies.

<https://www.ncbi.nlm.nih.gov/pubmed/32615564>

Increased Cell-Free DNA Plasma Concentration Following Liver Transplantation Is Linked to Portal Hepatitis and Inferior Survival

Krenzien F, Katou S, Papa A, Sinn B, Benzing C, Feldbrugge L, Kamali C, Brunnbauer P, Splith K, Lorenz RR, Ritschl P, Wiering L, Ollinger R, Schoning W, Pratschke J, Schmelzle M.

J Clin Med 2020; 9(5):1543

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Summary

Donor organ quality is crucial for transplant survival and long-term survival of patients after liver transplantation. Besides bacterial and viral infections, endogenous damage-associated molecular patterns (DAMPs) can stimulate immune responses. Cell-free DNA (cfDNA) is one such DAMP that exhibits highly proinflammatory effects via DNA sensors. This study measured cfDNA after liver transplantation and found elevated levels when organs from resuscitated donors were transplanted. High levels of cfDNA were associated with high C-reactive protein, leukocytosis as well as granulocytosis in the recipient. In addition to increased systemic immune responses, portal hepatitis was observed, which was associated with increased interface activity and a higher number of infiltrating neutrophils and eosinophils in the graft. In fact, the cfDNA was an independent significant factor in multivariate analysis and increased concentration of cfDNA was associated with inferior 1-year survival. Moreover, cfDNA levels were found to be decreased significantly during the postoperative course when patients underwent continuous veno-venous haemofiltration. In conclusion, patients receiving livers from resuscitated donors were characterised by high postoperative cfDNA levels. Those patients showed pronounced portal hepatitis and systemic inflammatory responses in the short term leading to a high mortality.

<https://www.ncbi.nlm.nih.gov/pubmed/32443763>

Effects of Circulating HMGB-1 and Histones on Cardiomyocytes-Hemadsorption of These DAMPs as Therapeutic Strategy after Multiple Trauma

Weber B, Lackner I, Baur M, Fois G, Gebhard F, Marzi I, Schrezenmeier H, Relja B, Kalbitz M.

J Clin Med 2020; 9(5):1421

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Summary

The aim of the study was to determine the effects of post-traumatically released nuclear proteins (High Mobility Group Box-1 protein (HMGB1)) and extracellular histones on cardiomyocytes (CM). The authors also evaluated a therapeutic option to capture circulating histones after trauma, using CytoSorb® hemadsorption to treat CM dysfunction. The results of the *in-vitro* study show clearly that both HMGB-1 and extracellular histones altered the calcium handling and reduced the cell viability as well as the mitochondrial respiration of human cardiomyocytes. A specially adapted CytoSorb® adsorber was applied either directly to eliminate exogenous extracellular histones *in-vitro* or to remove endogenous circulating histones from blood samples obtained from the trauma patients. CytoSorb® significantly reduced the histone concentrations *in-vitro*, depending on the dosage, as well as *ex-vivo* in plasma samples from injured patients. In summary, damage associated molecular patterns (DAMPs) such as HMGB-1 and extracellular histones impair human CM *in-vitro*. Hemadsorption as with CytoSorb® could be a therapeutic option to reduce high concentrations of these DAMPs thereby lessen the early myocardial damage post trauma.

<https://www.ncbi.nlm.nih.gov/pubmed/32403440>

In-Vitro Sorbent-Mediated Removal of Edoxaban from Human Plasma and Albumin Solution

Angheloiu AA, Tan Y, Ruse C, Shaffer SA, Angheloiu GO.
Drugs R D 2020; 20(3):217-223

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Summary

Based on previous experience of sorbent-mediated ticagrelor, dabigatran, and radiocontrast agent removal, the authors tested the effect of two 40-ml sorbent columns (containing either CytoSorb® or Porapak Q – a non-clinically available polymer) on the removal of edoxaban, a direct oral anticoagulant acting reversibly on factor Xa and being widely used in patients with atrial fibrillation. 100 mL of edoxaban solution was circulated during six (3 for each adsorber) first-pass cycles using human plasma (2 samples) and 4% bovine serum albumin solution (4 samples) as drug vehicles. Drug concentration was measured by liquid chromatography-tandem mass spectrometry. The average edoxaban concentration decreased from 407 ng/mL to 3.3 ng/mL ($p = 0.017$), for a removal rate of 99% across all six samples. The drug concentrations with CytoSorb® were undetectable if the cycle time was 60 mins. The authors conclude that sorbent-mediated technologies (including CytoSorb®) may represent a viable pathway for edoxaban removal from human plasma or albumin solution.

<https://www.ncbi.nlm.nih.gov/pubmed/32415538>

Bioassay for Endothelial Damage Mediators Retrieved by Hemoadsorption

Denzinger M, Staendker L, Ehlers K, Schneider JM, Schulz T, Hein T, Wiese S, Roecker A, Gross R, Munch J, Bracht H, Barth E, Weiss M, Georgieff M, Schneider EM.
Sci Rep 2019; 9(1):14522

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Summary

Microvascular endothelial cells form the innermost layer of vessels in the cardio-vasculature, serving protective and barrier functions, and interacting with factors in the blood to mediate wound healing and the inflammatory response. When the immune system attempts to combat invading pathogens, such as in septic conditions, substantial collateral damage leads to impaired barrier function in the endothelium. This scientific in-vitro study was aimed at the proof of concept that endothelial-specific damage mediators are adsorbed by the CytoSorb® adsorber, which could explain immediate recovery of microvascular endothelial cells' (mEC) function and rapid recovery from catecholamine-dependency and septic shock in patients. The study results demonstrated that CytoSorb® is able to eliminate circulating nucleic acids (bound to an as yet undefined protein), which are considered to have a significant deleterious effect on endothelial integrity and may constitute a major danger-associated molecular pattern (DAMP) in the exacerbation of inflammation when patients experience septic shock. Hemoadsorption with CytoSorb® may therefore limit endothelial damage, through the binding of these nucleic acid-bearing aggregates and thus contribute to improved endothelial barrier function in septic shock patients.

<https://www.ncbi.nlm.nih.gov/pubmed/31601835>

Cytokine Removal in Extracorporeal Blood Purification: An in vitro Study

Harm S, Schildbock C, Hartmann J.
Blood Purif 2020; 49(1):33-43

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Summary

The aim of this in-vitro study was to compare three different medical devices (CytoSorb®, the high cut-off filter EMiC2 - Fresenius Medical Care, Bad Homburg, Germany - and the hemofilter HemofeelCH 1.8 - Toray, Tokio, Japan) with respect to their clearance for the cytokines interleukin-6 (IL-6), IL-8, IL-1beta, and tumor necrosis factor alpha (TNFa) using a multiFiltrate machine with 1 litre human plasma for 8 hrs with samples for cytokine quantification taken at defined time points from the plasma pool. Each experiment was conducted in triplicate, and clearance was calculated for all tested cytokines. CytoSorb® showed the best adsorption kinetics and highest clearance for all cytokines. The authors describe a level of protein and albumin loss with CytoSorb® in this in-vitro setup, and call for further in-vitro experiments to specify the adsorptive removal of important plasma components such as hormones, coagulation factors, and immunoglobulins by membranes and adsorbents.

<https://www.ncbi.nlm.nih.gov/pubmed/31509822>

Removal of dabigatran using sorbent hemadsorption

Angheloiu AA, Angheloiu GO.
Int J Cardiol 2019; 293:73-75

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Summary

Recent studies have demonstrated the safety of drugs including dabigatran and ticagrelor for preventing strokes in patients with atrial fibrillation. However, these drugs place the patient at an increased risk of bleeding complications if emergency surgery is required. In this in-vitro study the authors looked at the use of CytoSorb® as a method for removing dabigatran from human blood. Dabigatran was passed through different sized experimental CytoSorb® columns and its concentration measured from the affluent and effluent solutions. For testing the effect of dabigatran removal on the aPTT value (coagulation of the blood) one human volunteer was administered oral dabigatran 150 mg aPTT was measured at baseline prior to and post drug administration. The dabigatran concentration decreased from 1456 to 67 nM ($P = 0.002$) with the smaller CytoSorb® column, and with the 40 mL column it dropped to undetectable levels (therapeutic level is 743 nM). The removal rate from only one pass through the adsorber was 99%. In the human volunteer the aPTT was 29.2 s in the baseline samples, 34.7s after oral dabigatran, and 25s after plasma was passed through CytoSorb® ($p = 0.000025$ and 0.0000002). In conclusion, dabigatran is robustly removed by CytoSorb®, a method already proven successful for the P2Y12 receptor antagonist ticagrelor. Dabigatran removal restores the aPTT to below baseline values, suggesting that CytoSorb® could clinically reverse the anticoagulant effect of this drug. <https://www.ncbi.nlm.nih.gov/pubmed/31296393>

In vitro removal of anti-infective agents by a novel cytokine adsorbent system

König C, Röhr A, Frey OR, Brinkman A, Roberts JA, Wichmann D, Braune S, Kluge S, Nierhaus A.
Int J Artif Organs 2019; 42(2):57-64

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Summary

The aim of this in vitro study was to describe the adsorption of anti-infective drugs (standardized, clinically used concentrations of vancomycin, gentamicin, meropenem, ciprofloxacin, piperacillin, flucloxacillin, voriconazole, rifampicin and fluconazole) by the CytoSorb® adsorber in either normal saline 0.9% (1st experiment) or human albumin 5% (2nd experiment) at a flow rate of 1.2L/h for 1.5h. In addition, the antibiotics meropenem and ciprofloxacin were also dissolved in reconstituted blood and run through a CytoSorb® cartridge (3rd experiment), which was integrated into a continuous renal replacement therapy (CRRT) circuit with a flow rate of 2L/h for 18h. Samples from the solution, pre- and post-filter, were quantified by high-performance liquid chromatography. The mean clearance of the drugs in normal saline was 1.22 ± 0.07 L/h and in human albumin, 1.29 ± 0.08 L/h. In reconstituted blood, clearance of meropenem decreased from 5.4 to 1.4 L/h and for ciprofloxacin from 6.3 to 4.3L/h within the first 1.5h because of early drug adsorption. Importantly the authors note that during the total observation period of 18 hrs, 394 mg of meropenem and 284 mg of ciprofloxacin were absorbed by CytoSorb®, however, in addition 2870 mg of meropenem and 235mg of ciprofloxacin were removed by the concomitant renal replacement therapy alone. In these in-vitro settings, all tested drugs were adsorbed by CytoSorb® in relevant amounts however, as noted by the authors, the results, particularly using saline and albumin cannot be extrapolated into clinical practice as they do not represent what happens in a human body. The identified maximum adsorptive capacity and the rapid decline in concentration during the first 1.5 h of CytoSorb® use suggest that the administration of an additional dose within the first hours of CytoSorb® treatment may be reasonable. In addition, early therapeutic drug monitoring should be considered. <https://www.ncbi.nlm.nih.gov/pubmed/30545255>

Removal of Bilirubin with a New Adsorbent System: In Vitro Kinetics

Gemelli C, Cuoghi A, Magnani S, Atti M, Ricci D, Siniscalchi A, Mancini E, Faenza S.
Blood Purif 2019; 47(1):10-15

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Summary

Many potentially toxic molecules accumulate in the blood during hepatic dysfunction including bilirubin, however this is difficult to remove, particularly in its unconjugated form when it is strongly bound to albumin. The aim of this in vitro study was to assess bilirubin adsorption using CytoSorb® in 4 separate but related experiments with different albumin-bilirubin solutions. Results showed that in all experiments the ability of CytoSorb® to adsorb unconjugated bilirubin led to efficient bilirubin removal with a removal rate up to 90% after 24 hrs and with minimal albumin loss. No sign of bilirubin release from the charged adsorber was detected, confirming the irreversibility of the adsorption. The authors conclude that CytoSorb® seems a

promising artificial liver support, due to its ability to adsorb bilirubin (and other liver toxins) and its proven ability to modulate the cytokines involved in hepatic and other organ dysfunctions.

<https://www.ncbi.nlm.nih.gov/pubmed/30219813>

Broad adsorption of sepsis-related PAMP and DAMP molecules, mycotoxins, and cytokines from whole blood using CytoSorb® sorbent porous polymer beads

Gruda MA, Ruggeberg K, O'Sullivan P, Guliashvili T, Scheirer AR, Golobish TD, Capponi VJ, Chan P.
PLoS One 2018; 13(1):e0191676

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Summary

In sepsis and septic shock, pathogen-associated molecular pattern molecules (PAMPs), including bacterial exotoxins, cause direct cellular damage and/or trigger an immune response in the host, often leading to excessive cytokine production, a maladaptive systemic inflammatory response syndrome (SIRS), and tissue damage. The released damage-associated molecular pattern molecules (DAMPs), such as activated complement and HMGB-1, into the bloodstream cause further organ injury. This study quantified the size-selective adsorption of a wide range of sepsis-related inflammatory bacterial and fungal PAMPs, DAMPs and cytokines, in an in-vitro whole blood recirculation system. Purified proteins were added to whole blood and recirculated through a device filled with CytoSorb® hemoadsorbent polymer beads or a control (no bead) device in vitro. Except for TNF-alpha trimer, hemoadsorption through CytoSorb® reduced the levels of a broad spectrum of cytokines, DAMPs, PAMPs and mycotoxins by more than 50 percent providing an additional means of reducing the uncontrolled inflammatory cascade that contributes to a maladaptive SIRS response, organ dysfunction and death in patients with a broad range of life-threatening inflammatory conditions such as sepsis, toxic shock syndrome, necrotizing fasciitis, and other severe inflammatory conditions.

<https://www.ncbi.nlm.nih.gov/pubmed/29370247>

Extracorporeal Hemoperfusion as a Potential Therapeutic Option for Critical Accumulation of Rivaroxaban

Koertge A, Wasserkort R, Wild T, Mitzner S.
Blood Purif 2018; 45:126-128

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Summary

Rivaroxaban is widely used as an oral anticoagulant for prevention of stroke, systemic and pulmonary embolism, and deep vein thrombosis. However, there are issues in patients with impaired renal clearance or overdose which potentially leads to an increased risk of bleeding. In this experimental work the authors applied a model device containing 60 mL of the CytoSorb® adsorbent in an in-vitro recirculation system to remove high plasma concentrations of rivaroxaban from citrate-anticoagulated human whole blood (1,000 mL, flow rate 40 mL/min) during 120 min of hemoperfusion. Results showed that within 1 hour of circulation 91.6% of the drug had been removed by the CytoSorb® adsorbent. The same circulation system without CytoSorb® showed only minor depletion and loss over a test period of 5 hrs. The results suggest that CytoSorb® hemadsorption columns may offer a suitable means to rapidly reverse the anticoagulant effect of rivaroxaban in-vivo.

<https://www.karger.com/Article/FullText/484923>

Removal of bile acids by extracorporeal therapies: an in vitro study

Hartmann J, Harm S.
Int J Artif Organs 2018; 41(1):52-57

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Summary

Bile acids (BAs) that accumulate in the circulation in patients with liver failure are considered to be responsible for direct toxic effects and pruritus. The aim of this study was the in vitro characterization of different BAs regarding their removability with high-flux dialysis and different adsorbents (including CytoSorb®). Dialysis experiments were conducted in pediatric circuits with human plasma. For the adsorption studies, batch tests using 10% adsorbent in spiked human plasma were carried out. The study found that with high-flux dialysis, only BAs such as glycocholic and taurocholic acid could be removed efficiently, while all tested BAs were removed by adsorption, including the CytoSorb® adsorbent. In conclusion, adsorption-based systems offer particular advantages for the removal of hydrophobic bile acids.

<https://www.ncbi.nlm.nih.gov/pubmed/28885663>

Hemoadsorption corrects hyperresistinemia and restores anti-bacterial neutrophil function

Bonavia A, Miller L, Kellum JA, Singbartl K.

Intensive Care Med Exp 2017; 5(1):36

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Summary

Resistin is an inflammatory cytokine and uremic toxin. Elevated levels of resistin (hyperresistinemia) in septic patients have been associated with greater disease severity and worse outcomes. Septic hyperresistinemia impairs neutrophil migration, a crucial first-line mechanism in the body's defense against bacterial infection. In this experimental study the effects of hyperresistinemia on other neutrophil defense mechanisms were studied, as well as the effects of hemoadsorption with CytoSorb® (and a second, clinically non-approved, adsorbent material) on hyperresistinemia and neutrophil dysfunction. Thirteen patients with septic shock and six control patients were analyzed for serum resistin levels and the effect on neutrophil migration. Patients with septic shock had higher serum resistin levels than the control patients. In vitro, neutrophils exposed to hyperresistinemia exhibited twofold lower bacterial clearance rate from the cells compared to controls. Hemoadsorption with CytoSorb® (and the second adsorbent material) reduced resistin levels and thereby restored normal intracellular bacterial clearance. CytoSorb® may therefore provide a therapeutic option to improve neutrophil function during septic hyperresistinemia and ultimately alleviate immunosuppression in this disease state.

<https://www.ncbi.nlm.nih.gov/pubmed/28779451>

Ticagrelor Removal From Human Blood

Angheloiu GO, Gugiu GB, Ruse C, Pandey R, Dasari RR, Whatling C.

JACC: Basic to Translational Science 2017; 2(2):135–145

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Summary

The authors devised a method for ticagrelor removal (platelet aggregation inhibitor) from blood using CytoSorb® hemadsorption in two sets of in-vitro experiments. The first was a first-pass experiment using bovine serum albumin (BSA) solution pre-incubated with ticagrelor, whereas the second set, performed in a recirculating manner, used human blood mixed with ticagrelor. In the recirculation set up, Ticagrelor removal from BSA solution and human blood reached values of over 90% after only 3 - 4 hours. CytoSorb® hemadsorption was found to robustly remove ticagrelor from both BSA solutions and human blood samples.

<https://www.ncbi.nlm.nih.gov/pubmed/30167561>

Polystyrene-Divinylbenzene-Based Adsorbents Reduce Endothelial Activation and Monocyte Adhesion Under Septic Conditions in a Pore Size-Dependent Manner

Eichhorn T, Rauscher S, Hammer C, Groger M, Fischer MB.

Inflammation 2016; 39(5):1737-1746

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Summary

The endothelium is the tissue that acts as a barrier between the blood stream and surrounding tissues. Endothelial activation with excessive recruitment and adhesion of immune cells plays a central role in the progression of sepsis. This study studied endothelial activation induced by plasma from highly septic patients and demonstrated the ability of polystyrene-divinylbenzene-based adsorbents (CytoSorb® and Amberchrom) to reduce endothelial activation in a pore size-dependent manner. Blood from septic patients was taken on admission to ICU, 1 hr and 24 hrs later. Primary monocytes were isolated and their purity and viability determined. Venous blood was obtained from healthy volunteers. Blood from both sets of patients was diluted and passed through the adsorbents. Following this the blood was then passed over an endothelial layer. Results showed that treatment of stimulated whole blood with polystyrene-divinylbenzene-based cytokine adsorbents prior to passage over the endothelial layer resulted in significantly reduced endothelial cytokine and chemokine release, plasminogen activator inhibitor-1 secretion, adhesion molecule expression, and in diminished monocyte adhesion. Plasma samples from septic patients differed substantially in their potential to induce endothelial activation and monocyte adhesion despite their almost identical interleukin-6 and tumor necrosis factor-alpha levels. Data support the potential of porous polystyrene-divinylbenzene-based, including CytoSorb®, to reduce endothelial activation under septic conditions by depletion of a broad range of inflammatory mediators.

<http://www.ncbi.nlm.nih.gov/pubmed/27503310>

Removal of bilirubin with a new adsorbent system: in vitro kinetics

Faenza S, Ricci D, Mancini E, Gemelli C, Cuoghi A, Magnani S, Atti M.
Crit Care 2016; 20(Suppl 2):P192

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Summary

The authors performed an in vitro study on bilirubin kinetics removal to verify the adsorption capacity of CytoSorb® and the ability to remove protein-bound solutes. The study showed the effectiveness of CytoSorb® in removing irreversibly bilirubin, without significant loss of albumin. CytoSorb® might represent a valid and simple aid in organ dysfunctions, without need of plasma separation. In vivo studies are ongoing to confirm the in vitro results.

[Link to Article](#)

Leukocyte capture and modulation of cell-mediated immunity during human sepsis: an *ex vivo* study

Rimmele T, Kaynar AM, McLaughlin JN, Bishop J, Fedorchak M, Chuasuwan A, Peng Z, Singbartl K, Frederick D, Zhu L, Carter M, Federspiel W, Zeevi A, Kellum JA.
Crit Care 2013; 17(2):R59

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Summary

This *ex vivo* study using human whole blood tested the hypothesis whether leukocyte capture modulates inflammatory cytokines and immune cell function. Specially designed miniaturized extracorporeal blood purification devices (including mini cartridges with CytoSorb® beads in two different sizes) were capable of capturing not only inflammatory mediators but also activated leukocytes (primarily neutrophils and monocytes). The effects of this therapy on inflammation and immune function were examined.

<http://www.ncbi.nlm.nih.gov/pubmed/23531333>

Modeling competitive cytokine adsorption dynamics within hemoadsorption beads used to treat sepsis

Kimmel JD, Harbert EM, Parker RS, Federspiel WJ.
J Chromatogr A 2011; 1218(44):8013-8020

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Summary

This study investigated in vitro whether competitive adsorption of serum solutes affected cytokine removal dynamics (IL-6) within the CytoSorb® beads and found that competitive adsorption effects seem negligible at physiologic cytokine concentrations (<1 ng/ml).

<http://www.ncbi.nlm.nih.gov/pubmed/21962329>

Characterizing accelerated capture of deoligomerized TNF within hemoadsorption beads used to treat sepsis

Kimmel JD, Lacko CS, Delude RL, Federspiel WJ.
J Biomed Mater Res B Appl Biomater 2011; 98(1):47-53

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Summary

This in vitro study examined the dynamics of TNF capture within the CytoSorb® beads and quantified how perturbation of TNF oligomeric structure accelerated TNF removal within the device. The authors found that dissociation of TNF into its smaller monomeric constituents significantly accelerated TNF capture rates and therefore propose strategies to promote localized TNF deoligomerization at the sorbent surface.

<http://www.ncbi.nlm.nih.gov/pubmed/21504054>

IL-6 adsorption dynamics in hemoadsorption beads studied using confocal laser scanning microscopy

Kimmel JD, Gibson GA, Watkins SC, Kellum JA, Federspiel WJ.
J Biomed Mater Res B Appl Biomater 2010; 92(2):390-396

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Summary

In this in vitro study the authors used confocal laser scanning microscopy (CLSM) to directly examine adsorption dynamics of fluorescently labeled IL-6 within hemoadsorption beads.

<http://www.ncbi.nlm.nih.gov/pubmed/19904819>

Characterization of a Novel Sorbent Polymer for the Treatment Of Sepsis

Valenti IE.

Master Thesis 2010

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Summary

Objective of this in vitro study was to characterize the CytoSorb® polymer with respect to its adsorption properties of cytokines in different media with increasing complexity (buffer, serum, whole blood).

[Link to Article](#)

A simple mathematical model of cytokine capture using a hemoadsorption device

DiLeo MV, Kellum JA, Federspiel WJ.

Ann Biomed Eng 2009; 37(1):222-229

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Summary

In this in silico study the authors presented a bio-mathematical model which can calculate adsorption/removal-dynamics of different cytokines (TNF, IL-6, IL-10) in the CytoSorb® cartridge. They state that the removal rate of individual cytokines only depends on a single cytokine-polymer specific parameter (Γ_i). The model and the theoretically calculated removal dynamics correlated well with experimental data from an in vivo-performed reference study (rats with endotoxemia).

<http://www.ncbi.nlm.nih.gov/pubmed/18949559>

In-Vitro Myoglobin Clearance by a Novel Sorbent System

Kuntsevich VI, Feinfeld DA, Audia PF, Young W, Capponi V, Markella M, Winchester JF.

Artif Cells, Blood Substitutes and Biotechnology 2009; 37(1):45-47

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Summary

Rhabdomyolysis (excessive break-down of muscle tissue due to crush injury, infection, drugs etc.) can result in acute kidney injury from myoglobinuria when the myoglobin released into the blood from damaged muscle passes through the glomerular filter and accumulates in the renal tubules. The aim of this in vitro study was to investigate, whether hemoadsorption (using CytoSorb®) was potentially useful to effectively reduce myoglobin levels (myoglobin dissolved in 1) Normal saline and 2. In serum of three donors).

<http://www.ncbi.nlm.nih.gov/pubmed/19132637>

Hemoadsorption to improve organ recovery from brain-dead organ donors: a novel therapy for a novel indication?

Venkataraman R, Song M, Lynas R, Kellum JA.

Blood Purif 2004; 22(1):143-149

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Summary

The usefulness of CytoSorb® for in maintaining organ function (liver, kidney, heart) in brain-dead donors is discussed in this study. As a 'proof of concept' in vitro experiment the authors tested the ability of hemoadsorption to remove S100B (released from damaged brain cells exhibiting cytokine-like properties) using two human glioblastoma cell lines.

<http://www.ncbi.nlm.nih.gov/pubmed/14732823>

Sorbents in acute renal failure and end-stage renal disease: middle molecule and cytokine removal

Winchester JF, Silberzweig J, Ronco C, Kuntsevich V, Levine D, Parker T, Kellum JA, Salsberg JA, Quartararo P, Levin NW.

Blood Purif 2004; 22(1):73-77

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Summary

This study discusses the use of hemoadsorption in acute and chronic renal failure (both inflammatory states) to reduce cytokine- and middle molecule levels. CytoSorb® is discussed in detail. Data are presented that show the use of CytoSorb® as well as CytoSorb® plus conventional high-flux dialysis in patients with chronic renal failure. Results confirm that removal of β_2 -microglobulin, angiogenin, leptin and IL-18 is much more effective when using combined therapy (CytoSorb® plus conventional high-flux dialysis). Levels of leucocytes, thrombocytes and albumin were hardly affected.

<http://www.ncbi.nlm.nih.gov/pubmed/14732814>

In vitro removal of therapeutic drugs with a novel adsorbent system

Reiter K, Bordoni V, Dall'Olio G, Ricatti MG, Soli M, Ruperti S, Soffiati G, Galloni E, D'Intini V, Bellomo R, Ronco C.

Blood Purif 2002; 20(4):380-388

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Summary

Aim of this in vitro study was to investigate the potential of CytoSorb® to effectively eliminate therapeutically administered drugs (mainly in intensive care) of middle molecular weight from uremic blood. In addition, the authors emphasize the good biocompatibility of CytoSorb®.

<http://www.ncbi.nlm.nih.gov/pubmed/12169849>

3. Background & Reviews

NEW; Systematic review with expert consensus on use of extracorporeal hemoadsorption in septic shock: An Indian perspective

Mehta Y, Ansari AS, Mandal AK, Chatterjee D, Sharma GS, Sathe P, Umraniya PV, Paul R, Gupta S, Singh V, Singh YP.

World J Crit Care Med 2024; 13(1):89026

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Summary

The aim of this expert consensus panel was to formulate consensus statements on the use of CytoSorb hemoadsorption from best available evidence, contextualized to the Indian scenario. Based on a systematic literature search covering articles published between January 2011 to March 2023, nine consensus statements were developed and considered by 11 expert members from critical care and emergency medicine. After three voting rounds using a Delphi approach, consensus was achieved on all nine statements. These included the following recommendations and statements; ideally starting CytoSorb within 24 hrs of refractory septic shock, not making interleukin (IL) 6 levels a mandatory parameter to decide on starting CytoSorb, the potential need for more than one adsorber in some patients, change of adsorber 6 – 24 hrs depending on clinical course, that CytoSorb is a generally safe therapy, and evaluation of efficacy be based on proximal endpoints such as hemodynamic stabilization, inflammatory biomarkers and/or improvements in organ function rather than mortality. The consensus expert panel also recognised the necessity to form an association or society that can keep a registry regarding the use of CytoSorb for all indications. The authors conclude that it is hoped that this consensus statement will help in facilitating proper treatment, initiation and maintenance of CytoSorb therapy for the optimization of management of refractory septic shock patients in India.

[Link to article](#)

Hemoadsorption in infective endocarditis: a systematic review

Thielmann M, Dohle DS, Czerny M, Bonaros N, Wendt D, Folliguet T, Baufreton C, Lebreton G.

Indian J Thoracic and Cardiovascular Surg 2024; epub

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Summary

This systematic review included literature published on the use of CytoSorb in patients undergoing surgery for infective endocarditis (IE). Thirteen studies were identified, including three randomized control trials (RCTs), with single case reports excluded. All the literature is then described in detail, in chronological order, before a basic research, budget impact publication and previous review and meta-analysis are also discussed. Overall, it is noted that evidence is mixed regarding CytoSorb use in IE, particularly in routine elective surgery and low-risk patients. However, in at-risk patients, there is evidence of reduced rates of sepsis and / or sepsis associated mortality, and reductions in plasma cytokine levels. There is also evidence of reduced overall mortality, reduced inotropic support (better hemodynamic stability), and lesser amounts of transfused blood products. It is concluded that appropriate selection criteria be developed for the use of CytoSorb to target the right patient population (e.g patients with an ongoing infection on antibiotic therapy). Timing and dosing also need to be further evaluated, including potential post-operative use. Finally, the advantage of hemoadsorption is that it offers the possibility of stabilizing hemodynamics, reducing sepsis-related mortality and protecting organ function.

[Link to Article](#)

A Contemporary Review of the Use of Extracorporeal CytoSorb® Hemoadsorption Therapy in Patients with Infective Endocarditis

Gong A, Li Y, Yang M, Wang S, Su B.

J Clin Med 2024; 13(3):763

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Summary

In this review the use of CytoSorb as an adjuvant hemoadsorption therapy to mediate the inflammatory response in patients with infective endocarditis (IE) undergoing cardiac surgery is described. The authors explain the rationale and clinical evidence for hemoadsorption in such patients, and then take an in-depth look at the various publications in this field. The authors note that there are conflicting results in the literature, highlighting the fact that the use of hemoadsorption should be in properly selected cardiopulmonary bypass (CPB) patients, taking into account the treatment timing, duration, and dose. CytoSorb was found to be safe and well tolerated with no device related adverse events during or after CPB. Health economic benefits are also described, although need confirming with further prospective analysis. It is noted that the majority of clinical evidence includes only European participants and therefore future trials should also take into account differences in genetics and clinical practice patterns across different populations and countries. In conclusion, although the safety profile is strong, the effect of CytoSorb. on some patient-centered outcomes remains controversial in IE patients who undergo cardiac surgery with CPB. Therefore, additional evidence from large, well-designed randomized controlled trials, including the timing of initiation, treatment duration, frequency of filter change, and dose adjustment of antibiotics, is recommended to clarify the best patient groups who will benefit from CytoSorb hemoadsorption in the future.

<https://www.ncbi.nlm.nih.gov/pubmed/38337456>

Hemoadsorption in Organ Preservation and Transplantation: A Narrative Review

Garcia-Villegas R, Arni S.

Life (Basel) 2023; 14(1):65

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Summary

In this comprehensive narrative review the authors explore how the role of cytokine adsorption can resolve different complications that occur in transplantation medicine, either during the surgical procedure, or before surgery with ex-vivo graft treatment, including potential cytokine storm activation, blood ABO and immune incompatibilities. Different methods of cytokine adsorption are included, including CytoSorb, Jafron adsorbers, oXiris, Molecular Adsorbent Recirculating System (MARS) and polymyxin B. It is noted that cytokine adsorption is also performed for the treatment of various life-threatening conditions, such as endotoxic septic shock, acute respiratory distress syndrome, and cardiogenic shock, all potentially leading to adverse clinical outcomes during transplantation. The review considers all research done in-vivo, in animals and in humans, with CytoSorb being by far the most commonly used form of adsorption. There are multiple benefits of adsorption listed for lung, heart, kidney and liver transplantation including decreases in cytokines, vasopressor use, in-hospital mortality, decreases in bilirubin (liver transplant) and increases in lung compliance (for lung transplant). The authors note that after surgery, dysmetabolism and stress response limit successful graft survival and can lead to primary or secondary graft dysfunction. In this clinical context, and given that a major problem in transplant medicine is that the demand for organs far exceeds the supply, a technological innovation such as a hemoadsorption system could greatly contribute to increasing the number of usable organ donors. In summary, this review describes the specific advantages and disadvantages of the application of cytokine adsorption in the context of transplantation and examine, before and/or after organ transplantation, the benefits of the addition of a cytokine adsorption therapy protocol.

<https://www.ncbi.nlm.nih.gov/pubmed/38255680>

Hemoadsorption in acute respiratory distress syndrome patients requiring venovenous extracorporeal membrane oxygenation: a systematic review

Li W, Chen Y, Li D, Meng X, Liu Z, Liu Y, Fan H.

Respir Res 2024; 25(1): 27

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Summary

This systematic review included all publications with patients on venovenous extracorporeal membrane oxygenation (VV ECMO) for severe acute respiratory distress syndrome (ARDS) plus hemoadsorption. In total eight articles were

included with 189 patients. In all studies CytoSorb hemoadsorption was used. Most studies described reductions in inflammatory markers and fluid resuscitation requirements in ARDS patients with Coronavirus disease 2019 (COVID-19) or sepsis following hemoadsorption as well as reduced doses of hemodynamic related drugs. Because studies included patients with different pathologies the authors are very careful with their conclusions that hemoadsorption therapy may enhance hemodynamic stability in ARDS patients with COVID-19 or sepsis receiving VV ECMO support, while the results do not allow any conclusions to be drawn that hemoadsorption could reduce inflammation and mortality. In the future larger multicenter randomized prospective studies are needed, however, the authors end with stating that the combination of ECMO and hemoadsorption may be a new strategy to reduce cytokine storm, promote lung rest, and prolong the time to the next targeted treatment for ARDS patients.

<https://www.ncbi.nlm.nih.gov/pubmed/38217010>

Hemoadsorption Therapy for Critically Ill Patients with Acute Liver Dysfunction: A Meta-Analysis and Systematic Review

Turan C, Szigetváry CE, Kóti T, Engh MA, Atakan I, Zubek L, Terebessy T, Hegyi P, Molnár Z.
Biomedicines 2024; 12(1):67

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Summary

This systematic review and meta-analysis assessed the evidence on clinical outcomes following hemoadsorption therapy in patients with acute liver dysfunction as part of multiorgan failure sequelae. The search yielded 30 eligible publications from between 2011 and 2023, reporting on the use of hemoadsorption in 335 patients presenting with liver dysfunction related to acute critical illness. CytoSorb was the main hemoadsorption technique used (23 datasets, n = 232), next to Coupled Plasma Filtration Adsorption (4, n = 88), oXiris (2, n = 2), and CytoSorb + oXiris (1, n = 1). Of those 30 publications, 26 were case presentations (n = 84), 3 were observational studies (n = 142), and 1 was a registry analysis (n = 109). Data pooled from 160 patients showed a significant reduction in total bilirubin levels post treatment (mean difference of -4.79 mg/dL (95% CI: -6.25; -3.33), p = 0.002). Analysis of the data from individual cases showed a significant reduction in levels of aspartate transaminase (p = 0.03) and vasopressor need (p = 0.03) and a tendency to lower levels of total bilirubin, alanine transaminase, C-reactive protein, and creatinine. The authors conclude that the use of hemoadsorption for critically ill patients with acute liver dysfunction or failure seems to be safe and yields a trend towards improved liver function after therapy, but more high-quality evidence is crucially needed.
<https://www.ncbi.nlm.nih.gov/pubmed/38255174>

The potential role of extracorporeal cytokine removal with CytoSorb® as an adjuvant therapy in Acute Respiratory Distress Syndrome

Tomescu D, Popescu M, Akil A, Nassiri AA, Wunderlich-Sperl F, Kogelmann K, Molnar Z, Alharthy A, Karakitsos D.

Int J Artif Orgs 2023; 46(12):605-617

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Summary

In this narrative review the role of CytoSorb® in the management of patients with acute respiratory distress syndrome (ARDS) is summarized. An overview of the pathophysiology and rationale for the use of CytoSorb® in patients with hyperinflammatory ARDS is given along with a summary of the literature published so far on this topic. The authors note that there are an increasing number of published case series and case reports that shed light on promising clinical effects. Of interest, most of the available data is derived from ARDS patients requiring extracorporeal membrane oxygenation (ECMO) therapy as well as from critically ill Coronavirus Disease 2019 (COVID-19) patients. One common phenotype of ARDS is that of a secondary injury to a dysregulated inflammatory host response, so - in cases of hyperinflammation - immunomodulation by extracorporeal cytokine removal such as with the CytoSorb® hemoadsorption cartridge could conceptually enhance lung recovery during the early course of the disease. In summarizing the literature, the authors state that an earlier start of CytoSorb® therapy seems to be advantageous. As ARDS is often associated with severe hemodynamic instability and also with septic shock, it is recommended to continue CytoSorb® therapy until there is sufficient hemodynamic stabilization, with the option to use additional adsorbers if required. In the most severe cases, changing the first and second adsorber after 8-12 hours may ensure maximum removal capacity, however this should be addressed in future studies. Treatment duration is often for 2 – 3 days. The combined and early use of ECMO and hemoadsorption could also represent a novel strategy to promote enhanced lung rest in patients with ARDS. The review supports the concept of adjuvant hemoadsorption

therapy in patients with severe ARDS as it has shown consistently positive findings in regards to improvement in lung function and oxygenation, attenuation of the inflammatory response as well as a positive effect on hemodynamic stabilization and metabolic parameters while having a very good safety profile without major device-related adverse events being reported to date.

<https://www.ncbi.nlm.nih.gov/pubmed/38037333>

A potential approach toward the management of sepsis: The extracorporeal cytokine hemadsorption therapy

Yildiz AB, Copur S, Tanriover C, Yavuz F, Vehbi S, Hasbal NB, Kanbay M.

Semin Dial 2024; 37(2):117

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Summary

In this narrative review the authors look at the role extracorporeal cytokine hemoabsorption (with CytoSorb®) has in patients with hyper-inflammatory response syndromes caused by sepsis and septic shock. They note that despite the improvements in treatments and diagnostic modalities, morbidity and mortality rates remain relatively high among intensive care unit (ICU) patients. The authors evaluate the current pre-clinical and clinical literature regarding CytoSorb® use in patients with septic shock and also COVID-19. Issues such as timing, optimal duration and careful patient selection are discussed in order to maximum therapy response and outcome. Benefits of CytoSorb® use are given as reductions in cytokines and inflammatory parameters, vasopressors and invasive mechanical ventilation need, and increase in oxygenation (PF ratio). Finally the authors state that 'extracorporeal cytokine hemoabsorption systems are promising therapeutic alternative for critically ill patients despite the lack of clear beneficial effects on mortality based on the current literature'.

<https://www.ncbi.nlm.nih.gov/pubmed/38084784>

Adjunctive hemoabsorption therapy with CytoSorb in patients with septic/vasoplegic shock: A best practice consensus statement

Mitzner S, Kogelmann K, Ince C, Molnar Z, Ferrer R, Nierhaus A.

J Clin Med 2023; 12(23):7199

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Summary

In this consensus statement, the authors summarize the existing evidence on the use of CytoSorb® in patients with septic / vasoplegic shock in order to provide consensus guidance based best practice. The properties of the CytoSorb® device are discussed before its effects on circulating cytokines and also regarding improvements in hemodynamic stability are described. Evidence regarding patient selection, timing of therapy initiation and dosing duration is also examined. The therapeutic strategy of CytoSorb® is described as modulating the host response to infection and mitigating organ dysfunction at an early time point. The safety profile of CytoSorb® appears favorable, with ongoing efforts to further expand knowledge regarding use through prospective and retrospective data collection, including registries. In summary, this consensus statement describes the insights gained from the clinical use of the device in patients with septic vasoplegic shock over the past decade. CytoSorb® is described as a promising and safe adjuvant treatment option for critically ill patients with severe hyperinflammatory conditions that are not responding to standard medical therapy.

<https://www.ncbi.nlm.nih.gov/pubmed/38068250>

Hemoabsorption as Adjuvant Therapy in Acute Respiratory Distress Syndrome (ARDS): A Systematic Review and Meta-Analysis

Szigetváry CE, Turan C, Kovács EH, Kóti T, Engh MA, Hegyi P, Csukly G, Ruzskai Z, Molnár Z.

Biomedicines 2023; 11(11):3068

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Summary

The aim of this systematic review and meta-analysis was to investigate the effects of adjunctive hemoabsorption (HA) on clinical and laboratory outcomes in patients with acute respiratory distress syndrome (ARDS). The authors performed a systematic literature search in PubMed, Embase, CENTRAL, Scopus, and Web of Science for studies including patients receiving HA therapy for ARDS. The primary outcome was the change in PaO₂/FiO₂ before and after HA therapy as a measure of respiratory function. Secondary outcomes included the before and after values for C-reactive protein (CRP), lactate, interleukin-6 (IL-6), and norepinephrine (NE) doses. Twenty six publications, with 243 patients (198 undergoing HA therapy and 45 controls) were included. From this 23 studies were with CytoSorb®, and the rest with HA330 and HA380 and oXiris®. There was a significant improvement in PaO₂/FiO₂ ratio following HA therapy (p = 0.005) and a

reduction in CRP levels ($p = 0.026$) and NE dose ($p = 0.028$). The authors found a non-significant reduction in mortality in patients receiving HA therapy with a 'very low' certainty of evidence. A (non-significant) reduction in platelets was noted in three publications but these were not reported as adverse events. It remains uncertain whether this was the result of the extracorporeal circulation or the hemoadsorption device. The authors conclude that use of HA resulted in a significant improvement in oxygenation and a reduction in NE dose and CRP levels in patients treated with ARDS without any serious adverse events reported. This data could be useful for designing high-quality trials in the future.

<https://pubmed.ncbi.nlm.nih.gov/38002070/>

An In-Depth Analysis of the Multi-Faceted Benefits of CytoSorb Filter Utilization during Cardiopulmonary Bypass

Butt SP, Pandey G, Aziz R, Phillips S, Saleem Y, Ashiq F, Darr U, Bhatnagar G.

Journal of Critical Care & Emergency Medicine 2023;2(9):1-6

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Summary

This review describes the use of CytoSorb® as a potential adjunctive therapy to mitigate inflammation triggered by cardiopulmonary bypass (CPB). A literature review was conducted and various databases were searched using relevant keywords. Results showed mixed results regarding CytoSorb®'s efficacy in reducing pro-inflammatory cytokines and for improving clinical outcomes. Some studies reported reduced cytokine levels, improved hemodynamics, and decreased need for vasopressors, however, others found no significant cytokine reduction or clinical improvement. For all studies, CytoSorb® was generally well-tolerated with no device-related serious adverse events reported. Additionally, CytoSorb® demonstrated potential benefits in reducing bleeding complications when used during cardiac surgery in patients taking antiplatelet or anticoagulant medications. The authors state that the use of CytoSorb® in cardiac surgery with CPB offers potential benefits but requires further research. Future directions should include evaluating long-term benefits and safety, refining patient selection criteria, conducting comparative studies, standardizing guidelines for CytoSorb® integration, and exploring its utility in other cardiac surgery scenarios.

[Link to Article](#)

Cytokine hemoadsorption with CytoSorb® in patients with sepsis: a systematic review and meta-analysis

Saldana-Gastulo JJC, Llamas-Barbaran MDR, Coronel-Chucos LG, Hurtado-Roca Y.

Crit Care Sci 2023; 35(2):217-225

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Summary

The objective of this study was to analyze the effect of CytoSorb® on mortality, interleukin levels, vasopressor use and adverse events in patients with sepsis. The authors searched MEDLINE®, Embase and the Cochrane Library for randomized controlled trials and cohort studies that reported the use of CytoSorb® among septic patients. In total 6 studies enrolling 413 patients were included. Assessment for risk of bias indicated variations in study quality from high to moderate. The overall mortality rate was 45% (42% intervention group and 48% control group), with no significant effect on mortality found at 28 - 30 days. A meta-analysis for other outcomes was not done due to the small number of studies found or the lack of data. The authors conclude that there was a very low certainty evidence, due to imprecision, risk of bias, and heterogeneity in the studies analyzed, showing no benefit of CytoSorb® use in terms of mortality at 28 - 30 days. It is recommended that high-quality randomized trials with a common intervention arm are needed to evaluate the influence of CytoSorb® in this population.

<https://www.ncbi.nlm.nih.gov/pubmed/37712812>

Hemoadsorption Using CytoSorb® in Patients with Infective Endocarditis: A German-Based Budget Impact Analysis

Rao C, Preissing F, Thielmann M, Wendt D, Haidari Z, Kalisnik JM, Daake L, Traeger K.

J Cardiovascular Development and Disease 2023; 10(9):366

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Summary

The purpose of this analysis was to theoretically investigate the budget impact of a reduced intensive care stay in infective endocarditis (IE) patients treated with intraoperative CytoSorb® in the German Healthcare System. Use of intraoperative hemoadsorption was found to result in 2,298€ saved per patient in the base-case scenario without therapy reimbursement. Savings increased to 3,804€ per patient where there was full device-specific reimbursement. Deterministic and probabilistic sensitivity analyses confirmed the robustness of savings, with a probability of savings of 99% and 100% in the base-case and full reimbursement scenarios, respectively. In summary, intraoperative hemoadsorption in IE patients might have relevant economic benefits

related to reduced ICU stay, resulting in improved resource use. Further evaluations in larger prospective cohorts are warranted.

<https://pubmed.ncbi.nlm.nih.gov/37754795/>

The Effect of CytoSorb on Inflammatory Markers in Critically Ill Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Heymann M, Schorer R, Putzu A.

Crit Care Med 2023; 51(12):1659-1673

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Summary

The purpose of this systematic review and meta-analysis was to review the literature reporting on the effectiveness of CytoSorb® at removing inflammatory mediators in critically ill patients. Electronic databases were searched to May 2023 and randomized controlled trials reporting on inflammatory parameters in critically ill patients with hyperinflammatory conditions on CytoSorb® included. Seventeen trials (n = 855) were identified with 7 performed in medical ICU patients with hyperinflammatory conditions and 10 in complex cardiovascular surgery under cardiopulmonary bypass. Overall, the reported levels of interleukin (IL)-6 were low. Hemoadsorption with CytoSorb® was not associated with lower IL-6 at (mean difference -5.98 [95% CI, -30.44 to 18.48] pg/mL) after initiation of the treatment, as well as the concentration of procalcitonin. The levels of C-reactive protein were not lower with CytoSorb® use. The use of CytoSorb® was associated with higher mortality at latest follow-up (relative risk = 1.22 [95% CI, 1.02-1.45]) and at 30 days. However, as the authors note, the certainty of evidence (CoE) in this regard was very low and generally ranged from low to very low only. The authors noted that heterogeneity could arise from the different time points and techniques used to measure markers. Also, that analysis based on changes from baseline is often more efficient and powerful than comparing post intervention values, but the lack of individual patient data or of aggregate change-from-baseline data did not allow further exploration in this analysis. In conclusion the authors state that the use of CytoSorb® hemoadsorption in a mixed population of critically ill patients with hyperinflammatory conditions does not exhibit a consistent decrease in IL-6 and other inflammatory parameters within the first 5 days of treatment. The uncertainty surrounding these findings highlights the need for further investigation.

Comment from CytoSorbents:

Despite being published in March 2023, the recent RCT by Jansen et al., *Crit Care* 2023; 27(1):117 that provides irrevocable mechanistic proof that treatment with CytoSorb® has an impact in hyperinflammation with high levels of cytokines, was not included in the analysis.

<https://www.ncbi.nlm.nih.gov/pubmed/37607074>

Cost-Effectiveness and Budget Impact of a Novel Antithrombotic Drug Removal System to Reduce Bleeding Risk in Patients on Preoperative Ticagrelor Undergoing Cardiac Surgery

Cohen BG, Chingcuanco F, Zhang J, Reid NM, Lee V, Hong J, Deliarhyris EN, Padula WV.

Am J Cardiovasc Drugs 2023; 23(4):429-440

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Summary

This aim of this article was to estimate the cost-effectiveness and budget impact of using CytoSorb® intraoperatively versus standard practice for reducing the risk of perioperative bleeding during and after coronary artery bypass grafting from the US healthcare sector perspective. The well established and recognised Markov model was used to analyze the cost-effectiveness and budget impact of CytoSorb® in three cohorts: (1) surgery within 1 day from last ticagrelor dose; (2) surgery between 1 and 2 days from last ticagrelor dose; and (3) a combined cohort. The model analyzed costs and quality-adjusted life years (QALYs). Results were interpreted as both incremental cost-effectiveness ratios and net monetary benefits (NMBs) at a cost-effectiveness threshold of \$100,000/QALY. Results showed that CytoSorb® hemoadsorption was dominant for each cohort. Patients with less than 1 day of washout in the device arm gained 0.017 QALYs at a savings of \$1748 (USD), for an NMB of \$3434. In patients with 1-2 days of washout, the device arm yielded 0.014 QALYs and a cost savings of \$151, for an NMB of \$1575. In the combined cohort, device gained 0.016 QALYs and a savings of \$950 for an NMB of \$2505. Per-member-per-month cost savings associated with device was estimated to be \$0.02 for a one-million-member health plan. On the basis of the probabilistic sensitivity analyses, use of CytoSorb® had a 91% likelihood of being dominant for patients with less than 1 day of washout, and a 99% likelihood of being cost-effective at a \$100,000/QALY threshold. For patients with 1–2 days of washout, use of the device had a 54% likelihood of being dominant and a 90% likelihood of being cost-effective at a \$100,000/QALY threshold. The authors conclude that the use of intraoperative extracorporeal

hemoadsorption is a dominant strategy compared with standard of care for CABG patients on ticagrelor with less than 2 days of washout. Thus, this novel device can be adopted for cardiac surgery patients on ticagrelor to provide better clinical outcomes at lower healthcare costs.

<https://www.ncbi.nlm.nih.gov/pubmed/37204675>

Efficacy of CytoSorb®: a systematic review and meta-analysis

Becker S, Lang H, Vollmer Barbose C, Tian Z, Melk A, Schmidt BMW.

Crit Care 2023; 27:215

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Summary

In this meta-analysis the authors searched various databases regarding the efficacy of the CytoSorb® device with regard to mortality in various settings between 2010 to May 2022. All randomized controlled trials and intervention studies with control groups were considered, with the longest reported mortality defined as the primary endpoint. All studies were analyzed together as well as divided into the subgroups: sepsis, cardiac surgery, other severe illness, SARS-CoV-2 infection, and recovery from cardiac arrest. From 1295 publications, 34 studies were found eligible, including 1297 patients treated with CytoSorb® and 1314 controls. It was found that CytoSorb® did not lower mortality in all studies together, or in the subgroups. In patients with cardiac arrest, a significant survival advantage of the untreated controls was found. The authors note that there was wide heterogeneity between the studies with substantial differences found in the results. Use of CytoSorb® (number of adsorbers, time to initiation of adsorber, length of use etc.) also differed greatly. They conclude that to date there is no evidence for a positive effect of the CytoSorb® adsorber on mortality across a variety of indications that justifies its widespread use in intensive care medicine.

<https://www.ncbi.nlm.nih.gov/pubmed/37259160>

Reversal and removal of oral antithrombotic drugs in patients with active or perceived imminent bleeding

Cao D, Amabile N, Chiarito M, Lee VT, Angiolillo DJ, Capodanno D, Bhatt DL, Mack MJ, Storey RF, Schmoedel M, Gibson CM, Deliargyris EN, Mehran R.

Eur Heart J 2023; 44(20):1780-1794

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Summary

Remarkable progress has been made in the pharmacological management of patients with cardiovascular disease, including the frequent use of antithrombotic agents. Nonetheless, bleeding complications remain frequent and potentially life-threatening. This state of the art review describes the therapeutic interventions that rely on prompt antithrombotic drug reversal or removal that have been developed to assist clinicians in treating patients with active bleeding or an imminent threat of major bleeding due to urgent surgery or invasive procedures. Therapeutic interventions such as reversal agents for antithrombotic drugs as well as other hemostatic agents are described, along with their drawbacks. These include the possible prothrombotic effects associated with the withdrawal of the antithrombotic protection. The clinical implications of reversal strategies for patients with ongoing major bleeding (e.g. intracranial bleed or gastrointestinal bleed) or threat of major bleeding (e.g. non-deferable surgery) are discussed. Drug removal via hemoadsorption is then discussed on base of available preclinical and clinical results. Although not mentioned by name, the references and a diagram showing the integration into a cardiopulmonary bypass all pertain to the CytoSorb® adsorber. The authors conclude that understanding the ischemic-bleeding risk tradeoff of antithrombotic drug reversal and removal strategies in the context of urgent high-risk settings requires dedicated clinical investigations, but challenges in trial design remain, with relevant practical, financial, and ethical implications.

<https://www.ncbi.nlm.nih.gov/pubmed/36988155>

Extracorporeal blood purification strategies in sepsis and septic shock: An insight into recent advancements

Mehta Y, Paul R, Ansari AS, Banerjee T, Gunaydin S, Nassiri AA, Pappalardo F, Premuzic V, Sathe P, Singh V, Vela ER.

World J Crit Care Med 2023; 12(2):71-88

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Summary

In this study the use of extracorporeal therapies (ECT) for the treatment of dysregulation of the immune system in sepsis / septic shock is reviewed. 68 articles from the last two decades were identified where ECT was used for the removal of inflammatory mediators in sepsis. Results showed that ECT techniques such as high-volume hemofiltration, coupled plasma adsorption/filtration, resin or polymer adsorbers, and CytoSorb® are emerging as adjunct therapies to

improve hemodynamic stability in septic shock. The authors note that CytoSorb® has the most published data regarding use in the field of septic shock with reports of improved survival rates and lowered sequential organ failure assessment (SOFA) scores, lactate levels, total leucocyte count, platelet count, interleukin- IL-6, IL-10, and TNF levels. In clinical practice, however, timing of ECT is still often delayed as doctors see it more as a final rescue therapy. So better guidance with patient selection, timing and dosing has to be compiled and provided to the user at the bedside. Importantly and considering the different ECT systems available in the market, it has to be stated that clinical results, but particularly safety relevant aspects, are not transferable between various hemoadsorption products due to technical differences. In summary, clinical acceptance of ECT in sepsis and septic shock is currently still limited due to a lack of large random clinical trials. In addition to patient-tailored therapies, future research developments with therapies targeting the cellular level of the immune response are expected.

<https://www.ncbi.nlm.nih.gov/pubmed/37034019>

Management of severe perioperative bleeding guidelines from the European Society of Anaesthesiology and Intensive Care

Kietaibl S, Ahmed A, Afshari A, Albaledejo P, Aldecoa C, Barauskas G, De Robertis E, Faraoni D, Filipescu D, Fries D, Godier A, Haas T, Jacob M, Lancé MD, Llau MD, Meier J, Molnar Z, Mora L, Rahe-Meyer N, Samama CM, Scarlatescu E, Schlimp C, Wikkelsø AJ, Zacharowski K.

Eur J Anaesthesiol 2023; 40: 226-304

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Summary

These updated guidelines (previous guidelines 2017) aim to provide an evidence based set of recommendations to help ensure clinical management of patients with perioperative bleeding. A group of experts met and literature from between 2015 – 2021 searched. These searches identified 130,407 articles. All articles were assessed, and the existing guidelines revised to incorporate new evidence. Sixteen recommendations derived from the systematic literature search, and four clinical guidances retained from previous ESAIC guidelines were formulated. Using the Delphi process on 253 sentences of guidance, strong consensus (>90% agreement) was achieved in 97% and consensus (75 to 90% agreement) in 3% of the recommendations. In the section; How should intra-operative and postoperative bleeding be stopped and anaemia be managed, the following recommendation is made for patients undergoing cardiac surgery:

'In patients on ticagrelor or rivaroxaban undergoing emergency cardiac/aortic surgery on CPB, haemoadsorption may be considered as an adjuvant therapy to reduce bleeding complications. 2C'

In conclusion these guidelines aim to provide specific guidance for bleeding management in a variety of clinical situations.

<https://www.ncbi.nlm.nih.gov/pubmed/36855941>

Sepsis-associated acute kidney injury: consensus report of the 28th Acute Disease Quality Initiative workgroup

Zarbock A, Nadim MK, Pickkers P, Gomez H, Bell S, Joannidis M, Kashani K, Koyner JL, Pannu N, Meersch M, Reis T, Rimmel T, Bagshaw SM, Bellomo R, Cantaluppi V, Deep A, De Rosa S, Perez-Fernandez X, Husain-Syed F, Kane-Gill SL, Kelly Y, Mehta RL, Murray PT, Ostermann M, Prowle J, Ricci Z, See EJ, Schneider A, Soranno DE, Tolwani A, Villa G, Ronco C, Forni LG.

Nat Rev Nephrol 2023; 19(6):401-417

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Summary

This is a consensus report on sepsis-associated acute kidney injury (SA-AKI) from a quality initiative workgroup that met in the summer of 2022 to try and develop consensus agreements on a number of issues on this topic using a modified Delphi approach. There were 33 experts in the group from all over the world. A number of consensus were agreed, including definition and epidemiology, pathophysiology (including the role of pathogen and damage-associated molecular patterns -PAMPS and DAMPs leading to dysregulated activation of the immune system), fluid management, biomarkers for diagnosis and guiding treatment, pediatric SA-AKI and the role of extracorporeal therapies (ECT) in SA-AKI. Under this topic, the characteristics of the various technologies used for ECT in SA-AKI are given as well as various consensus statements, two of which address specifically extracorporeal blood purification (EBP):

- **Consensus statement 5a;** EBP techniques can be used to remove pathogens, microbial toxins, inflammatory mediators and toxic metabolites from the blood as well as replenish solutes (grade 1A)
- **Consensus statement 5d** Initiation of EBP in sepsis might be considered for immunomodulatory support in patients who meet explicit and timely clinical and/or biological criteria, such as high

concentrations of damage-associated molecular patterns and pathogen-associated molecular patterns, as well as other targets of systemic inflammation (not graded)

Furthermore the authors state that investigators should refrain from choosing mortality as the primary end point for future clinical studies because of the well-known variation in mortality across centres, sepsis and AKI phenotypes. Randomized control trials (RCTs) examining the effects of EBP, in which patient heterogeneity is reduced through specific inclusion criteria with clinically relevant endpoints, including hemodynamic and organ function improvement, as well as intensive care stay rather than only mortality, should be performed. <https://www.ncbi.nlm.nih.gov/pubmed/36823168>

Rationale for sequential extracorporeal therapy (SET) in sepsis

Ronco C, Chawla L, Husain-Syed F, Kellum JA.

Crit Care 2023; 27(1):50

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Summary

Sepsis and septic shock remain drivers for morbidity and mortality in critical illness. The clinical picture of patients presenting with these syndromes evolves rapidly and may be characterised by a number of factors including:

- (a) microbial host invasion
- (b) establishment of an infection focus
- (c) opsonisation of bacterial products (e.g. lipopolysaccharide)
- (d) recognition of pathogens resulting in an immune response
- (e) cellular and humoral effects of circulating pathogen and pathogen products
- (f) immunodysregulation and endocrine effects of cytokines
- (g) endothelial and organ damage
- (h) organ crosstalk and multiple organ dysfunction.

Each step may be a potential target for a specific therapeutic approach. At various stages, extracorporeal therapies may target circulating molecules for removal in the following ways:

- (a) pathogen removal from the circulation with affinity binders and cartridges (specific)
- (b) circulating endotoxin removal by hemoperfusion with polymyxin B adsorbers (specific)
- (c) cytokine removal by hemoperfusion with sorbent cartridges or adsorbing membranes (non-specific),
- (d) extracorporeal organ support with different techniques for respiratory and cardiac support (CO(2) removal or extracorporeal membrane oxygenation), and renal support (hemofiltration, haemodialysis, or ultrafiltration).

The authors note that the use of different techniques at different points for specific targets would require trials with endpoints other than mortality, where the primary objective should be to achieve the desired action by using extracorporeal therapy at a specific point. The following devices are discussed in detail: Seraph 100, polymyxin B filter, CytoSorb®, Jafron HA330/HA380, and oXiris®.

<https://www.ncbi.nlm.nih.gov/pubmed/36750878>

Targeting circulating high mobility group box-1 and histones by extracorporeal blood purification as an immunomodulation strategy against critical illnesses

Li Y, Chen Y, Yang T, Chang K, Deng N, Zhao W, Su B.

Crit Care 2023; 27(1):77

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Summary

High mobility group box-1 (HMGB1) and histones are major damage-associated molecular patterns (DAMPs) that mediate lethal systemic inflammation, activation of the complement and coagulation systems, endothelial injury and multiple organ dysfunction syndrome in critical illnesses. Although animal models show that targeting HMGB1 or histones by their specific antibodies or inhibitors could significantly mitigate aberrant immune responses, routine clinical use of such agents is still not recommended by any guidelines. This review summarizes the extracorporeal blood purification technologies used in intensive care that may exert an immunomodulatory effect by eliminating inflammatory mediators such as cytokines, endotoxin, HMGB1 and histones in patients with critical illnesses. CytoSorb® is one such adsorber that is described, and after summary and analysis of the literature, the authors describe CytoSorb® as maybe offering a therapeutic approach in critically ill patients via control of the massive release of various DAMPs, such as extracellular HMGB1 and histones.

<https://www.ncbi.nlm.nih.gov/pubmed/36855150>

The Techniques of Blood Purification in the Treatment of Sepsis and Other Hyperinflammatory Conditions

Berlot G, Tomasini A, Zanchi S, Moro E.
J Clin Med 2023; 12(5):1723

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Summary

Even in the absence of strong indications deriving from clinical studies, the removal of mediators is increasingly used in septic shock and in other clinical conditions characterized by a hyperinflammatory response. Despite the different underlying mechanisms of action, they are collectively indicated as blood purification techniques. Their main categories include blood- and plasma processing procedures, which can run in a stand-alone mode or, more commonly, in association with a renal replacement treatment. The different techniques and principles of function, the clinical evidence derived from multiple clinical investigations, and the possible side effects are reviewed and discussed along with the persisting uncertainties about their precise role in the therapeutic armamentarium of these syndromes. <https://www.ncbi.nlm.nih.gov/pubmed/36902510>

CytoSorb in patients with coronavirus disease 2019: A rapid evidence review and meta-analysis

Wei S, Zhang Y, Zhai K, Li J, Li M, Yang J, Zhang R, Li Y, Li Z.
Front Immunol 2023; 14: 1067214

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This is a systematic review and meta-analysis to combine all the evidence available in the published literature to date on the treatment of COVID-19 patients with CytoSorb®. Literature published between 1 December 2019 to 31 December 2021 and stored in the Cochrane Library, Embase, PubMed, and International Clinical Trials Registry Platform (ICTRP) were searched for all relevant studies that included cases where COVID-19 patients were treated with CytoSorb®. In total, 14 studies with 241 COVID-19 patients from eleven different countries treated with CytoSorb® hemoadsorption were included. The pooled incidence of concomitant extracorporeal membrane oxygenation (ECMO) support was 73.2%. Findings revealed that combined in-hospital mortality was 42.1%. The pooled mean C-Reactive Protein (CRP) level decreased from 147.55 to 92.36 mg/L (before versus after CytoSorb®), and interleukin - IL-6 decreased from 339.49 to 168.83 pg/ml. CytoSorb® could be easily integrated into extracorporeal circuits including continuous renal replacement therapy (CRRT) and ECMO. The authors state that CytoSorb® is also suitable for patients with renal dysfunction or cardiopulmonary failure and should be explored when conventional treatment fails to provide adequate clinical stability.

<https://www.ncbi.nlm.nih.gov/pubmed/36798138>

Use of CytoSorb® Hemoadsorption in Patients on Veno-Venous ECMO Support for Severe Acute Respiratory Distress Syndrome: A Systematic Review

Akil A, Napp LC, Rao C, Klaus T, Scheier J, Pappalardo F.
J Clinical Med 2022; 11(20):5990

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Summary

In this review, data on the use of CytoSorb® in patients with acute respiratory distress syndrome (ARDS) treated with veno-venous extracorporeal membrane oxygenation (V-V ECMO) were analysed. After screening all available studies, 13 were included that fulfilled in the inclusion criteria (12 published and 1 abstract). Where possible, a before and after analysis for relevant biomarkers and clinical parameters was carried out. CytoSorb® use was found to be associated with significant reductions in the inflammatory markers, C-reactive protein (CRP – p= 0.039) and interleukin 6 (IL-6 p= 0.049). Increases in the PaO₂/FiO₂ ratio also reached significance (p=0.028), while norepinephrine levels showed a trend towards reduced levels. Mortality rates in the CytoSorb® group also tended to be lower than in the control group of most included studies. In an exploratory analysis on 90-day mortality in COVID-19 patients supported with V-V ECMO, the therapy was associated with a significantly reduced risk of death. In brief: This is the first comprehensive review that summarizes the clinical effects of CytoSorb® in patients with severe ARDS treated with V-V ECMO. Despite low patient numbers, there was a trend towards effective inflammatory biomarker reduction, decreased vasopressor dosage and improved lung function with adjunctive hemoadsorption. Exploratory analyses suggest that the aforementioned clinical benefits may also translate into lower mortality, potentially improving survival. Early initiation of CytoSorb® in the ECMO circuit might offer a new approach to enhance lung rest and promote recovery in these difficult to treat patients.

<https://www.ncbi.nlm.nih.gov/pubmed/36294309>

Adverse outcomes with extracorporeal adsorbent blood treatments in toxic systemic inflammation: a perspective on possible mechanisms

Matson J, Lange P, Honore PM, Chung KK.

Ann Intensive Care 2022; 12(1):105

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Summary

This review discusses extracorporeal blood purification (EBP) treatments used in patients with sepsis and related conditions to mitigate toxic systemic inflammation, prevent or reverse vital organ injury, and improve outcome. Although generally considered safe, since 2020 four clinical studies including adsorbent EBP treatment have reported significantly increased patient mortality associated with the adsorbent treatments. Published criticisms have focused on study design and execution but none have considered the possible toxic effects of the adsorbent treatments per se. The authors theorise that the science of cytokine molecular dynamics suggest that immobilization of inflammatory proteins on solid scaffolds or molecular carriers may stabilize protein structure and preserve or amplify protein function. It is unknown if these mechanisms are operative in EBP adsorbent treatments. If these mechanisms are operative, then the adsorbent medium could become reactive, promoting inflammatory activity which could result in negative outcomes. Considering the recent reports of harm with adsorbent treatments in diverse inflammatory conditions, caution urges investigation of these potentially harmful mechanisms in these devices. Candidate mechanisms for possible inquiry are discussed.

<https://www.ncbi.nlm.nih.gov/pubmed/36370238>

Use of Cytokine Filters During Cardiopulmonary Bypass: Systematic Review and Meta-Analysis

Naruka V, Salmasi MY, Arjomandi Rad A, Marczin N, Lazopoulos G, Moscarelli M, Casula R, Athanasiou T.

Heart, Lung and Circulation 2022; 31(11):1493-1503

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Summary

In this systematic review and meta-analysis, the use of hemoadsorption during cardiopulmonary bypass was assessed. In total 8 randomized control trials (RCTs) and 7 observational studies were included. Although all forms of adsorption therapies were allowed to be included in the analysis, 12 of the 15 studies were using CytoSorb®. There was also no restriction on the types of cardiac procedures, including cardiac trans-plantation and infective endocarditis. Subgroup analysis of non-elective surgeries across the observational studies (emergency and infective endocarditis) significantly favoured hemoadsorption in terms of 30-day mortality ($p=0.01$) and shorter ICU stay ($p=0.001$), while comparing hemoadsorption and controls across all studies showed no significant differences in this regard. According to the authors this illustrates that cytokine adsorption may be preferentially more effective in patients with high inflammatory response, such as infective endocarditis or cardiac transplant patients. The authors conclude that a significant reduction in 30-day mortality and ICU stay could be obtained by using hemoadsorption therapy during non-elective cardiac surgery, especially emergency surgery and in patients with higher inflammatory burden such as infective endocarditis. They recommend designing well-conducted, large scale RCTs in patients with infective endocarditis which will likely provide further results on the benefits of cytokine filters use.

<https://www.ncbi.nlm.nih.gov/pubmed/36041987>

Management of perioperative bleeding risk in patients on antithrombotic medications undergoing cardiac surgery – a systematic review

Matejic-Spasic M, Hassan K, Thielmann M, Geidel S, Storey RF, Schmoeckel M, Adamson H, Deliarogiris EN, Wendt D.

J Thorac Disease 2022; 14(8):3030-3044

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Summary

The aim of this review was to evaluate perioperative bleeding complications in patients on dual antiplatelet therapy (DAPT) or direct-acting oral anticoagulants (DOACs) undergoing high-bleeding risk cardiovascular surgery and to present currently available potential solutions to mitigate antithrombotic therapy-related bleeding complications. Relevant articles on bleeding complications in cardiac surgery from last 10 years in Medline (PubMed) were screened. An additional search evaluating potential solutions to mitigate bleeding complications was also performed. From all reviewed studies, a total of 19 articles could be included evaluating the risk for bleeding in cardiac surgery related to DAPT or DOACs, and 10 papers evaluating antithrombotic drug reversal or removal in this setting. Reported bleeding rates ranged between 18% and 41%, a remarkably

wide variability. New costly reversal agents are available but have not been sufficiently tested in this setting. Antithrombotic removal by innovative intraoperative hemoadsorption has been shown to be associated with a significant decrease in re-thoracotomy rate, overall procedure duration, administered transfusion volumes, chest-tube drainage, and length of hospitalization. Results from ongoing trials should provide more informed insights concerning the efficacy and safety of several potential solutions.

<https://pubmed.ncbi.nlm.nih.gov/36071758/>

Extracorporeal hemoadsorption with the CytoSorb device as a potential therapeutic option in severe intoxications: review of the rationale and current clinical experiences

Mitrovic D, Huntjens D, de Vos E, van Tellingen M, Franssen E.

Journal of Clinical Pharmacy and Therapeutics 2022; 47(9):1444-1451

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Summary

This review summarizes all the published data so far on CytoSorb® use in acute severe intoxications from accidental and intentional drug exposure. Due to the nature of the problem, randomized controlled trials are not feasible in this field of clinical use. It is noted that for a lot of substances there are no known reversal agents, or antidotes. Hence the use of CytoSorb® was considered a therapeutic option, especially considering its strong safety profile and the high acuity of these life-threatening situations. The authors note that besides an intended direct removal of the toxic compound itself from the blood compartment, the therapy also holds a massive potential in also treating secondary complications of poisonings. So far there have been 13 publications including 17 patients that have used CytoSorb® in several intoxication scenarios. Pre and post adsorber drug levels confirm the direct removal of various drugs by CytoSorb®. Drugs reported on include beta blockers, antihypertensives, antidepressants, antiarrhythmic, antipsychotics, anticonvulsants, and MDMA (ecstasy).

<https://www.ncbi.nlm.nih.gov/pubmed/35924306>

Hemoperfusion in the intensive care unit

Ricci Z, Romagnoli S, Reis T, Bellomo R, Ronco C.

Intensive Care Med 2022; 48(10):1397-1408

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Summary

This review describes the evolution of knowledge and current understanding regarding technical concepts, safety, and clinical results of the use of hemoperfusion. The review includes a summary of various hemoperfusion techniques including the polymyxin B cartridge, coupled plasma filtration adsorption (CPFA), Jafron HA series, Seraph -100® and CytoSorb®. The most recent literature regarding adsorption applied in critically ill patients and their indications are summarized, including recent randomized controlled trials and future areas of investigation. It is recommended that clinical trials for the assessment of efficacy of hemoperfusion in septic patients should apply the explanatory approach which includes a highly selected homogenous patient population, enrichment criteria such as applying genetic signature and molecular biomarkers which identify subphenotypes of patients. The authors conclude that as our understanding of critical care pathophysiology and hyperinflammatory diseases has evolved, it is now clear that each patient requires a tailored approach. They suggest that it appears likely that hemoperfusion research will switch from large-scale randomized trials to tailored, adaptive studies that include only patients meeting specific and objective criteria (i.e., biomarkers, clinical phenotypes) that offer plausible indications for treatment and/or endpoints for the assessment of the biological efficacy of blood purification.

<https://www.ncbi.nlm.nih.gov/pubmed/35984473>

Mortality and adverse events of hemoadsorption with CytoSorb® in critically ill patients: a systematic review and meta-analysis of randomized controlled trials

Heymann M, Schorer R, Putzu A.

Acta Anaesthesiol Scand 2022; 66(9):1037-1050

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Summary

In this review the authors performed a systematic search along with a meta-analysis and trial sequential analysis (TSA) of randomized-controlled trials to assess the mortality and safety of CytoSorb® therapy in critically ill patients with inflammatory conditions. Electronic databases were searched up to April 2022. The primary outcome was mortality at longest follow-up and secondary outcomes included various adverse event (AE) outcomes, *even if this wasn't the focus of the original study*. Where data on mortality was not included in the original study, the original authors were

contacted for further data. Conflicts of interest and funding of each trial were assessed and a relative risk (RR) and 95% confidence interval (CI) calculated by the authors. Fourteen published (n=764) and 4 unpublished (n=111) trials were included, with 8 trials in medical ICU patients and 10 in complex cardiac surgery. Hemoadsorption was associated with higher mortality at latest follow-up (29.85% vs. 24.20%). However, the authors note that overall, the certainty of evidence was insufficient to draw firm conclusions on mortality effects. Although under-reported (or not systematically evaluated in the included studies), the risk of serious and non-serious adverse events was not higher with the use of CytoSorb®. The authors list the limitations of their analysis as; issues with the quality and quantity of the randomized trials included, that most were single centre, few were at low risk of bias, and all were not powered for mortality as an endpoint. Finally, they state that considerable uncertainty about the findings does not allow firm conclusions to be made and suggest a need for high-quality randomized trials to clarify mortality and adverse events related to CytoSorb®. <https://www.ncbi.nlm.nih.gov/pubmed/35788557>

Survival of patients treated with extracorporeal hemoadsorption and ECMO – results from a nation-wide registry

Heidenreich A, Kaier K, Bode C, Zehender M, von zur Mühlen C, Duerschmied D, Wengenmayer T, Stachon P, Supady A.

ASAIO J 2023; 69(3):339-343

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Summary

Information from a German Research Data Centre dataset was retrospectively collected between 2017 – 2019 for all patients treated with veno-venous (VV) extracorporeal membrane oxygenation (ECMO) either with or without CytoSorb®. During this time 7,699 patients were treated with VV ECMO, of which 684 (9%) were also treated with CytoSorb®. Use of CytoSorb® increased year on year (2017: 6.6%, 2018: 8.4%, 2019: 11.8%). Patients supported with ECMO either with or without CytoSorb® were of similar age and about one third of the patients in both cohorts were female. When combined with CytoSorb®, ECMO was initiated later than in patients without CytoSorb®. Overall mortality was higher for VV ECMO compared to other data from large trials (53.08% v 35%), which may be due to the unselected nature of the dataset. CytoSorb® use was associated with higher mortality and increased treatment costs, however, there was limited information regarding the severity of disease which may have impacted on this. Therefore direct comparisons of outcomes between these patients should, as the authors note, be interpreted with caution.

CONCLUSIONS (from CytoSorbents): For appropriate interpretation of these comparisons a better understanding of the patients underlying disease status that led to the initiation of VV ECMO and CytoSorb® therapy is mandatory.

<https://pubmed.ncbi.nlm.nih.gov/35857288/>

Application of Adsorptive Blood Purification Techniques during Cardiopulmonary Bypass in Cardiac Surgery

Liu MH, Yu H, Zhou RH.

Oxid Med Cell Longev 2022: 6584631

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Summary

In this review, the use of blood purification techniques (BPTs) in cardiopulmonary bypass (CPB) for mitigating the systemic inflammatory response (SIRS) is described. Different devices used for this are covered, including the AN69 nonselective membrane, PMMA membrane, oXiris® semi-selective membrane, polymyxin B hemoperfusion selective cartridge, and CytoSorb® as a nonselective cartridge. CytoSorb® is described as the most representative and most recent device of adsorption BPTs and as the only specially approved extracorporeal cytokine adsorber in the European Union. A further, detailed description is including the facts that it has the widest adsorption spectrum and also that it is convenient for installing in the extracorporeal circulation circuit. A literature search between 2016 and 2021 was done regarding the use of CytoSorb® during CPB surgery and the results summarized in detail. They note that the current level of evidence of CytoSorb® in adult cardiac surgery is insufficient, with inconsistencies which may be related to the small sample size, inappropriate setting of admitting-exclusion criteria, and insufficient duration of CytoSorb® intervention. The authors discuss a number of issues that need addressing including indications for treatment, appropriate treatment time, optimal flow conditions, selection of clinically meaningful endpoints and defining a possible target treatment population. In conclusion, the authors note that there is no denying that adsorptive extracorporeal blood purification technology opens a new door for the ongoing fight against CPB-associated SIRS. More prospective, large-sample randomized controlled trials are needed to evaluate the safety and efficacy of this technique in CPB.

<https://www.ncbi.nlm.nih.gov/pubmed/35663201>

Sepsis Management in Southeast Asia: A Review and Clinical Experience

Mehta Y, Paul R, Rabbani R, Acharya SP, Withanaarachchi UK.

Journal of Clinical Medicine 2022; 11(13); 3635

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Summary

This review summarizes the literature that focuses on the diagnosis and treatment of sepsis, issues with colistin resistance, the increasing use of chloramphenicol, antibiotic abuse, resource constraints and finally the association of sepsis with COVID-19 in Southeast Asia. A panel of five experts discussed the literature and made the following recommendations:

- Data on the incidence of sepsis in this region be collected and shared
- The management of sepsis be personalized
- Use of conventional approaches and innovative therapeutic alternatives to sepsis management be employed

In particular a personalized approach and innovative therapeutic alternatives such as CytoSorb® are highlighted as potential options for the treatment of patients with sepsis in Southeast Asia. CytoSorb® is described in detail, along with all the publications on these patients from this region. It is noted that it is now well established that absence of evidence is not evidence of absence. Therefore, adopting a personalized treatment approach wherever and whenever desirable and embracing novel extracorporeal blood purification technologies could further enhance patient outcomes and alleviate the burden of sepsis. In support of this, the authors state that instead of randomized control trials, that real-world evidence be used to show the benefit in determining the potential of CytoSorb® for the management of sepsis.

<https://pubmed.ncbi.nlm.nih.gov/35806919/>

Mechanistic Considerations and Pharmacokinetic Implications on Concomitant Drug Administration During CytoSorb Therapy

Scheier J, Nelson PJ, Schneider A, Colombier S, Kindgen-Milles D, Deliargyris EN, Nolin T.

Crit Care Explorations 2022; 4(5):e0688

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Summary

This review article on concomitant drug administration during CytoSorb® therapy summarizes mechanistic principles, available preclinical and clinical data and provides guidance for clinical management. The authors included human, animal and bench-top studies with PK or drug removal data and did not consider reports of CytoSorb® usage to treat drug overdose. They reviewed PK data of CytoSorb® hemoadsorption for more than 50 drugs of various categories like analgesics, antiarrhythmics, anticonvulsants, antidepressants, antihypertensives, anti-infectives, antithrombotics, anxiolytics, and immunosuppressants. By classifying PK data according to different removal rates and clearance they could differentiate between four removal categories. First, they list drugs with “insignificant *in vivo* removal”. Category two “low *in vitro* removal” comprises drugs for which clinically significant removal by CytoSorb® therapy cannot be excluded. In the third category “moderate or high *in vitro* removal” the authors grouped drugs for which clinically significant removal is possible and lastly, they classify drugs into category four for which “significant *in vivo* removal” was demonstrated. For the last three categories, the authors recommend TDM (therapeutic drug monitoring) to guide dosing wherever available. In conclusion, the authors highlight that CytoSorb® therapy may increase drug elimination through active removal. They discuss that the extent of removal is heterogeneous, and its clinical significance, if any, depends on various aspects and the broader clinical context, including a patient’s specific endogenous drug clearance and the underlying extracorporeal platform used. With their collection on available data, they allow for general guidance on dosing adjustments during CytoSorb® therapy. They point out that any treatment decisions should always be complemented by clinical judgment and therapeutic drug monitoring, when available.

<https://www.ncbi.nlm.nih.gov/pubmed/35783552>

Hemadsorption for removal of ticagrelor and direct oral anticoagulants in cardiac surgery

Jackson R, Trus RM, El-Diasty M.

Expert Rev Cardiovasc Ther 2022; 20(2):141-150

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Summary

This review describes the issue of an increasing number of cardiac patients on antiplatelets or oral anticoagulation undergoing emergent cardiac surgery without an appropriate washout period who are at increased risk for developing perioperative bleeding, increased transfusion requirements, longer surgical operating times, prolonged intensive care unit (ICU) and hospital lengths of stay, and higher mortality rates. It is estimated that due to their critically unstable condition, around 33% of patients undergo their cardiac procedures before the recommended 3 day washout period. This review evaluates and reviews current evidence for applying CytoSorb® in removing ticagrelor and direct oral anticoagulants (DOACs) including 4 in vitro studies, 3 case reports, one retrospective clinical study and 2 cost analysis studies. Based on this evidence, the authors conclude that CytoSorb® is safe, and may be effective in reducing perioperative bleeding as demonstrated by reducing chest tube output, blood product transfusions, and re-thoracotomy rates. CytoSorb® can also reduce length of intensive care unit (ICU) and hospital stay. Although, CytoSorb® has an initial upfront cost, it has been proven to be cost effective due to potential health resource savings on both short- and long-term projections. In conclusion, CytoSorb® is a feasible means for the removal of ticagrelor and DOACs in patients requiring emergency cardiac surgery. It can be incorporated into a cardiopulmonary circuit intraoperatively. The authors note that if the use of CytoSorb® to reduce bleeding complications in cardiac surgery is proven to be safe and efficient in larger ongoing studies, it has the potential to change clinical practice guidelines and enhance high standard patient care.

<https://www.ncbi.nlm.nih.gov/pubmed/35179425>

The Effects of Hemoadsorption on the Kinetics of Antibacterial and Antifungal Agents.

Berlot G, Di Bella S, Tomasini A, Roman-Pognuz E.

Antibiotics (Basel) 2022; 11(2):180

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Summary

In this review paper the basic principles of ultrafiltration and hemoadsorption are described including the devices Toraymyxin®, oXiris® and CytoSorb®. Existing experimental and clinical studies are presented, which, when considered together, show that it is hard to draw definitive conclusions. As drug removal is maximal in the initial phase of hemoadsorption and decreases with time due to the saturation of the binding sites, it could be advisable to administer a loading dose followed by a continuous infusion. The authors conclude that different blood purification techniques are currently used to treat clinical conditions characterized by an overwhelming inflammatory reaction. It should be recognized that anti-infective agents can be removed along with mediators; thus, the use of therapeutic drug monitoring (TDM) and adjustment of the dosing regimens of anti-infective drugs is warranted.

<https://www.ncbi.nlm.nih.gov/pubmed/35203783>

Blood purification could tackle COVID-19?

Yamada H, Ohtsuru S

J Intensive Care 2021; 9(1):74

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Summary

In this review the authors discuss the impact on coronavirus disease 2019 (COVID-19) globally, and the challenges that this has brought including establishing effective treatments. Various blood purification techniques have been applied including therapeutic plasma exchange (TPE), CytoSorb®, AN69 surface-treated membrane, and polymyxin b hemoperfusion. In regards to CytoSorb® the authors note that a recent critical published randomized trial may have issues with its design and therefore results, so that it might be 'premature to rush to negative conclusions about the efficacy of CytoSorb®'. In conclusion the authors state that blood purification has excellent potential to fight the COVID-19 pandemic, however further research is needed to elucidate the actual effects of these applications.

<https://www.ncbi.nlm.nih.gov/pubmed/34895343>

Therapeutic Modulation of the Host Defense by Hemoadsorption with CytoSorb® - Basics, Indications and Perspectives - A Scoping Review

Köhler T, Schwier E, Praxenthaler J, Kirchner C, Henzler D, Eickmeyer C.

Int J Mol Sci 2021; 2021(22):12786

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Summary

This review summarizes the theoretical knowledge, in vitro results, and clinical findings of the CytoSorb® adsorber for the treatment of massively elevated cytokine levels and other indications, in order to provide the clinician with

pragmatic guidance for daily practice. According to the authors CytoSorb® is the most widely used hemoadsorption procedure at present that specifically targets hyperinflammation by extracorporeal removal of pro-inflammatory substances, i.e., cytokines. A search of PubMed yielded 170 publications for final inclusion in this review. CytoSorb® therapy appears to be safe and useful in various disease states (e.g., rhabdomyolysis, liver failure, intoxications or life threatening bleeding under direct oral anticoagulants – DOAC use) as well as in septic shock or cytokine release syndrome, although a conclusive assessment of treatment benefit is not possible and no survival benefit has yet been demonstrated in randomized controlled trials. In this regard a selection of current studies that have investigated the use of CytoSorb® therapy in sepsis and septic shock is presented in a table in the article. The authors conclude that further high-quality randomized controlled trials of hemoadsorption are urgently needed and should consider factors such as blood flow, dose (amount of blood purified (ABP)), average adsorber use time, and total duration of hemoadsorption. Potential side effects or interactions, in addition to a patient population clearly defined by indication and disease severity, should equally be investigated.

<https://pubmed.ncbi.nlm.nih.gov/34884590/>

Hemoperfusion and blood purification strategies in patients with COVID-19: A systematic review

Sanfilippo F, Martucci G, La Via L, Cuttone G, Dimarco G, Pulizzi C, Arcadipane A, Astuto M.
Artif Organs 2021; 45(12):1466-1476

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Summary

This is a systematic review of studies that treated COVID-19 patients with extracorporeal cytokine removal (hemoperfusion - HP). Eleven clinical studies and case series that had enrolled at least five patients were included including two CytoSorb® studies (Rampino et al. and Alharthy et al.). In total, 226 patients were identified, while another 59 patients functioned as controls in some of the included studies. Of the patients receiving HP therapy, the most frequently used approaches were artificial liver support (ALS, n = 62) and CytoSorb® (n = 55). They found wide variability in the clinical and biological outcomes reported with most studies describing decreasing levels of interleukin - IL-6 after HP treatment. The authors suggest that prospective randomized data are recommended to establish further the role of HP in COVID-19 patients.

<https://www.ncbi.nlm.nih.gov/pubmed/34632596>

The Use of CytoSorb Therapy in Critically Ill COVID-19 Patients: Review of the Rationale and Current Clinical Experiences

Ruiz-Rodríguez JC, Molnar Z, Deliargyris EN, Ferrer R, Tisherman SA.
Critical Care Research and Practice 2021; 7769516

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Summary

The purpose of this review was to provide an overview of the pathophysiological background of the hyperinflammation seen in a subset of patients with COVID-19, and to summarize the currently available evidence on the effects of hemoadsorption with CytoSorb® in these patients. In this regard an overview lists 12 sources including > 150 COVID-19 patients treated with CytoSorb® therapy. The authors note that serious, potentially life-threatening complications are often due to the dysregulated hyperinflammatory host immune response causing vasoplegic shock, severe hypoxemia, and elevated inflammatory marker levels. In this population, the use of extracorporeal cytokine adsorption appears to provide significant benefits including hemodynamic stabilization and improvement in oxygenation. Observed mortality in general was lower than predicted and better than in control patients without CytoSorb®, however, comparisons of reported mortalities under CytoSorb® therapy with other reports on mortality in COVID-19 patients should be done with caution and are likely to be inconclusive. All reports agree that the therapy is safe and well tolerated. Although several open questions remain, early evidence with the use of CytoSorb® in these critically ill patients is encouraging.

<https://pubmed.ncbi.nlm.nih.gov/34336280/>

Reducing antithrombotic-related bleeding risk in urgent and emergency cardiac surgery

Harky A, Badran A.
Br J Cardiol 2021; 28(2):26

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Summary

This review focuses on the role CytoSorb® for purifying extracorporeal blood, particularly for preventing bleeding complications during on-pump cardiac surgery, including removal of the antiplatelet agent, ticagrelor, and the oral anticoagulant, rivaroxaban, from the blood. Current guidelines recommend stopping such agents

at least two to five days prior to surgery and delaying urgent / emergency surgery so that the risk of perioperative bleeding is minimised. However, stopping these medications isn't always possible in the setting of urgent and emergent cases. It is not only bleeding that can significantly impact on the outcomes, but the accompanying inflammatory and cytokine response can fulminate the coagulopathic process during and post cardiac surgery further affecting outcomes. The authors summarise the literature around CytoSorb® use in this field of application including potential cost savings before going on to outline the recent medtech innovation briefing (MIB) from the National Institute for Health and Care Excellence (NICE) which considers CytoSorb® as the first device to demonstrate safe and effective removal of ticagrelor from the circulation. According to the NICE MIB, CytoSorb® provides significant advantages in reducing the risk of bleeding in emergency cardiac surgery in patients treated with ticagrelor and lowers the utility of bleeding resources. CytoSorb® can, therefore, also reduce in-hospital stay for urgent cases awaiting cardiac surgery, which would be associated with significant cost savings. The authors conclude with stating that while currently there is limited evidence, there appears to be a trend that the novel approach of CytoSorb® use can be an effective tool to minimize bleeding risk in emergency cardiac surgery patients treated with ticagrelor or rivaroxaban.

<https://www.ncbi.nlm.nih.gov/pubmed/35747456>

The Potential Role of Extracorporeal Cytokine Removal in Hemodynamic Stabilization in Hyperinflammatory Shock

Hawchar F, Rao C, Akil A, Mehta Y, Rugg C, Scheier J, Adamson H, Deliaroyis E, Molnar Z.

Biomedicines 2021; 9(7):768

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Summary

In this review, hemodynamic instability due to a dysregulated host response ("hyperinflammatory shock") is discussed as a life-threatening condition requiring vasopressors and vital organ support. Hemoadsorption with CytoSorb® has proven to be effective in reducing cytokines and possibly in attenuating the devastating effects of the cytokine storm originating from the immune over-response to the initial insult. A literature search of all publications in the PubMed database was made to assess evidence of the impact of CytoSorb® on norepinephrine needs in the critically ill. Analysis of studies that included data on control cohorts in a comparative pooled analysis was also made and treatment effect was defined as a reduction in vasopressor dosage at 24 h. The literature search found 33 eligible articles including 353 patients with evidence of a significant reduction in norepinephrine requirements after treatment: median before, 0.55; after, 0.09 µg/kg/min, $p < 0.001$. Analysis of 4 studies with control groups that included 140 patients overall revealed a large and significant pooled effect size at 24 hrs though characterized by high heterogeneity. The authors share the concerns of many experts that - based on an improved understanding of the underlying pathophysiologic mechanisms - mortality may no longer be the only appropriate primary endpoint for clinical trials in this setting. In conclusion the presented data indicate the important contribution of early hemoadsorption in achieving rapid hemodynamic stabilization in patients with refractory vasoplegic shock.

<https://www.ncbi.nlm.nih.gov/pubmed/34356830>

Opportunities, Controversies and Challenges of Extracorporeal Hemoadsorption with CytoSorb® during ECMO

Napp LC, Lebreton G, De Somer F, Supady A, Pappalardo F.

Artif Organs 2021; 45(19):1240-1249

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Summary

In this interdisciplinary debate article, the use of extracorporeal membrane oxygenation (ECMO) around the world for various indications is initially described with prognosis often poor even with all the supportive therapies. Clinical deterioration is often associated with inflammation. Hemoadsorption with CytoSorb® is discussed as a way to limit this inflammatory response, as the device can be safely and easily installed into ECMO circuits. CytoSorb® has been used more than 130,000 times to date, but since randomized controlled trials are largely lacking, there is substantial debate on its use. Several experts from critical care medicine, cardiology, cardiac surgery, and perfusion technology discussed the pros and cons of CytoSorb® therapy and outline future aspects for its clinical application and research. For example, it is recommended that future studies look at defining a better starting point for CytoSorb® integration and duration of use, and the fact that ECMO *per se* is not a reason to start CytoSorb®, rather the underlying pathological condition. Potential fields of application are listed as e.g. profound shock on ECMO, extracorporeal cardio-pulmonary resuscitation, post-cardiotomy ECMO in patients with infection and ECMO in the context of organ donation.

<https://www.ncbi.nlm.nih.gov/pubmed/34152637>

Sepsis-Pathophysiology and Therapeutic Concepts

Jarczak D, Kluge S, Nierhaus A.

Front Med (Lausanne) 2021; 2021:8:628302

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Summary

Sepsis is a life-threatening condition and a global disease burden. Despite all efforts of experimental and clinical research during the last three decades, the ability to positively influence course and outcome of the syndrome remains limited. This review provides an overview of sepsis immune pathophysiology, including acute respiratory distress syndrome, sepsis-induced acute kidney injury and cardiac dysfunction. Various therapeutic concepts covering causal therapy as well as supportive therapy are then discussed with a section on the role of adsorption techniques and in particular CytoSorb®. Immunotherapies and immunoglobulins are also described before, finally, the role of artificial intelligence in sepsis is briefly explored. In the summary the authors note that the previous approach of using exclusively anti-inflammatory therapies has been disappointing, and that the investigation of strategies that aim to re-balance the profound immune dysregulation during sepsis and septic shock seems to be a promising goal.

<https://www.ncbi.nlm.nih.gov/pubmed/34055825>

Extracorporeal Cytokine Adsorption Therapy As a Preventive Measure in Cardiac Surgery and As a Therapeutic Add-On Treatment in Sepsis: An Update Systematic Review of Comparative Efficacy and Safety

Goetz G, Hawlik K, Wild C.

Crit Care Med 2021; 49(8):1347-1357

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Summary

In this systematic review of cytokine adsorption, four databases (Medline, Embase, Cochrane Library, and the European Network for Health Technology Assessment) were searched on December 2019, and any randomized controlled trials and prospective studies with a concurrent control in patients with sepsis or undergoing cardiac surgery were included. Results showed for the preventive treatment of extracorporeal cytokine adsorption therapy in cardiac surgery, very low-quality inconclusive evidence for mortality, length of intensive care stay, and length of hospitalization. Very low-quality inconclusive evidence was found for (serious) adverse events. For the therapeutic treatment of extracorporeal cytokine adsorption therapy in patients with sepsis/septic shock, the authors found very low-quality inconclusive evidence for mortality up to 60-day follow-up, organ function and length of stay in the ICU. Very low-quality inconclusive evidence was again found for (serious) adverse events. The authors strongly recommend that well-powered studies with patient-relevant endpoints be encouraged. They note that it is also potentially a wrong interpretation of the evidence to discredit the additive measure fully, as absence of evidence of effect should not be confused with evidence of absence, so evidence of no effect.

<https://www.ncbi.nlm.nih.gov/pubmed/33935160>

Effect of Extracorporeal Blood Purification on Mortality in Sepsis: A Meta-Analysis and Trial Sequential Analysis

Snow TAC, Littlewood S, Corredor C, Singer M, Arulkumaran N.

Blood Purif 2021; 50(4-5):462-472

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Summary

The objective of this study was to conduct a meta-analysis and trial sequential analysis (TSA) of published randomized controlled trials (RCTs) to determine whether mortality benefit exists for extracorporeal blood purification techniques in sepsis. Thirty-nine RCTs were identified, including 2,729 patients. Fourteen studies used hemofiltration (n = 789), 17 used endotoxin adsorption devices (n = 1,363), 3 used nonspecific adsorption (n = 110), 2 used cytokine removal (CytoSorb®) (n = 117), 2 used coupled plasma filtration adsorption (CPFA) (n = 207), 2 combined hemofiltration and perfusion (n = 40), and 1 used plasma exchange (n = 106). Using conventional meta-analysis, hemofiltration, endotoxin removal devices and nonspecific adsorption devices were associated with mortality benefit, however, the use of TSA revealed that, based on the number of existing patients recruited for RCTs, neither hemofiltration, endotoxin removal devices, nor nonspecific adsorption devices were associated with mortality benefit. Due to the low number of studies/patients, TSA was not performed for the two CytoSorb® studies. The authors conclude that there are inadequate data for any

technique at present to conclude that the use of extracorporeal blood purification techniques in sepsis is beneficial. Further adequately powered RCTs are required to confirm any potential mortality benefit, which may be most evident in patients at greatest risk of death.

<https://www.ncbi.nlm.nih.gov/pubmed/33113533>

(Hemoadsorption for blood purification - incomparability of the clinically offered methods)

Original Article in German. English or Spanish translations available on request

Krenn CG, Steltzer H.

Med Klin Intensivmed Notfmed 2021; 16(5):449-453

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Summary

In this review article, the authors highlight the different aspects between hemoadsorption products on the market and take a critical look at the available evidence. Technical features, applications specific characteristics and existing evidence of the adsorption technologies including CytoSorb® (CytoSorbents™ Inc., Monmouth Junction, NJ, USA), Jafron® HA series (Jafron Biomedical Co., Guangdong, China) and the Biosky® MG series (Biosun® Medical Technology Co., Foshan City, Guangdong Province, China) were analysed. A comprehensive analysis of these criteria showed that there are significant differences between the available technologies in terms of materials used, adsorption characteristics, application and available data on safety and clinical experience. Furthermore, it became clear that for blood purification technologies not only their efficacy should be considered in the light of an effect price/performance ratio, but also, and in particular, the clinical safety of the individual processes is of crucial importance. Among the technologies analyzed, CytoSorb® currently represents, according to the authors, the best investigated and clinically most established procedure. In addition, it should be noted that not only clinical results, but especially also safety-relevant aspects are not transferable between the products due to the technically different procedures.

<https://www.ncbi.nlm.nih.gov/pubmed/32583037>

Hemoadsorption efficacy for uncomplicated high-risk cardiac surgery

Redant S, Legrand M, Langman Y, Aguilar AG, Angoulvant F, Kaefer K, De Bels D, Attou R, Kashani K, Honore P.

Crit Care 2019; 23(1):343

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Summary

In this letter the authors comment on the paper by Poli et al., *Crit Care* 2019; 23(1): 108 which, whilst it didn't show a clinical or laboratory benefit, states that there was no association with any complications of intraoperative CytoSorb® use either. They note that the perioperative peak levels of interleukins in the patients were low, which may explain why there was no obvious benefit. They then list a number of publications from various CytoSorb® application fields in patients with higher levels of interleukins, which showed a positive clinical course with an improvement in hemodynamic parameters such as mean arterial pressure, cardiac index, and need for catecholamines. Finally they state that the patients who will most likely benefit most from CytoSorb® are those a significant systemic inflammatory response, and agree with the authors that the device should be tested in patient populations with high levels of circulating cytokines, such as IL-6.

<https://www.ncbi.nlm.nih.gov/pubmed/31684994>

Ticagrelor Removal by CytoSorb® in Patients Requiring Emergent or Urgent Cardiac Surgery: A UK-Based Cost-Utility Analysis

Javanbakht M, Trevor M, Rezaei Hemami M, Rahimi K, Branagan-Harris M, Degener F, Adam D, Preissing F, Scheier J, Cook SF, Mortensen E.

Pharmacoeconomics - Open 2020; 43(2):307-319

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Summary

Acute coronary syndrome patients receiving dual antiplatelet therapy who need emergent or urgent cardiac surgery are at high risk of major bleeding, which can impair postoperative outcomes. CytoSorb® has been demonstrated to remove ticagrelor, one of these antiplatelet therapies, from blood during on-pump cardiac surgery. The aim of this study was to evaluate the cost utility of intraoperative removal of ticagrelor (using CytoSorb®) versus usual care among patients requiring emergent or urgent cardiac surgery in the UK. A de novo decision analytic model was developed to estimate the short- and long-term costs and outcomes. Results from randomised clinical trials and national standard sources such as National Health Service (NHS) reference costs

were used to inform the model. Results of the model calculations showed that in emergent cardiac surgery, intraoperative removal of ticagrelor using CytoSorb® was less costly (£12,933 vs. £16,874) and more effective (0.06201 vs. 0.06091 quality-adjusted life-years) over a 30-day time horizon than cardiac surgery without prior natural washout of ticagrelor. For urgent cardiac surgery, the use of CytoSorb® was less costly than any of the three comparators (delaying surgery for natural washout without adjunctive therapy, adjunctive therapy with short-acting antiplatelet agents, or adjunctive therapy with low-molecular-weight heparin). Results showed that CytoSorb® has a high probability of being cost saving (99% in emergent cardiac surgery and 53–77% in urgent cardiac surgery, depending on the comparators). Cost savings derive from fewer transfusions of blood products and re-thoracotomies, and shorter stay in the hospital/intensive care unit. Therefore the implementation of CytoSorb® as an intraoperative intervention for patients receiving ticagrelor undergoing emergent or urgent cardiac surgery is a cost-saving strategy, yielding improvement in perioperative and postoperative outcomes and decreased health resource use.

<https://www.ncbi.nlm.nih.gov/pubmed/31620999>

Recommendations for the management of hemophagocytic lymphohistiocytosis in adults

La Rosee P, Horne A, Hines M, von Bahr Greenwood T, Machowicz R, Berliner N, Birndt S, Gil-Herrera J, Girschikofsky M, Jordan MB, Kumar A, van Laar JAM, Lachmann G, Nichols KE, Ramanan AV, Wang Y, Wang Z, Janka G, Henter JL.

Blood 2019; 133(23):2465–2477

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Summary

Hemophagocytic lymphohistiocytosis (HLH) is a severe hyperinflammatory syndrome induced by over-activated macrophages and cytotoxic T cells. The primary (genetic) form is most common in children, whereas the secondary (acquired) form is most frequent in adults. Secondary HLH is commonly triggered by infections or malignancies but may also be induced by autoinflammatory/autoimmune disorders, in which case it is called macrophage activation syndrome (MAS; or MAS-HLH). HLH in adults may present with a phenotype indistinguishable from sepsis or multiple organ dysfunction syndrome. Treatment algorithms targeting hyperinflammation are frequently based on pediatric protocols, which may result in overtreatment and unnecessary toxicity in adults. In adults, HLH-associated mortality remains high, especially in patients with underlying malignancies. Although the drugs used in pediatric HLH are effective in adult HLH, there is still a need for novel agents and interesting trials testing alternative therapeutic approaches have been initiated. In this paper, expert consensus recommendations derived from an interdisciplinary working group on adult HLH are presented, to facilitate knowledge transfer between physicians caring for pediatric and adult patients with HLH, with the aim to improve the outcome for adult patients affected by HLH. Noted with a couple of case references in the section, ‘Salvage treatment of relapsed and refractory HLH’ is the comment that ‘the use of cytokine adsorption columns may aid in rescuing critically ill patients from a deleterious cytokine storm’.

<https://www.ncbi.nlm.nih.gov/pubmed/30992265>

Rationale of Hemoadsorption during Extracorporeal Membrane Oxygenation Support

Napp LC, Ziegeler S, Kindgen-Milles D.

Blood Purif 2019; 48(3):203-214

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Summary

In this review the role of CytoSorb® with the use of extracorporeal membrane oxygenation (ECMO) and extracorporeal life support (ECLS) is explored. ECMO and ECLS are increasingly being used for treating various forms of shock, lung failure, and life support including resuscitation. However, most patients on ECMO are affected by a systemic inflammatory response caused by the underlying disease as well as the ECMO support itself, which contributes to vasoplegia, multi-organ failure, deterioration and death. The rationale, available data and technical aspects of CytoSorb® use is described with ECMO and ECLS, as a way of reducing excessive levels of inflammatory molecules such as interleukins, cytokines as well as damage- and pathogen-associated molecular patterns. Finally, the authors give recommendations based on their existing experience.

<https://www.ncbi.nlm.nih.gov/pubmed/31096211>

Cytokine removal in human septic shock: Where are we and where are we going?

Honore PM, Hoste E, Molnar Z, Jacobs R, Joannes-Boyau O, Malbrain M, Forni LG.

Ann Intensive Care 2019; 9(1):56

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Summary

The use of blood purification therapies to improve immune homeostasis and therefore mortality in septic patients has recently become more available. In this executive summary of an expert meeting held at the 6th International Fluid Academy Days in Antwerp, Belgium (Nov 23-25, 2017), the current understanding regarding the use of such adsorbers, and in particular, CytoSorb® in humans with septic shock was explored in detail. All available literature was summarized, and the topics discussed included; pathophysiology of the inflammatory response, rationale for cytokine removal, and whether the use of CytoSorb® in patients with sepsis or septic shock demonstrate any clinical benefit. Results from the consensus meeting included discussion regarding which patient benefits most from cytokine removal, when to start CytoSorb®, for how long, in which study population, which severity of patient, which biomarkers to observe and recommendations for future research. The authors conclude that while clinical results are thus far not yet satisfactory, more research is needed to answer various open questions.

<https://www.ncbi.nlm.nih.gov/pubmed/31089920>

What Have We Learned about the Use of Cytosorb Adsorption Columns?

Ankawi G, Xie Y, Yang B, Xie Y, Xie P, Ronco C.

Blood Purif 2019; 48(3):196-202

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Summary

The aim of this review was to summarize the published literature on the use of CytoSorb® (CS). The authors describe the main studies that use CytoSorb® in sepsis (Schädler 2013 & 2017, Friesecke and Kogelmann) where they note that observational data suggest improved hemodynamics and a trend towards improved mortality. They also summarize the main cardiac surgery papers (Träger 2016, Bernardi, Träger 2017, Calabro) before reporting on the Nemeth and Kellum 2008 studies in regards to organ transplantation, the use of CytoSorb® in liver failure, in drug removal including ticagrelor, and finally the Registry. The authors note that the body of evidence to support the safety and effectiveness of CS continues to grow and that sorbents offer clear advantages compared to other extracorporeal techniques: the capacity for removal of a wide range of molecular weights; enhanced clearance due to large surface area of sorbents material; and that sorbents do not rely on the removal of fluid for the clearance of toxins, potentially avoiding the time limitations of dialysis and the replacement fluid requirements of hemodiafiltration. CytoSorb® adsorption therapy may be of utmost benefit when applied early in the clinical course, for an adequate duration, and frequently repeated until hemodynamic stability is achieved. Among the important potential side effects associated with the use of sorbents in general, including CytoSorb®, is the removal of antibiotics, and other beneficial molecules, which should be carefully monitored with drug levels (when possible), and supplemented with additional doses as needed. Finally, although evidence to support the use of extracorporeal blood purification techniques (in general) in sepsis/other acute conditions is insufficient at this point, potential benefits (in particular, control of the exaggerated immune response, which typically translates into hemodynamic stability) cannot be ignored. Overall, CytoSorb® therapy seems to be safe and effective, with further studies to expand the knowledge on novel indications, such as management of the cytokine release syndrome, which complicates adoptive immunotherapies such as chimeric antigen receptor T cells (CAR T cells) warranted.

Comments by CytoSorbents

- It should be noted, that the article states that 25 (and not 20) patients were included in the Friesecke study, and that the Schädler 2013 data is reported as a separate patient study rather than interim analysis for the 2017 publication.
- The article states that CytoSorb® does not remove IL-10. The reference used for this is Kellum et al., 2008 where they reported that systemic levels of IL-10 did not decrease over 1 hr of CytoSorb® use in 8 brain dead subjects. However, the same article proves that there is indeed IL-10 removal by CytoSorb®, as shown by the comparison of simultaneous pre- and post adsorber measurements. So, despite a lack of decrease of systemic levels in these subjects, there is clear evidence that CytoSorb® removes IL-10.

<https://www.ncbi.nlm.nih.gov/pubmed/30253409>

Why do we need extracorporeal blood purification for sepsis and septic shock?

Simoni J.

Artif Organs 2019; 43(5):444-447

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Summary

In this invited editorial the author discusses the fact that there are still a lot unknowns in the field of sepsis and septic shock, mortality remains unacceptably high, there is a lack of efficacious drugs and a cure impossible given current knowledge. As an adjunctive therapy, blood purification technology is logical and urgently needed for the removal of sepsis and septic shock mediators: (i) pathogenic microorganisms, (ii) microbial toxins, (iii) inflammatory mediators (eg, anaphylatoxins, cytokines, other activators of leukocytes and platelets, (iv) vasoactive substances (eg, NO), and (v) other factors (eg, plasma free Hb, bilirubin, ammonia, uremic toxins, etc). The primary goal of blood purification is hemodynamic stabilization and attenuation of systemic inflammation and subsequent immunosuppression. In this review various forms of hemoadsorption are described including Polymyxin B®, oXiris®, and CytoSorb®. The lesson today is that “monotherapy” directed at attenuating a single molecule or a very narrow group of molecules, cannot overcome the damaging effects of an entire cascade of sepsis and septic shock mediators. To overcome this problem a much broader approach is necessary including safe and effective blood purification devices. According to the author, despite the present lack of data on significant outcome improvements, their positive role in the treatment of septic shock patients remains undisputed.

<https://www.ncbi.nlm.nih.gov/pubmed/30908693>

Hemoadsorption with CytoSorb®

Poli EC, Rimmel T, Schneider AG.

Intensive Care Med 2019; 45(2):236-239

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Summary

This review article focuses solely on hemoadsorption with CytoSorb®. The authors describe how CytoSorb® works and that it is currently marketed in 53 countries. Scientific evidence of CytoSorb® use in sepsis is given, including the RCT from Schädler et al., where it is noted that the short treatment time may have limited findings. The CytoSorb® Registry is also mentioned along with the studies from Friesecke et al. and Kogelmann et al. Use of CytoSorb® is also discussed in cardiac surgery, including the Bernardi et al. study, where it is again noted that the cytokine levels in these patients were not particularly high, perhaps explaining the lack of cytokine removal. Drug removal is also discussed however it is noted that potential removal of antibiotics should be monitored. Beneficial removal of medications in situations of intoxication (venlafaxine, dabigatran, ticagrelor, rivaroxaban) is briefly discussed. Finally, the recent approval for use for CytoSorb® for removal of myoglobin and bilirubin is also mentioned. The review notes that post marketing surveillance in over 20,000 patients has not reported any major adverse events. Future studies, the authors feel, should focus on patients with very high inflammatory responses, ideally pre-confirmed before inclusion in order to determine the ideal target population. The authors conclude that, until more evidence from RCTs becomes available, the users of CytoSorb® in clinical practice should be aware that there are still some open questions to be answered concerning clear evidence of benefit and potential undesired effects.

<https://www.ncbi.nlm.nih.gov/pubmed/30446798>

Extracorporeal techniques for the treatment of critically ill patients with sepsis beyond conventional blood purification therapy: the promises and the pitfalls

Ankawi G, Neri M, Zhang J, Breglia A, Ricci Z, Ronco C.

Crit Care 2018; 22(1):262

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Summary

Understanding the complex pathophysiology behind a sepsis induced dysregulated immune response (caused by both pathogen- and damage – associated molecular patterns – PAMPS and DAMPS that trigger both pro- and anti-inflammatory cytokines) has led to the development of therapeutic strategies aimed at restoring a balanced immune response by eliminating and/or deactivating these inflammatory mediators. Different extracorporeal techniques have been studied in recent years in the hope of maximizing the effect of renal replacement therapy in modulating the exaggerated host inflammatory response, including high volume hemofiltration (HVHF), high cut-off (HCO) membranes, adsorption alone, and coupled plasma filtration adsorption (CPFA). This review provides a comprehensive overview of the technical aspects, clinical applications, and associated side effects of these techniques. In regards to CytoSorb®, the evidence is described as limited at the moment, but growing. Literature suggests an improvement in hemodynamics and trend towards decreased mortality, with reductions in IL6 levels observed. Reasons for the to date neutral results

from the CytoSorb® randomized controlled trials are clearly explained, while a table summarizes the available main studies that report on the effectiveness and limitations of the adsorber.

<https://www.ncbi.nlm.nih.gov/pubmed/30360755>

Clinical Utility of Extracorporeal Cytokine Hemoadsorption Therapy: A Literature Review

Bonavia A, Groff A, Karamchandani K, Singbartl K.

Blood Purif 2018; 46(4):337-349

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Summary

Extracorporeal cytokine hemoadsorption is an emerging technology utilized in the treatment of dysregulated inflammatory states such as sepsis. In this review article the authors assess the literature relating to cytokine hemoadsorption in the context of sepsis. Three blood purification techniques are available including filtration, dialysis and adsorption however, this article focuses on adsorption and primarily CytoSorb® in particular. The CytoSorb® therapy is described in depth, its mode of action, as well as a review of literature supporting its various fields of application. Whilst larger and in particular randomized control trials are lacking, the authors provide a table describing the clinical reports relating to CytoSorb® therapy in peer reviewed articles. They also discuss ongoing trials, including the REFRESH II randomized controlled multicenter trial in the USA, as well as the CytoSorb® Registry. The latest interim analysis of the registry showed that none of the patients were affected by any device-associated side effects. Given the widespread reported use of this technology thus far, the authors are hopeful that the rate of clinician self-reporting increases in the future.

<https://www.ncbi.nlm.nih.gov/pubmed/30176653>

Neonatal and Pediatric General and Cardiac Anaesthesia and ICU: what's new in 2017/2018 ? -Bari Pediatric Hospital Experience-Italy

Milella L.

Journal of Pediatrics and Neonatal Care 2018; 8(1):00309

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Summary

This is a review of the current protocols and studies, recently published or in progress at the Neonatal and Pediatric General and Cardiothoracic Intensive Care Unit in Bari, Italy. In recent years pediatric units have adapted some of the techniques used to treat adults, including hemodiafiltration and new blood purification techniques for septic shock and sepsis treatment. The article describes some of these adaptations, such as how it successfully used the CytoSorb® in a patient with hemophagocytotic lymphohistiocytosis (HLH). As a result a pilot study has been conducted with CytoSorb® used in patients with sepsis, systemic inflammatory response syndrome (SIRS) and multi-organ failure or inflammatory changes caused by ECMO or ventricular assist devices. Cytokine levels were measured in the blood before, during and after CytoSorb® use with results appearing to confirm its reliability and effectiveness.

[Link to Article](#)

Extracorporeal membrane oxygenation and cytokine adsorption

Datzmann T, Traeger K.

Journal of Thoracic Disease 2018; Suppl 5:S653-S660

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Summary

Extracorporeal membrane oxygenation (ECMO) is increasingly used for mechanical support of respiratory and cardio-circulatory failure, but its use may lead to a similar excessive systemic inflammatory response as observed during sepsis and after cardiopulmonary bypass which may lead to multiple organ damage and failure. Therefore, controlling these excessively increased cytokines may be considered a valuable treatment option. This review article describes the mechanism of hemoadsorption therapy with CytoSorb® to decrease cytokine levels, as well as removal of other substance such as myoglobin, free hemoglobin and bilirubin. They describe how controlling the pro-inflammatory response with hemoadsorption may have a positive impact on the endothelial glycocalyx, and maintenance of the vascular barrier function. The authors acknowledge that whilst published data thus far on the use of CytoSorb® in ECMO is based on individual cases, it appears to offer a promising new option for the treatment of overwhelming inflammatory response, leading to faster hemodynamic and metabolic stabilization, finally resulting in preserved organ function.

<https://www.ncbi.nlm.nih.gov/pubmed/29732183>

Extracorporeal Sorbent Technologies: Basic Concepts and Clinical Application

Clark WR, Ferrari F, La Manna G, Ronco C.

Contrib Nephrol 2017; 190:43-57

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Summary

In this review article the basic principles that apply to sorbents are discussed, including composition, structure, fundamental mechanisms of solute removal and the importance of sorbent biocompatibility. The clinical application of sorbents is discussed. New sorbent-based clinical approaches for acute conditions are presented, including a chapter on CytoSorb® which is described and its use summarized in brief.

<https://www.ncbi.nlm.nih.gov/pubmed/28586767>

Continuous hemoadsorption with a cytokine adsorber during sepsis - a review of the literature

Houschyar KS, Pyles MN, Rein S, Nietzsche I, Dusche D, Maan ZN, Weissenberg K, Philipps HM, Strauss C, Reichelt B, Siemers F.

Int J Artif Organs 2017; 40(5):205-211

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Summary

Sepsis is a well-recognized worldwide healthcare issue, ultimately resulting in significant mortality, morbidity and resource utilization. In its most severe form, sepsis causes multi-organ dysfunction. Sepsis induces the activation of complement factor and the release of inflammatory cytokines such as tumor necrosis factor alpha (TNF- α) and interleukin-1beta (IL-1 β), resulting in a systemic inflammatory response. This review article analyzes the efficacy of CytoSorb® in reducing the inflammatory response during sepsis. CytoSorb® is known to have excellent adsorption rates for inflammatory cytokines such as IL-1 β , IL-6, IL-8, IL-10, and TNF- α . Studies have demonstrated that treatment with CytoSorb® has beneficial effects on the survival rate and inflammatory responses in animal septic models. Several cases have been reported in which treatment with CytoSorb® is very effective in the stabilization of organ failure and hemodynamics in critically ill patients. Therefore, treatment with CytoSorb® may play an important role in the treatment of sepsis in the future.

<https://www.ncbi.nlm.nih.gov/pubmed/28525674>

Extracorporeal renal replacement therapies in the treatment of sepsis: where are we?

Forni LG, Ricci Z, Ronco C.

Semin Nephrol 2015; 35(1):55-63

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Summary

This review outlines the use of extracorporeal therapies in the treatment of sepsis and septic AKI, considering the classic aspects of extracorporeal renal replacement therapy including indications, timing, and delivered dose but also discussing the various techniques that are currently used to achieve immune homeostasis. The authors discuss evidence accumulated to date and suggest possibilities for the future treatment of these patients. In this context, CytoSorb® therapy is mentioned as one of the most promising approaches, due to its improved biocompatibility and therefore the opportunity for whole blood perfusion, its efficiency in removing multiple inflammatory mediators shown in animal studies as well as in case reports, and its beneficial effects on chemokine gradients which may restore gradients towards infected tissue and away from healthy organs through leukocyte trafficking control.

<http://www.ncbi.nlm.nih.gov/pubmed/25795499>

Blood Purification and Mortality in Sepsis: A Meta-Analysis of Randomized Trials

Zhou F, Peng Z, Murugan R, Kellum JA.

Crit Care Med 2013; 41(9):2209-2220

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Summary

This is a systematic review and meta-analysis of randomized trials to determine the association between various blood purification techniques including hemofiltration, hemoperfusion, plasma exchange, and hemodialysis and all-cause mortality in humans with sepsis. A key finding of the review is that blood purification techniques were associated with lower mortality in patients with sepsis. These results were driven

mainly by hemoperfusion and plasma exchange. Noteworthy, polymyxin B hemoperfusion studies from Japan had the biggest influence on the results.

<http://www.ncbi.nlm.nih.gov/pubmed/23860248>

Newly Designed CRRT Membranes for Sepsis and SIRS-A Pragmatic Approach for Bedside Intensivists Summarizing the More Recent Advances: A Systematic Structured Review

Honore PM, Jacobs R, Joannes-Boyau O, De Regt J, De Waele E, van Gorp V, Boer W, Verfaillie L, Spapen HD. *ASAIO J* 2013; 59(2):99-106

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Summary

Since continuous renal replacement therapy (CRRT) in the treatment of sepsis and systemic inflammation response syndrome (SIRS) have shown relatively negative results, attention is now drawn to new membranes and sorbents that may better eliminate massive amounts of unbound mediators in a wider spectrum and also in greater magnitudes. This review summarizes the use and evidence of these newly designed technologies i.e. high cutoff CRRT membranes, high non-selective adsorptive CRRT membranes, high selective adsorptive CRRT membranes and cytokine-adsorbing columns. The authors state, that “CytoSorb® might be seen as the most promising although not having the ability to fix endotoxin”.

<http://www.ncbi.nlm.nih.gov/pubmed/23438770>

Moving from a Cytotoxic to a Cytokinic Approach in the Blood Purification Labyrinth: Have We Finally Found Ariadne's Thread?

Honore PM, Jacobs R, Joannes-Boyau O, Boer W, De Waele E, Van Gorp V, De Regt J, Spapen HD. *Mol Med*. 2012; 18:1363-1365

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Summary

In this article the authors discuss the new “cytokinik” approach introduced by Namas et al. potentially explaining the mode of action of hemoadsorption using large surface-area polymer (i.e. CytoSorb®) compared to the hitherto propagated “cytotoxic” hypotheses.

<http://www.ncbi.nlm.nih.gov/pubmed/23052299>

New membranes for extracorporeal blood purification in septic conditions

Bello G, Di Muzio F, Maviglia R, Antonelli M. *Minerva Anestesiol* 2012; 78(11):1265-1281

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Summary

This review discusses the use of available technologies for extracorporeal blood purification (hemoadsorption, coupled plasma filtration adsorption, high cut-off- and hemofiltration membranes) in sepsis. The authors specifically address the medical/scientific evidence of CytoSorb®, but also of all other procedures.

<http://www.ncbi.nlm.nih.gov/pubmed/22772857>

Clinical review: blood purification for sepsis

Rimmelé T, Kellum JA. *Crit Care* 2011; 15(1):205

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Summary

This review discusses the latest advances in blood purification for sepsis and how they relate to current concepts of disease. The authors review the underlying mechanisms and the current medical/scientific evidence for high-volume hemofiltration, cascade hemofiltration, hemoadsorption, coupled plasma filtration adsorption, high-adsorption hemofiltration and high-cutoff hemofiltration/hemodialysis. Though all technologies are biocompatible and effective (reduction of cytokines and in part bacterial toxins, improvement of physiological parameters such as hemodynamics and oxygenation), there is an urgent need for confirming large multi-center trials evaluating the ability of these therapies to improve clinical outcomes. Regarding CytoSorb®, the authors mainly discuss the two Kellum in vivo studies (endotoxin and cecal ligation and puncture model).

<http://www.ncbi.nlm.nih.gov/pubmed/21371356>