



Current Trends in Hemoadsorption Treatment for Critically Ill Patients: are We Moving Forward?

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Hemoadsorption is an extracorporeal therapy that uses specialized adsorptive filters to eliminate harmful substances, such as cytokines and toxins, selectively or non-selectively from a patient's bloodstream. In doing so, it aims to mitigate the systemic effects of severe inflammatory conditions. It represents a groundbreaking advancement in critical care medicine; its clinical applications are growing in various severe inflammatory conditions as an important adjuvant treatment to the standard of care in the last few years.

Accumulating evidence suggests that classical blood purification therapies do not eliminate middle- to large-sized cytokines in critical illnesses. When evaluating the role of cytokines in the pathophysiology of sepsis, studies have focused on reducing the cytokine levels by extracorporeal blood purification techniques.¹ In 1993, Bellomo et al.² suggested that continuous veno-venous hemofiltration via dialysis can remove both tumor necrosis factor- α and interleukin-1 beta from circulation in critically ill patients with sepsis. Further studies using both dialysis and high-volume hemofiltration were unable to strongly demonstrate their outcome benefits in patients with sepsis or in septic shock.³ Other than diffusion and convection, extracorporeal blood purification can occur by absorption via solid agents (sorbents). There are various commercially available hemoadsorption filters with sorbents having different physical properties. Sorbents are usually produced as granules, beads, or fibers, ranging in diameter from 50 μ m to 1.2 cm. These offer a significantly high surface area relative to their volume, providing a significant capacity and substantial surface for interactions with target substances (Figure 1). As blood or plasma is circulated through the sorbent bed, solutes are removed via adsorption, which occurs on the bead surfaces. Sorbent cartridges are either used alone or placed in the proximal part of a hemofiltration circuit (Figure 2).

The polymyxin-B endotoxin-absorbing column is a blood purification technique that was developed based on the fact that polymyxin-b molecules are capable of binding to lipopolysaccharide endotoxins. Polymyxin-B hemoperfusion studies have shown contradictory results in patients with sepsis. The last Surviving Sepsis Campaign Guidelines recommend against the use of polymyxin-B hemoperfusion therapy due to new evidence of the associated higher mortality rate when compared with past clinical studies.⁴

Hemoadsorption therapies have clinical applications in several systemic hyperinflammatory conditions, including sepsis/septic shock, non-infectious vasoplegic shock (such as in cardiac surgery), acute respiratory distress syndrome, coronavirus disease-19 (COVID-19), multitrauma, rhabdomyolysis, severe burn, severe acute pancreatitis, drug elimination for antithrombotic reversal, and ECMO for the prevention of a hyperinflammatory state. Current studies suggest that hemoadsorption beneficially affects the duration of intensive care unit and hospital stay, hemodynamics, and duration of mechanical ventilation. However, its effect on mortality remains uncertain. In a retrospective cohort study,

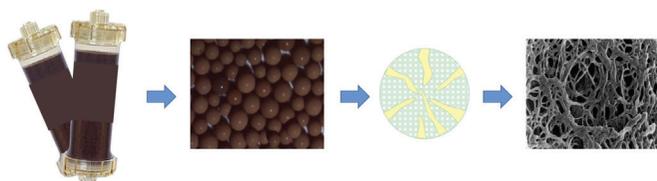


FIG. 1. The cartridges contain sorbents in the form of solid granules or powder, which have a significantly high surface area. It interacts with the target substances that need to be removed from the blood.



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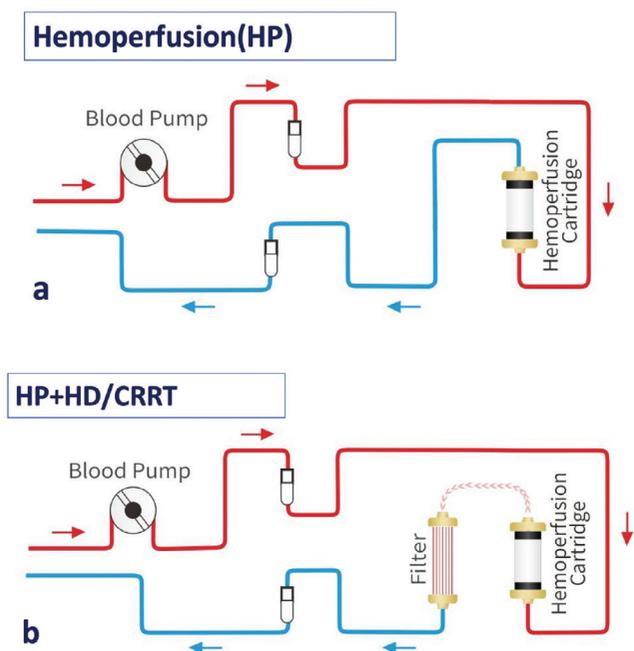


FIG. 2. Technical aspect of hemoabsorption treatment. a) Patient's blood is circulated through the sorbent unit (cartridge) by a pump so directly contacts with the particles or b) Cartridge is integrated into the hemodialysis or continuous renal replacement therapy (CRRT) circuit before the filter for absorption
 *HP: Hemoperfusion, **HD: Hemodialysis

high-dose hemoabsorption (6 l/kg) improved the survival rate in patients with septic shock.⁵ In another single-center retrospective study, patients who underwent hemoabsorption therapy had lower mortality rates and catecholamine levels than those who did not undergo hemoabsorption.⁶ Furthermore, hemoabsorption of ticagrelor/rivaroxaban in patients undergoing emergency open-heart operations reportedly reduces the risk of bleeding complications.⁷ Saller et al.⁸ determined that hemoabsorption therapy in patients undergoing aortic surgery with hypothermic circulatory arrest reduced the vasopressor and transfusion requirements and improved the acid-base balance. There have been case reports and series about its use in patients following a trauma, indicating its potential benefits in avoiding further renal injury.⁹ Randomized controlled trials (RCTs), consensus, and meta-analyses have determined that hemoabsorption is associated with improved dialysis complications, quality of life, and survival.^{10,11} Because COVID-19 worsens with marked severe systemic inflammation, there is significant scope for hemoabsorption studies in patients with COVID-19. Although some studies have shown clinical improvement and reduced inflammatory markers with hemoabsorption use in patients with COVID-19, some RCTs have failed to demonstrate an improvement in the outcomes because of the dysregulated overactivation of the systemic immune

system.^{12,13} Hemoabsorption in the pediatric population has also been studied. One study showed that hemoabsorption improved the severity scores of multiorgan dysfunction in children with septic shock.¹⁴

Despite the small studies and case series that have demonstrated positive results with hemoabsorption, meta-analysis studies have been unable to demonstrate this benefit. Thus, hemoabsorption is not used in routine clinical practice. In a 2023 meta-analysis of 34 studies, which included 1,297 patients who had received hemoabsorption and 1,314 who were controls, hemoabsorption did not lower the mortality rate in all the studies combined as well as in each subgroup (sepsis, cardiopulmonary bypass surgery, severe illness, and COVID-19).¹⁵ A significant limitation of this meta-analysis was the small number and quality of the studies included, in which the sample sizes were small and the populations were heterogeneous. This may have affected the conclusion. Mortality reduction alone cannot be considered an adequate end point because it might be affected by several other variables.

There are limitations to hemoabsorption therapy for a more extended clinical use. Heterogeneity of critical care patients poses a significant challenge to the selection of patients who are likely to benefit from this therapy. Till date, studies have been unable to clearly identify such a subgroup. Various underlying diseases and comorbidities can influence treatment outcomes, making it difficult to identify a criteria for the initiation and cessation of therapy and for the evaluation of the therapy's effectiveness across all patient groups. Another limitation of hemoabsorption therapy is the lack of a standardized protocol for its administration. Variability in the adsorbent material type or commercially available cartridge used, optimal treatment duration, and timing of the intervention can affect the efficacy of hemoabsorption therapy; thus, it is challenging to compare the results of different studies. Therapeutic drug monitoring is essential to maintain a constant concentration because the device may adsorb some antibiotics, antivirals, or antifungals. The high cost associated with hemoabsorption therapy is also a significant concern. Specialized equipment as well as personnel and expensive consumable cartridges can limit its widespread use, especially in healthcare systems with limited resources.

Although there is considerable uncertainty regarding the timing of administration and the phenotypes of patients to be treated, hemoabsorption regulates immune homeostasis. Thus, new clinical studies related to hemoabsorption are very important. Studies involving potential therapeutic targets in the field of microcirculatory dysfunction; such as glycocalyx, which maintains vascular permeability and modulates inflammatory responses; are urgently required. To overcome the limitations of hemoabsorption, further large-scale, well-designed, and powerful clinical trials that focus on the kinetics and transportation properties of sorbents, adsorption mechanism, and potential side effects and timing of treatment are urgently required. Future studies could identify certain patient groups that may benefit from hemoabsorption therapy with a more standardized administration protocol.

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