

COVID-19: Hyperinflammatory Syndrome and Hemoadsorption with CytoSorb

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Following the emergence of a novel coronavirus from Wuhan, China, the world faced a major problem, so many countries were shocked by the outbreak of this virus. Unlike the rest of its dangerous family, it has a higher reproductive number than Middle East respiratory syndrome, which is estimated to be approximately 3.28 with a median of 2.79 and IQR of 1.16 [1]. Since August 29, 2020, the virus has infected more than 24 million people and killed more than 841,000.

At present, very few drugs have been effective in treating the disease, and no drug has been developed for definitive treatment [2, 3]; the most important treatment for these patients is supportive care [4]. The first cause of death in these patients was acute respiratory failure syndrome (ARDS) [5], and the second reason has been found to be hyperinflammatory syndrome [6, 7]. This complication is due to the high secretion of cytokines in relation to overactive immune response of the immune system, which leads to the multiple organ dysfunction syndromes, which may be the cause of acute respiratory failure. Hyperinflammatory syndrome is sometimes triggered by other viral infections in adults, with acute respiratory failure occurring in approximately 50% of cases [8].

According to recent findings, the characteristics of hemophagocytic lymphohistiocytosis are similar to the crit-

ically ill patients with COVID-19; therefore, these 2 diseases may have a common treatment. The cytokines observed in the critically ill patients with COVID-19 are increased interleukin (IL)-1, IL-2, IL-6, IL-7, granulocyte colony-stimulating factor, interferon- γ inducible protein 10, monocyte chemoattractant protein 1, macrophage inflammatory protein 1- α , and tumor necrosis factor- α [7, 9–11]. A study also found that the patients who died of coronavirus had higher levels of ferritin and IL-6 than those who survived [5]. Therefore, the idea may come to mind that patient survival may increase by suppressing the immune system. However, as in the MERS outbreak corticosteroids were not used routinely, even though in the COVID-19 outbreak immunosuppressive drugs have been used in a limited way and the results have been acceptable, these drugs also have their own side effects, which may worsen the patient's condition [6, 12]. Studies have also shown this hyperinflammatory syndrome can be prevented by IL-1 and IL-6 blockade [13, 14]. A meta-analysis study suggested a cutoff of more than 55 pg/mL of IL-6 for identifying patients at high risk of severe COVID-19 and more than 80 pg/mL can be used for identifying patients at high risk of mortality [15].

Hemoadsorption is a method used to purify the blood and separate the substances. To this end, different car-

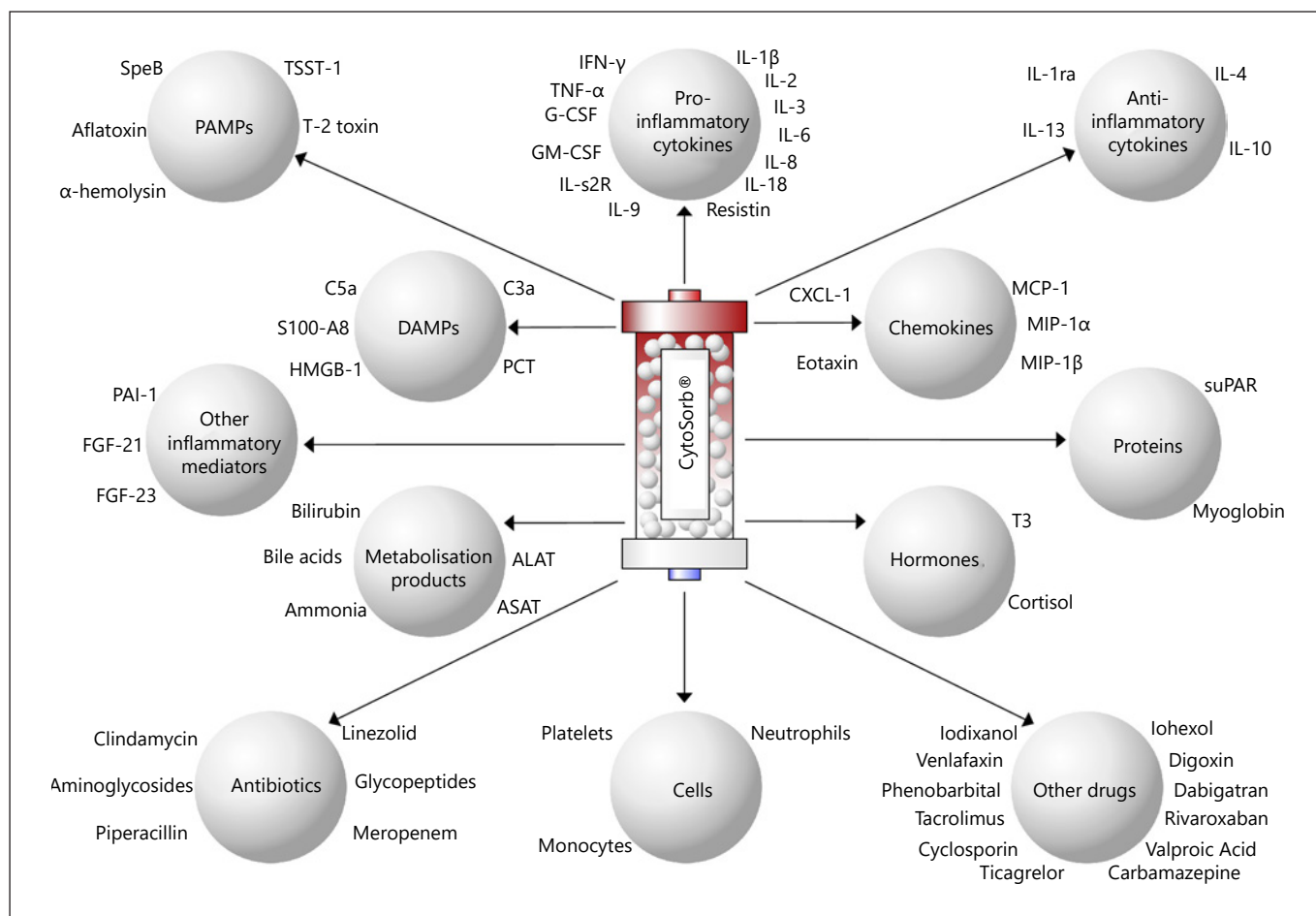


Fig. 1. Function of CytoSorb [photo was taken from Poli EC, Rimmele T, Schneider AG. Hemoadsorption with CytoSorb®. *Intensive Care Med.* 2019;45(2):236–9].

tridges are used, and the HA-330 type is designed to absorb the cytokines [16]. CytoSorb is a recent device designed to remove the cytokine from the blood using hemoadsorption. CytoSorb cartridges contain biocompatible polystyrene divinylbenzene copolymer beads capable of adsorbing the molecules of medium molecular weight using a combination of size exclusion and hydrophobic interactions [17]. CytoSorb can absorb a large number of inflammatory and pre-inflammatory factors and proteins [18] (Fig. 1).

In one study, the ability of this method to treat ARDS was confirmed [19]. However, this procedure is not without complications similar to other treatment methods, so removal of antibiotics and other beneficial molecules might lead to thrombocytopenia and leukopenia which are the side effects of hemoadsorption with CytoSorb [10].

Based on the above-mentioned points, it is hypothesized that this treatment modality is effective in treating critically ill patients with COVID-19 with ARDS and hyperinflammatory syndrome by removing inflammatory factors from the plasma. To date, definitive criteria for initiating hemoadsorption with CytoSorb in COVID-19 critically ill patients have not been established. However, it seems that the start of this treatment cannot be decided solely by considering the clinical condition and acute respiratory failure; it requires confirmation of the relationship between the level of inflammatory factors and ARDS.

Conflict of Interest Statement

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Author Contributions

Behnam Masmouei: study design and drafting the final version. Mehdi Harorani and Mohammad-Rafi Bazrafshan: gathering information and checking the accuracy of studies. Zahra Karimi: writing the first draft.

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