



Mortality Rate and Acute Kidney Injury Prevalence Reduction in COVID-19 Critical Patients Treated with Hemoperfusion

Abstract

Introduction: Coronavirus disease 2019 (COVID-19) induces organic damage mainly through the patient's immune overreaction. Hemoperfusion (HPF) can remove inflammatory cytokines and can reduce the negative effects of cytokine storm in COVID-19. We compared the mortality rate, inflammatory response, and acute kidney injury (AKI) prevalence among patients suffering from respiratory insufficiency secondary to COVID-19 treated with and without HPF with HA330 cartridge. **Methods:** Mortality rate, serum creatinine, and ferritin values were compared between patients suffering from respiratory insufficiency secondary to COVID-19 who received conventional treatment and another group of patients who additionally received four sessions of HPF with HA330. **Results:** Of 116 patients suffering from acute respiratory insufficiency secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), one group ($n: 84$) received support treatment and the other group ($n: 32$) additionally received HPF with HA330 cartridge. Both groups had no renal disease and similar age and comorbidities at admission, except for obesity and mechanical ventilation requirement, which were significantly higher in the HPF group. Mortality rate (61% vs. 31%, $P: 0.008$), serum creatinine (1.4 vs. 0.5 mg/dl, $P < 0.001$), and post-HPF serum ferritin (2868 vs. 1675, $P < 0.001$) were significantly lower in the HPF group. **Conclusion:** Mortality rate, serum ferritin, and AKI were significantly reduced in critical COVID-19 patients who received HPF with HA330 cartridge than in those who did not receive it. These results were obtained despite the HPF group risk factors, such as obesity and mechanical ventilation, worsening its prognosis.

Keywords: Acute kidney injury, COVID-19, hemoperfusion

Introduction

Coronavirus disease 2019 (COVID-19)-induced organic compromise is generated by a series of inflammatory mediators released by a patient's immune overreaction (cytokine storm).¹⁻⁵

Hemoperfusion (HPF) is an extracorporeal technique that involves the passage of blood (or plasma) through an adsorption cartridge, where solutes are removed by direct binding to the sorbent material. HA330 cartridge can bind cytokines.^{6,7} Previous studies have proposed the utility of HPF with HA330 cartridge in reducing the negative effects of cytokine storm in different settings, including COVID-19.⁶⁻⁹

Therefore, we decided to compare the mortality rate, inflammatory response, and acute kidney injury (AKI) prevalence between critical patients suffering from respiratory insufficiency secondary to COVID-19 who were treated with and without HPF-HA330.

Materials and Methods

This study was performed between March 2020 and March 2021 in the critical care units (CCU) of two Colombian medical centers. Adult (age >18 years) subjects who presented with respiratory insufficiency secondary to COVID-19 (PCR) requiring ventilation and a sequential Organ Failure Assessment (SOFA) score <8 at admission were admitted.

Mortality rate, serum creatinine, and ferritin values were compared between one group of patients suffering from respiratory insufficiency secondary to COVID-19 who received conventional treatment support, which consisted of inotropic substances, corticosteroids, antibiotics, and respiratory or renal artificial support (if required), in Clínica de la Costa (Barranquilla, Colombia) and another group of patients who additionally received four consecutive sessions of

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HPF–HA330 (Jafron® – Colombianmedicare®) initially every 12 h (sessions 1 and 2) and then every day (sessions 3 and 4). Informed consent was obtained from all patients included in the study, and this study was approved by the ethics committees of the Clínica de la Mujer (Bogotá) and the Clínica de la Costa (Barranquilla), Colombia.

All procedures performed in this study involving were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Results

A total of 116 patients with acute respiratory insufficiency secondary to SARS-CoV-2 were studied. The mean age was 57 years (range: 47–71 years) with males constituting 65%). One group ($n = 84$) received conventional support treatment (Barranquilla) and the other group ($n = 32$) additionally received complete HPF–HA330 treatment (Bogotá). Both groups had similar basal serum creatinine (0.9 mg/dl) and prevalence of hypertension (49%), diabetes mellitus (26%), chronic respiratory disease (12%), and cardiopathy (9%). However, the HPF group had higher prevalence of obesity (72% vs. 44%, $P = 0.013$) and mechanical ventilation requirement (90% vs. 48%, $P < 0.001$) than the non-HPF group.

Finally, the mortality rate (61% vs. 31%, $P = 0.008$), serum creatinine level (1.4 vs. 0.5 mg/dl, $P < 0.001$), and post-HPF serum ferritin value (2868 vs. 1675, $P < 0.001$) were significantly lower in the HPF group.

Discussion

Host inflammation response can produce harm not only by cytokine-induced cytotoxic effect, but also by perpetuating and expanding the immune cellular activation. This phenomenon leads to systemic inflammation, and thrombosis.⁸⁻¹⁰ Thus, it has been proposed that reducing cytokine activity could improve patient prognosis.¹⁰ Extracorporeal cytokine removal consists of blood purification procedures based on transmembrane hydrostatic pressure gradient which leads to solvent drag: convection, or solute adsorption to cartridge: hemoperfusion (HPF). The HPF with HA330 resin cartridge absorbs most inflammatory cytokines, and has been applied to sepsis, acute lung injury, hepatitis, pancreatitis, showing significant reduction of inflammatory cytokines with improvement in patient's clinical evolution.⁷ Additionally, HPF with HA330 reduced the circulating and alveolar cytokines levels, improved oxygenation, and attenuated lung injury.^{6,7}

COVID-19–associated inflammatory response can affect many organs, particularly the lungs.¹¹⁻¹³ IL-6 and ferritin are among the main characteristic parameters of the systemic inflammatory syndrome associated with COVID-19. Serum

ferritin is responsible for stimulating innate immunity cells such as macrophages. Consequently, macrophages secrete cytokines, generating the so-called cytokine storm, which induces severe multi-organ damage through the massive release of inflammatory mediators.^{1-5,8} In this sense, it has been observed that HPF-treated patients improved their clinical evolution, and reduced serum inflammatory mediators, in comparison to those patients treated without HPF.^{8,9} The prompt reduction of serum IL-6 level induced by HPF points to its effective removal through the cartridge resin absorption as the mechanism causing clinical improvement, but it has also been speculated that this improvement could also be attributed to a reset of blood cytokine levels, perhaps due to the inhibitory effect of HA–HPF on cytokines' production.^{8,9} However, HPF should be applied at the appropriate time of the inflammatory process, only when their SOFA score was lower than 8 at ICU admission.⁹ In our study, it has also been observed that despite the HPF-treated patients showing increased risk factors, such as a significantly higher prevalence of obesity ($P = 0.013$) and the requirement of mechanical ventilation ($P < 0.001$), they finally presented with significantly lower mortality ($P = 0.008$) and AKI incidence ($P < 0.001$). In addition, these benefit outcomes were associated with a significant reduction in post-HPF serum ferritin level ($P < 0.001$) with respect to the control group. It is worth mentioning that none of the potential adverse effects (hemolysis, thrombocytopenia, leukopenia, fever) reported in HPF-treated patients was observed in our study.⁹

Limitations

Instead of cytokines, ferritin was measured as inflammatory marker.

Conclusion

Mortality rate, serum ferritin levels, and AKI were significantly reduced in critical COVID-19 patients who received HPF–HA330 than those who did not.

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Nil.

Conflicts of interest

Juan P. Cordoba MD. has served as an external scientific consultant for Colombianmedicare, which is Jafron representative in Colombia, and he has received honoraria for his services, and Adriana Barriga MD. has been a speaker for Colombianmedicare.

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