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Review Article

A Review of the Potential of Hemoperfusion for the Treatment of Patients with Respiratory Infectious Diseases with COVID-19 Approach

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ABSTRACT

Severe infection with COVID-19 disease can be associated with respiratory failure, kidney disorders, and in more advanced stages, organ failure and death. Unfortunately, there is currently no definitive cure for this disease, and damage to the immune system caused by inflammatory storms leads to widespread and varied complications that make an early diagnosis of the disease difficult. Therefore, eliminating or inhibiting the production of factors involved in inflammatory storms can be effective in improving the clinical condition of patients. According to specialized studies on the role of hemoperfusion in inhibiting advanced levels of COVID-19 disease, the present study was performed to investigate the use of hemoperfusion as a potential treatment option for this disease.

The growing trend in the number of patients with COVID-19 disease in 2020 indicates the need to equip medical centers with appropriate intensive care systems for this disease (1, 2 Studies show that about five percent of patients suffer from advanced respiratory distress syndrome and need intensive care [1-6]. Despite the valuable experiences that the medical staff of intensive care units in medical centers has gained since the beginning of the outbreak of this disease, the mortality rate of patients requiring intubation as well as those admitted to the ICU is still increasing. Although the use of some nonspecific therapies for patients with COVID-19 has resulted in a relative improvement in the clinical condition of these patients, the antiviral effects of these drugs are unclear [2,5]. Damage to the immune system of these patients can lead to multi-organ failure by activating inflammatory mediators [3]. Therefore, early detection and modulation of immune system activity and inhibition of inflammation-causing pathways through accurate monitoring of patients' clinical symptoms can play a significant role in preventing disease progression [7]. Various studies have been performed on ARDS caused by COVID-19 [3]. Some of these studies suggest that blood transfusion and the use of convalescent plasma may improve the relative clinical condition of patients with Covid-19 [4,8]. However, in some cases, this can make lung damage worse. Researchers have reported two types of lung injury, including low and high, based on the right to left shunt, elasticity, and lung weight [5]. The researchers acknowledged that patients in the H classification responded better to high levels of PEEP [9]. Hypoxia in such conditions is a syndrome with heterogeneous characteristics [10]. Studies have shown that the use of hemoperfusion alone or in combination with dialysis or continuous renal replacement therapy can prevent the progression of acute respiratory distress syndrome and renal and hepatic injury as well as a septic shock by inhibiting inflammatory mediators [11-15]. Besides, this method, by modulating the immune system, greatly

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inhibits multi-organ failure and significantly reduces the need for invasive ventilation [6].

Hemoperfusion and Inflammatory effect

Cytokine Storm Syndrome (CSS), which is caused by abnormal inflammatory responses following severe infections due to various factors such as the presence of infectious organisms in the body and can lead to sepsis, acute respiratory distress syndrome, and organ failure [16]. Inflammation is the body's physiological response to infectious agents and the onset of this process is associated with the diagnosis of infection and any tissue damage by immune system cells. During inflammation, cytokines including IL-1, 6, 8, 11, 12, interferon γ, and TNF-α are released, resulting in increased macrophage production. This leads to the dilation of the arteries and the migration of neutrophils to the infected tissues [17-21]. In the next stage, with the disappearance of the proinflammatory stimulus, protective reactions to control inflammation are produced by producing biomarkers such as IL-1RA, IL-4, and IL-10 [3,7,17,22]. In conditions such as sepsis, burns, acute lung injury, influenza, liver, and pancreatic insufficiency, as well as cytokine release syndrome, pro-inflammatory pathway balance and subsequent response are not properly regulated and inflammation is associated with life-threatening complications [23]. If this condition persists, the production of additional inflammatory mediators, especially cytokines, will increase [24].

Cytokines, which include chemokines, interferons, factors involved in tumor necrosis, lymphokines, and interleukins, are among the molecules involved in the pathways of the immune system that can play an active role in controlling the inflammatory process [25-29]. Despite the positive role of cytokines in inflammation, overproduction of these molecules can lead to vascular damage, increased vascular permeability, and ultimately cell death following edema and necrosis [30]. Therefore, the patient's clinical symptoms change and fever occurs, leukocytes accumulate and clots form in the arteries, and blood pressure and concentration decrease. In such cases, the patient needs to receive oxygen and, in many cases, pulmonary acidosis, alveolar hemorrhage, and pleural effusion are observed [29,31].

Hemoperfusion is a treatment method to purify and eliminate the toxicity of a patient's blood through the transfer of large volumes of blood, which is used to control conditions such as antibiotic-resistant secondary septic shock when infected with H1N1 influenza [32-33]. Hemoperfusion cartridges can control the progression of acute respiratory distress syndrome by absorbing cytokines and preventing these molecules from attaching to the alveoli and vessel walls, thus reducing the mortality rate of patients [34]. Hemoperfusion is also used in many surgeries and transplants of organs such as the heart, kidneys, and liver [35]. Also, the use of biocompatible compounds, as well as industrial resins in the preparation of hemoperfusion cartridges due to compatibility with the hemodynamic function of organs, can have better results [36].

Although the role of hemoperfusion therapy in diseases such as COVID-19 has been proven in many studies, understanding the mechanism of this method of treatment in the treatment of such infections requires more detailed studies [37-38]. Hemoperfusion devices can remove pro-inflammatory and anti-inflammatory cytokines that differ in patients and at different levels of the disease [39]. Hemoperfusion can lead to adverse effects by eliminating anti-inflammatory mediators and over-suppressing the immune system by increasingly reducing the pro-inflammatory response. Also, the role of this treatment in altering cytokines, endotoxins, or pathogens to provide an appropriate biological response is not yet clear [40-41]. The results of a study of patients with severe sepsis and acute respiratory distress syndrome showed that although interleukin-6 is eliminated through hemoperfusion, this method has no effect on reducing the level of this biomarker in the blood [42].

Also, based on the results of the previous study, the use of hemoperfusion in patients with septic shock has led to improved clinical conditions and increased patient survival [43]. However, past efforts to control inflammation in these patients have generally failed [43]. Although the use of methods such as hemofiltration and hemodiafiltration more successfully removes molecules such as cytokines than hemodialysis, they do not significantly improve the patient's clinical condition [44]. Similar therapies, such as plasma-assisted cytokine and interleukin therapy, are on the agenda for patients with COVID-19 [45]. But there are drawbacks to using these methods. Studies have shown that cytokine storms can destroy many of the proteins and immunoglobulins in plasma and thus weaken the immune system [46]. Another problem with plasma therapy is the change in the patient's hemodynamic status and severe hypotension like these methods, hemoperfusion can remove inflammatory cytokines by preserving important immunological proteins in the patient's plasma and maintaining the patient's hemodynamic status unchanged. This method can also be used in patients with hypotension and people with unstable hemodynamic conditions such as patients on dialysis [47-49].

Another advantage of using hemoperfusion is its ease of use in any treatment center that depends only on the dialysis machine. Other methods, such as plasma therapy, require special facilities such as special centrifuges in addition to the many benefits, these methods are associated with limitations and problems, including the removal of beneficial as well as harmful cytokines and some interleukins during plasma therapy and hemoperfusion [50]. Another method that combines hemoperfusion and plasma therapy is Plasma Filtration

Absorption (CPFA). In this method, the patient's plasma is removed from the blood with the help of a special filter and then in cytokines and inflammatory biomarkers free of hemoperfusion cartridge. This purified plasma is then transferred back to the patient [51-52]. This method is more successful in removing cytokines than hemoperfusion and does not cause hypotension and protein and immunoglobulin depletion due to plasma re-transfer to the patient [53].

Conclusion

According to the results of the present study, despite the positive role of hemoperfusion in the improvement of infectious diseases associated with severe inflammatory symptoms, however, the positive role of this method in the treatment of COVID-19 disease cannot be definitively reported. The use of clinical trials by members of treatment and research teams in the use of hemoperfusion for the treatment of this disease can pave the way to achieve the optimal treatment pathway of COVID-19 and similar infections.

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