Continuous Hemodiafiltration with a Cytokine-Adsorber During Sepsis

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Disclosure

Speaker contract with CytoSorbents Europe
Introduction

• Sepsis is a well-recognized worldwide healthcare issue, ultimately resulting in significant mortality, morbidity and resource utilization during and after critical illness
• Although mortality related to severe sepsis and septic shock have reduced slightly in the past decade, it remains more than 20%
Causes of Sepsis

• Bacterial infections are the most common cause of sepsis, but sepsis can also be caused by fungal, parasitic, or viral infections

• The infection can originate from anywhere in the body
Causes of Sepsis

- **Sepsis**: Systemic inflammatory response syndrome (SIRS) resulting from infection (bacterial, viral, fungal, or parasitic).
- **Severe Sepsis**: Sepsis associated with at least one acute organ dysfunction, hypoperfusion, or hypotension.
- **Death**: Presence of altered function of two or more organs in an acutely ill patient, such that homeostasis cannot be maintained without intervention.
- **Septic Shock**: Sepsis with hypotension, despite adequate fluid resuscitation, along with the presence of perfusion abnormalities or organ dysfunction.
- **Multiple Organ Dysfunction Syndrome (MODS)**
Risk factors for developing sepsis

- Elderly
- Newborn
- Chronic illnesses such as Diabetic, cancer
- Immunocompromised such as after organ transplant, Splenectomy or those with HIV or AIDS
- Patients receiving immunosuppresive therapy such as chemotherapy
- Malnourished
- Debilitated patients
Systemic Inflammatory Response Syndrome

Criteria for the systemic inflammatory response syndrome (SIRS)

Two or more of the following:

- Temperature $>38^\circ C$ or $<36^\circ C$
- Heart rate $>90$ beats/min
- White blood cell count (WBC) $>12$ K or $<4$ K, or $>10\%$ bands
- Respiratory rate $>20$ or $\text{PaCO}_2 < 32$ mmHg
CytoSorb- Adsorber

1. Extracorporeal cytokine adsorber, approved in the European Union and broadly indicated for use in any clinical situation where cytokines are elevated

2. Represents a potentially major advance in the control of deadly inflammation in critically-ill patients and those undergoing complex cardiac surgery
CytoSorb-Adsorber

<table>
<thead>
<tr>
<th>Technical data of the CytoSorb® adsorber according to the manufacturer information</th>
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<tbody>
<tr>
<td>Extracorporeal blood volume: 120 ml</td>
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<tr>
<td>Blood flow rates min-max: 100-400 ml/min</td>
</tr>
<tr>
<td>Max. treatment duration: 24 hours</td>
</tr>
<tr>
<td>Anticoagulation: possible with heparin or citrate</td>
</tr>
<tr>
<td>Sterilization: Gamma sterilization</td>
</tr>
<tr>
<td>Further details: Latex- and PHT free product</td>
</tr>
<tr>
<td>Storage conditions: 1°C to 40°C; upright storage</td>
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</tbody>
</table>
CytoSorb-Adsorber
Case Study 1

Admission of a 72-year-old patient on March 19, 2016:
Scalding during cooking

**Diagnosis:**
2a-2b gradual scalding of 8% body surface

**Affected areas:**
Thorax on the right, back, thigh on both sides,
Buttocks on both sides, right foot, lower left leg
Secondary diagnoses

- Parkinson's disease of the akinetically-rigid type stage III with dysarthrophonia
- Omarthrosis on both sides
- Coronary heart disease
Operations

Day 2: Tangential debridement of the left thigh grafted with split skin graft

Day 5: Puncture tracheotomy
Course of IL-6

ng/l

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29
Course of IL-10

pg/ml

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29
Case Study 2

Admission of a 47-year-old patient on March 11, 2014:
Pneumococcal sepsis with intravascular coagulation

Diagnosis:
Waterhouse Friderichsen syndrome after dental treatment in pneumococcal sepsis
Condition after splenectomy after two-time splenic rupture after traffic accident 1989

Affected areas:
Both feet and lower legs, right hand
History diagnostics

- Catecholamine-compulsorily circulatory insufficiency
- Pneumonia (3 MRGN Pseudomonas)
- Transfusion-related anemia and thrombocytopenia in disseminated intravascular coagulation
- Herpes Simplex Infection
Operations

**Day 7:** Amputation in the area of both lower limbs in the middle third with septic microembolism of both feet and lower limbs

**Day 10:** Debridement in the area of the right lower limb

**Day 20:** Revision of both stumps and defect cover with split-thickness skin graft, amputation of the right thumb
Operations

Day 28: Debridement of the right hand and secondary closure

Day 35: Debridement, residual defect cover on both lower limb stumps with split-thickness skin graft
Course of IL-6

ng/l

0 50 100 150 200 250 300 350 400 450 500

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48

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Course of IL-10

pg/m

120
110
100
90
80
70
60
50
40
30
20
10
0

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48
Case Study 3

Admission of a 21-year-old patient on 06.03.2014, 0.30 am:
Apartment fire with explosion

Diagnosis:
2b-3 graded burn of 60% body surface

Affected areas:
Arms on both sides, face, thorax, back, thigh on both sides, genitalia

Inhalation trauma second grade (bronchoscopically secured)
Secondary diagnoses

- Depression
- Epilepsy
- Well-known drug abuse (Crystal Meth)

History diagnostics
- Thigh thrombosis left
- Heparin-induced thrombocytopenia (HIT)
Operations

Day 2: Epifascial debridement, MEEK 1:6/1:4 Abdomen and upper arm on both sides, ventral thorax and lower arms on both sides

Day 4: Epifascial debridement back, lower arms on both sides and MEEK transplant 1:4 on the back and 1:3 lower arms on both sides

Day 7: Tangential debridement of both hands, split-thickness skin graft 1:1.5, tangential debridement, thigh left with split-thickness skin graft 1:5, tangential debridement thigh right with MEEK transplant 1:4/1:3, split-thickness skin graft 1:1.5
Operations

**Day 16:** Epifascial necrectomy neck, groin region on the right, covering with 1:1 split-thickness skin graft

**Day 22:** Tangential debridement back, shoulders on both sides, thorax, axillae on both sides, left upper arm and cover by cultivated keratinocytes

**Day 27:** Tangential debridement of the remaining necrosis on both arms

**Day 31:** Tangential debridement back, shoulder, arms on both sides, split-thickness skin graft 1:3
**Germ spectrum**

<table>
<thead>
<tr>
<th>Day</th>
<th>Bacteria</th>
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<tbody>
<tr>
<td>Day 6</td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Day 16</td>
<td>Stenotrophomonas maltophilia</td>
</tr>
<tr>
<td>Day 16</td>
<td>Enterobacter cloacae</td>
</tr>
<tr>
<td>Day 19</td>
<td>Acinetobacter baumannii (4MRGN)</td>
</tr>
<tr>
<td>Day 19</td>
<td>Green Streptococci</td>
</tr>
<tr>
<td>Day 19</td>
<td>Coagulase negative staphylococci</td>
</tr>
<tr>
<td>Day 36</td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>Day 36</td>
<td>Klebsiella pneumoniae (3MRGN)</td>
</tr>
<tr>
<td>Day 48</td>
<td>Klebsiella pneumoniae (4MRGN)</td>
</tr>
</tbody>
</table>
Course of cytokines

Measured cytokines:
1. Proinflammatory: IL-6
2. Anti-inflammatory: IL-10
Interleukin 6

ng/l

0 500 1000 1500 2000 2500 3000 3500 4000

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42

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Interleukin 10

pg/ml

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Use of the CytoSorb-Adsorber
Discussion

• CytoSorb seems effective in reducing postoperative systemic inflammatory response syndrome

• In the present study, a successful outcome in a case of septic shock and multiorgan failure where CytoSorb was used as an adjuvant therapy is reported

• CytoSorb therapy in septic shock patients with multi-organ failure might be an option as rescue therapy

• However, further studies with prospective randomized control design would be necessary to establish the benefit of this therapy as an adjuvant treatment in septic shock
Conclusion

• Treatments have been considered safe and well-tolerated
• CytoSorb significantly reduced IL-6, a predictor of mortality in sepsis and surrogate for cytokine storm
• Improved hemodynamics as evidenced by a reduction in noradrenaline and a significant impact on the patients survival time
References


Thank you!