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Hemoadsorption in Critical Care – It Is a Useful or a Harmful Technique?

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Since ancient times it has been known that elimination of toxins from the body helps to relieve symptoms, heal patients; for that hot baths, sweating techniques, enemas, and phlebotomy were used in the treatment of severe diseases.

Blood purification is still practiced today, but using modern techniques. The theoretical basis for the elimination of toxins by osmosis and dialysis through a semipermeable membrane was laid by Thomas Graham in the 19th century, but the first "artificial kidney", was built and used successfully by Kolff only in 1943, in patients with acute renal failure [1, 2].

Since then, blood purification has developed a lot, today it is possible to eliminate endo- and exotoxins in acute and chronic renal failure, liver failure, intoxications with various substances, but also the elimination of mediators formed in excess in sepsis and systemic inflammatory syndrome of other etiologies, and elimination of immune complexes in autoimmune and graft versus host diseases.

In intensive care, we often encounter situations in which patients have a strong inflammatory response triggered either by a pathogen (bacterial endo/ or exotoxins, fungal beta-glycan or viral genetic material) through PAMP (Pathogen Associated Molecular Pattern), or through DAMP (Damage Associated Molecular Pattern), which is released in massive tissue injury in post-traumatic conditions, extensive burns, or caused by hypoperfusion in shock states. The systemic inflammatory syndrome can develop also by using advanced technology as vital support (extracorporeal membrane oxygenation - ECMO, cardiopulmonary bypass - CPB or even blood purification techniques that use extracorporeal circulation), triggered by the contact of blood with the foreign surfaces of extracorporeal circuit. This inflammatory syndrome is meant to defend the body against the invasion of microorganisms, to attenuate infection, to localize tissue necrosis, but in some conditions, these reactions are exaggerated, and instead of leading to recovery, they lead to multiple organ dysfunctions and even death [3, 4].

In the last decades, different methods, different drugs have been tried to alleviate this inflammatory syndrome, but without clear benefits. The lack of expected results is possible due to the fact that in these systemic inflammatory syndromes a series of cells are activated and dozens of pro- and anti-inflammatory mediators are released, so the elimination or neutralization of only one of them, will not improve the patient's condition. Ideally, they should be all eliminated by a single technique. Experimental and clinical trials in recent years show that hemoadsorption is close to this goal. Various filters capable of adsorption and elimination of cytokines and/ or endotoxins have been developed.

Toraymixin (Toray Industries, Tokyo, Japan) uses a polystyrene fiber column, which contains polymyxin B, capable to adsorb endotoxins. Several studies (EUPHAS I and II) have shown that after using these cartridges, hemodynamic parameters improved and 28 days-mortality decreased in patients with sepsis or septic shock caused by Gram-negative bacteria [5, 6]. In contrast, the ABDOMIX multicenter trial could not demonstrate any benefit, on the contrary, they observed an insignificant, but higher rate of death in those with endotoxin hemoadsorption than in the patients with conventional therapy [7].

Cytosorb cartridge (CytoSorbents Corporation, Monmouth Junction, NJ, USA) is the most commonly used and the most studied to date. It is able to ad-

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sorb cytokines, chemokines, complement, myoglobin, free hemoglobin, bilirubin and bile acids, toxins, and drugs up to 55 kDa. It has an area of 40,000 m2, being composed of polystyrene and divinylbenzene microspheres, and is able to absorb hydrophobic molecules, such as cytokines. The removal of substances is concentration-dependent, so normal levels of pro- and anti-inflammatory mediators are practically unaffected [8]. Several studies have demonstrated the effectiveness of hemoadsorption with Cytosorb cartridges, especially if hemoadsorption is established early in the evolution of sepsis [9, 10], but there are also studies in which no improvement was observed in septic patients [11].

The HA330 cartridges (Jafron, Zhuhai City, China) are composed of styrene divinylbenzene copolymers as adsorbent, and are able to remove cytokines, complement and free hemoglobin, as well as other molecules between 15-60 kDa [12].

Oxiris (Baxter, Meyzieu, France), an enhanced AN69 membrane cartridge copolymer, consisting of a hydrophobic molecule of acrylonitrile and a hydrophilic molecule of sodium methallylsulfonate, and thus is able to retain both positively charged molecules such as cytokines and also those negatively charged, such as endotoxins. It is treated on the surface with polyethyleneimine, which increases its adsorption capacity to endotoxins, and is treated also with heparin, which reduces its thrombogenicity and allows longer use. It is practically the only cartridge so far, which targets both the cause (endotoxins) and the consequences (cytokines and other pro- and anti-inflammatory mediators) of the systemic inflammatory syndrome [8].

Compared to Cytosorb, there are relatively few studies with Oxiris. Several studies have observed a decrease in the level of TNF-α, IL-6, IL-8, interferon, as well as an improvement in hemodynamic status, a decrease in lactate levels, and a decrease of the SOFA score in patients with septic shock [13, 14]. Schwindenhammer et al. show that even if the lactate level decreased and the pH returned to normal, no significant improvement of the SOFA score and hemodynamic status was observed [15].

An experimental study analyzing the 3 cartridges (Toraymyxin, Cytosorb and Oxiris) shows that the ability to absorb and eliminate inflammatory mediators of Cytosorb and Oxiris filters are comparable, with small differences in the elimination of TNF-α (90.1% by Oxiris, compared to 98.4% of Cytosorb), IL-1b (86.8% by Oxiris, compared to 97.2% by Cytosorb) and IL-12 (22.1% by Oxiris, compared to 76.5% by Cytosorb). Endotoxin adsorption is faster with Toraymyxin, but without significant differences comparing to Oxiris [16].

Regarding the use of hemoadsorption techniques, we must keep in mind that so far there are no large, randomized trials. Even multicenter studies have analyzed small groups of patients. So we have relatively few data on the effectiveness and safety of hemoadsorption techniques, and sometimes these studies are contradictory.

There are other concerns too, on which we don't have answers yet. If we disrupt the normal immune response by filtering pro- and anti-inflammatory mediators, what will happen in the organism? Eliminating proinflammatory mediators, we practically destroy the body's defense mechanisms. Adsorbing anti-inflammatory cytokines, we can maintain a continuous inflammatory state, promoting microvascular thrombosis, which leads to multiple organ dysfunction syndrome [8, 17].

We have different hemoadsorption techniques as useful tools, their use can help us change the prognosis of patients with sepsis and septic shock, and in the systemic inflammatory syndrome of other etiology. It is important to select carefully the patients for hemoadsorption, depending on their cytokine-level. These filters adsorb mediators that play a role in systemic inflammatory syndrome in a dose-dependent manner, so patients with increased levels of cytokines will benefit more. But cytokine-level monitoring is not yet a routine, not even in large centers. Early onset of hemoadsorption seems to influence the patients' prognosis more, but this goal is often difficult to achieve, given that patients at admission in intensive care can be far in advanced stages of sepsis or systemic inflammatory syndrome. Hemoadsorption seems to be a promising technology, so in the near future, we will have to find solutions to these problems. And it is also necessary to conduct large, multicenter, randomized trials to certify the effectiveness and safety of these filters.

Conflict of interest

None to declare.

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