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COVID-19 Pandemic Hemoperfusion Therapy versus Plasma Exchange Therapy in Intensive Care

Ali Esmaeili Vardanjani[1,2], Siamak Moayedi[3], and Mohamad Golitaleb[4]

[1] Department of Critical Care Nursing and Management, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran
[2] Department of Nursing, Faculty Member, Hamadan University of Medical Sciences, Hamadan, Iran
[3] Department of Emergency Medicine, University of Maryland School of Medicine, Baltimore, U.S.A
[4] Department of Critical Care Nursing, School of Nursing, Arak University of Medical Sciences, Arak, Iran

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TO THE EDITOR

Coronavirus disease 2019 (COVID-19) is a novel human infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus has affected the majority of countries worldwide. In a cohort study of Chinese patients with COVID-19 related pneumonia, 23% were admitted to the intensive care unit (ICU), 17% developed acute respiratory distress syndrome (ARDS), and 11% died of the disease complications.[1]

According to reports, 67% of critically ill patients with COVID-19 may develop organ failure partly due to a sepsis-like syndrome caused by high levels of circulating cytokines. This condition can affect many vital organs including the lungs, kidneys, heart, and liver.[2] The high levels of cytokines, commonly referred to as "cytokine storm", maybe indirectly triggered by sepsis or directly caused by the impact of the virus on the host's immune system. Previous experience with similar viruses influenza A virus subtype H1N1 (A/H1N1), SARS and Middle East Respiratory Syndrome (MERS) leads to the conclusion that the severity of the disease depends on patients' symptoms and immune system competency. Thus far, in the setting of severe hypoxic respiratory failure and septic shock caused by COVID-19, mechanical ventilation and hemodynamic support appears to be the only therapeutic options.[3]

The cytokine storm has been linked to the development and progression of ARDS, septic shock, and multi-organ failure in these patients. Therefore, timely removal of cytokines from the serum can potentially mitigate related complications.[4,5] Hemoperfusion (HP) is a treatment technique in which large volumes of the patient's blood are passed over an adsorbent substance to extract toxic substances. Hemoperfusion cartridges have been designed for the removal of cytokines in patients with antibiotic-resistant septic shock secondary to H1N1 influenza.[6,7] As H1N1-induced ARDS has been successfully treated with HP, this approach may prove to be helpful in the treatment of COVID-19 patients as well.[6] Hemoperfusion cartridges adsorb cytokines and impede their binding to alveoli and blood vessel endothelial. In turn, this may prevent the development and progression of ARDS, and reduce the mortality rate of the disease.[4,8] Extracorporeal methods such as hemofiltration or hemoperfusion provide a new opportunity to support various vital organs and prevent their dysfunction. In severe conditions, it may be possible to use specific extracorporeal devices and circuits to replace the heart, lungs, kidneys, and liver, or at least to preserve their functions.[8-10] According to reports from our Chinese colleagues, who have treated many patients with complicated COVID-19 related syndromes in the intensive care unit (ICU), it appears

Corresponding Author: Mohamad Golitaleb, MSc;
Department of Critical Care Nursing, School of Nursing, Arak University of Medical Sciences, P.O.Box: 3848176941, Arak, Iran. Tel: (+98 86) 3417 3504, Fax: (+98 86) 3417 3524, E-mail: m.golitaleb@arakmu.ac.ir

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that direct HP with the highly biocompatible sorbent and industrial resin cartridges has resulted in remarkable outcomes.[10] It seems that this approach is greatly beneficial to eliminate circulating cytokines and support hemodynamic and organ functions. Chinese scientists proposed using HA380 cartridges from the Jafron Biomedical company in a 2-1-1 manner (i.e. 2 units every 12 hours in the first 24 hours and 1 unit daily for 2 consecutive days).[8] As we are unable to constantly monitor cytokine levels, the reasonable approach may be to nonspecifically remove them with the assumption that cytokines with the highest concentration are removed at a higher rate. This strategy may mitigate organ dysfunction and augment the host's immune system response.[11]

In plasma exchange therapy (PET), along with cytokines and interleukins induced by the cytokine-storm, many other plasma proteins and immunoglobulins (IgG, IgM, IgA) are also removed. This weakens the immune system and makes the body vulnerable to pathogens. In addition, daily withdrawal of two to three liters of plasma affects the patient's hemodynamics and leads to hypotension.[12] On the other hand, HP primarily and specifically removes cytokines and other inflammatory mediators and spares plasma proteins. Furthermore, as no plasma volume is withdrawn from the patient with HP, it has a negligible effect on the patient's hemodynamics. Another point to be considered is that PET is contraindicated in patients with hypotension or those with hemodynamic disorders such as hemodialysis patients.[8,12,13] A further advantage of HP is that it does not require replacement of volume with a solution while with PET, the volume of harvested plasma must be replaced with 1-1.5 liters of crystalloids or 0.5-1 liter of colloidal (400 CC albumin 20%, gelatin product) solutions or 3-4 units of fresh frozen plasma (FFP) units. All of these replacement fluids options have their disadvantages. Meanwhile, during the coronavirus pandemic, we face a serious shortage of blood products, especially FFP and albumin.[8,12] HP is a much simpler procedure to be performed in comparison to PET. PET requires specific centrifuges which are limited in Iran, and most hospitals lack the instrument and trained staff to perform this procedure.[12-14] However, HP can be performed using a dialysis machine by trained dialysis staff in almost any hospital. Paradoxically, the cost of PET is covered by insurance but HP is not. Currently, the cost of each piece of HP cartridges is 3-4 times more expensive than PET filters. Both treatment modalities have considerable side effects. HP can lead to thrombocytopenia (usually rebounding within 24 to 48 hours), hypocalcemia, hypoglycemia, hypothermia, neutropenia, hypophosphatemia, and rarely hypotension (usually mild).[14] PET can cause a reduction in hemoglobin, fibrinogen, and antibodies Additionally it can lead to seizures, urticaria, chest pain, hypotension, and coagulation disorders.[13] A common disadvantage of both HP and PET is that they act indiscriminately by removing both harmful and beneficial cytokines and interleukins.[12-14] Coupled plasma filtration adsorption (CPFA) is an extracorporeal detoxification system that combines an HP cartridge and a plasma separator filter. In this method, the patient's plasma is withdrawn from the circulation by the separator filter and then enters into the HP cartridge. Then purified plasma depleted of cytokines and other inflammatory mediators returns to the patient. This method increases the efficiency of cytokine removal compared with HP alone. This is because instead of the whole blood, only plasma enters into the HP cartridge in CPFA. Because the plasma isolated in CPFA is returned to the patient (unlike PET), CPFA is not associated with hypotension and depletion of immunoglobulins and other proteins obviating the need for plasma volume replacement.[15] Ultimately, the most ideal approach would be to employ CPFA (i.e. combined PET & HP) instead of either HP or PET alone to optimize the efficacy of cytokine removal in patients with COVID-19 infection.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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