

Rationale of using CytoSorb therapy in critically ill COVID-19 patients

Background

There are two problems in severe COVID-19 infection. First, the virus infects the lower respiratory tract, causing direct pulmonary injury through viral replication, leading to viral pneumonia and pneumonitis. The virus can also be detected in the bloodstream, and may cause direct cardiac injury, liver injury, and other remote organ injury.

The second problem, as seen in influenza, other coronavirus infections (e.g. SARS, MERS), and now COVID-19 infection, is the development of a cytokine storm, driving systemic hyperinflammation with capillary leak syndrome, organ injury, and other complications. In critically-ill patients in the ICU, this contributes to a high risk of death due to a high incidence of complications such as ARDS, shock, kidney injury, acute cardiac injury and arrhythmias, and other organ dysfunction.¹⁾ Clinically there are usually 3 phases in severe courses. The early phase with rather mild signs of infection, the pneumonic phase, beginning with lymphocytic pneumonitis and the hyperinflammatory phase, which usually manifests itself from the 3rd week with a sepsis-like clinical picture.²⁾ Though not definitive, the cytokine and inflammatory marker profile associated with COVID-19 disease severity resembles secondary hemophagocytic lymphohistiocytosis (sHLH), a severe hyperinflammatory syndrome, which in nearly 30% of cases stems from a viral infection as the underlying condition.^{3,4)} Overall, cytokine storm seems to be a fundamental problem in quite some critically ill COVID-19 patients and controlling the inflammatory response may be as important as targeting the virus.⁵⁾

The mortality rate for critically-ill patients is very high and is directly related to age. Depending on the country, case mortality currently fluctuates between around 1.5 - 15 %⁶⁾

Rationale

CytoSorb is a European Union-approved extracorporeal cytokine adsorber, designed to broadly reduce cytokine storm and other inflammatory mediators in the blood that could otherwise lead to uncontrolled systemic inflammation, organ failure, and death in many life-threatening illnesses. CytoSorb is broadly indicated for use in situations where cytokines are elevated, which includes the treatment of COVID-19 complications. CytoSorb has been used safely in more than 98,000 treatments worldwide, primarily in the treatment of systemic hyperinflammation in a wide variety of life-threatening conditions such as septic shock, influenza, ARDS, secondary HLH, trauma, liver failure, pancreatitis and many others.

In the majority of reported cases, CytoSorb therapy has been used safely to treat many of the complications of organ dysfunction and failure in bacterial and viral sepsis, seen also in patients with COVID-19 infection, including ARDS, shock, and other complications. For example, CytoSorb therapy is associated with hemodynamic stabilization and a reversal of shock, as indicated by a reduction in vasopressor need and improvement in lactate clearance in many studies.⁷⁻¹⁶⁾ CytoSorb has also been used safely with positive clinical outcomes in the treatment of ARDS with both CRRT and ECMO.¹⁷⁻²⁴⁾ Animal and cell culture studies support a potential role of CytoSorb in protecting endothelial tight junctions against hyper-inflamed serum, which may translate into reduced capillary leak syndrome, as well as a modulation of pulmonary metabolism, edema formation, and cell-mediated infiltration and injury to the lungs.²⁵⁻²⁷⁾

CytoSorb therapy has also been used successfully in documented cases of secondary HLH.²⁸⁻³⁰⁾ Recent recommendations on the management of HLH patients³⁰⁾ mention cytokine adsorption, which may aid in rescuing critically-ill patients from a deleterious cytokine storm.

Experience in Treating Patients with COVID-19 infection

The rationale of using blood purification to treat cytokine storm in critically-ill COVID-19 patients was recently detailed by a recent publication that concluded, "Finally, a sepsis-like syndrome might occur frequently due to the virus itself or to a superimposed bacterial infection and in this case, since pharmacological approaches have shown poor results, new extracorporeal organ support therapies including haemoadsorption and haemoperfusion, with new sorbent cartridges designed to remove cytokines and other circulating mediators, should be considered."³²⁾

To date, more than 1200 critically-ill patients with COVID-19 infection have been treated with CytoSorb in various countries. Although official patient level data is mostly not yet available due to the extraordinary circumstances in these countries, the positive results in Italy have led to the formal recommendation by the Italy Brescia Renal COVID Task Force and published by the Italian Society of Nephrology and ERA-EDTA, to specifically use CytoSorb in severe COVID-19 patients with Stage 3 AKI receiving Continuous Renal Replacement Therapy (CRRT).³³⁾ Also, the recent National Guidelines on adult COVID-19 patients from Panama recommend CytoSorb therapy, as well as a recently published expert consensus from Colombia.^{34,35)} In addition, the recent Handbook of COVID-19 Prevention and Treatment from Zhejiang University School of Medicine, China, is also recommending blood purification to treat cytokine storm in critical cases of COVID-19 infection.^{36,37)} Previously published data indicate a rapid and sustained reduction of IL-6 levels, as well as an improvement in oxygenation and hemodynamics.^{38,39,40)}

Conclusion

In the light of all this, CytoSorb therapy may be a promising and important therapeutic option to help manage the serious complications caused by cytokine storm and hyperinflammation in critically-ill COVID-19 infected patients.

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