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ORIGINAL RESEARCH CORONA EXPERIENCE

Efficacy of hemoperfusion in COVID-19 patients with difficult weaning from mechanical ventilation

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ABSTRACT

Background: Weaning of ventilated COVID-19 patients from ventilators has been a major problem in some of these patients. We performed hemoperfusion in a selective group of COVID-19 patients to facilitate weaning from the mechanical ventilation (MV).

Methodology: The present study was a retrospective case series of 30 consecutive COVID-19 patients, who showed difficulty with weaning off the ventilator. Hemoperfusion was performed by the HA330 disposable hemoperfusion cartridge (Jafron, China). Before and after hemoperfusion, changes in patients' hemodynamics, improvement in consciousness level, oxygen saturation, hypercapnia, initiating spontaneous breathing, and changes in lung involvement were assessed.

Results: The patients average age was 48.38 ± 15.04 years, with 17 (56.7%) females. The post-hemoperfusion values of SpO_2 ($P < 0.001$), mean arterial pressure ($P = 0.003$), positive end-expiratory pressure ($P < 0.001$), heart rate ($P < 0.001$), and ratio of arterial oxygen partial pressure to fractional inspired oxygen ($P < 0.001$) were significantly different compared to their pre-hemoperfusion values. The outcome of patients showed a significant relationship with age ($P = 0.017$) and spontaneous ventilation ($P = 0.001$).

Conclusions: The findings endorse the implementation of hemoperfusion for ICU-hospitalized COVID-19 patients experiencing difficulty in weaning from mechanical ventilation. Hemoperfusion demonstrated significant improvements in vital signs for the majority of patients and was associated with a successful weaning and survival rate of 63.3%. While these results are promising, further evidence is needed to consider hemoperfusion as an accepted clinical approach.

Abbreviations: APACHE II, acute physiology and chronic health evaluation-II, ARDS: acute respiratory distress syndrome, HR: heart rate, IL: interleukin, MV: mechanical ventilation, MAP: mean arterial pressure, RR: respiratory rate, PEEP: positive end-expiratory pressure, TNF-α: tumor necrosis factor alpha,

Keywords: COVID-19; Difficult Weaning; Mechanical Ventilation; Hemoperfusion

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1. INTRODUCTION

The emergence of SARS-CoV-2, a novel coronavirus strain causing coronavirus disease 2019 (COVID-19), profoundly impacted healthcare systems worldwide.[1] Given the widespread prevalence of COVID-19 and the lack of a definitive and specific treatment posing a serious threat to human health, significant efforts were made to develop effective treatment methods to reduce mortality and improve clinical symptoms of critically ill patients.[2] Inflammation plays a crucial role in the pathogenesis of COVID-19 and exacerbates its outcomes. An excessive immune response and cytokine storm can cause severe damage to lung tissue and other organs and lead to acute respiratory distress syndrome (ARDS) and multiorgan failure, thereby significantly increasing the risk of patient mortality.[3] Studies have shown that inflammation in the body is initiated by cytokines, including interleukins (ILs) 1, 6, 8, 11 and 12, interferon-gamma, and tumor necrosis factor alpha (TNF-α), and is modulated by anti-inflammatory mediators such as IL-1Ra, IL-4Ra, and IL-10Ra.[4] Dysregulation of the pro-inflammatory/anti-inflammatory cytokine axis triggers a cytokine storm, which can aggravate the patient's condition and cause organ dysfunction. These complications lead to prolonged ICU stays, increased dependence on mechanical ventilation, and higher mortality of these patients.[3,5]

Various methods, collectively known as extracorporeal clearance, are available to clear inflammatory mediators from the bloodstream, including hemodialysis, hemofiltration, hemoperfusion, and plasma exchange.[6] Among them is hemoperfusion, which can reduce pre-inflammatory cytokines that cause sepsis and shock, resulting in widespread inflammation and organ failure in patients.[7] This treatment method has been used historically as a life-saving last resort for drug poisonings such as salicylate and ethylene glycol poisonings where antidotes are not available, and physical removal of the toxic substance from the blood is inevitable.[8] Hemoperfusion has been proposed as a therapeutic method for alleviating the cytokine storm in patients with septic shock induced by drug-resistant H1N1 influenza virus infection.[9] It has also been successfully used to treat hypercytokinemia in patients with severe respiratory distress due to H1N1 influenza.[10] Thus, hemoperfusion is thought to be potentially effective for COVID-19 illness. Initial evidence has also indicated that hemoperfusion may be effective in reducing mortality rate among individuals with COVID-19.[11-14]

The practical experience of the authors during the pandemic showed that some critically ill COVID-19 patients who received mechanical ventilation experienced difficulty weaning from the ventilator after completing the treatment course. Suspecting the potential impact of cytokines in the patient's body on impeding weaning from the ventilator, the authors utilized hemoperfusion in this group of patients, which resulted in positive outcomes. The current research seeks to evaluate the efficacy of hemoperfusion in ICU-hospitalized COVID-19 patients with difficult weaning from mechanical ventilation.

2. METHODOLOGY

The present study was a retrospective case series of 30 consecutive COVID-19 patients hospitalized in the ICU of Imam Khomeini Hospital (Ardabil, Iran) from March 20, 2020 to March 20, 2021, who experienced difficulty weaning off the ventilator. The study was approved by the ethics committee of the Ardabil University of Medical Sciences (No.: IR.ARUMS.MEDICINE.REC.1401.074).

The inclusion criteria were: (1) Despite passing seven days from the first attempt at weaning, the patient could not successfully be weaned off the ventilator; (2) After complete implementation of the standard weaning protocol, the patient was in stable cardiopulmonary and electrolyte status and showed the necessary readiness for weaning from the ventilator but experienced unexplained weaning failure; (3) Age between 20-75 years, and (4) Ferritin levels above 2000 mg/dL. In addition, all patients were evaluated for weaning-related underlying diseases and were stable, without any underlying disease affecting weaning.

They underwent hemoperfusion once or twice at intervals of 48-72 hours. Hemoperfusion was performed by the HA330 disposable hemoperfusion cartridge (Jafron, China). All hemoperfusion procedures were performed under the supervision of the hospital's scientific committee, including respiratory, infectious disease, anesthesia, and hematology services. The standard protocol of weaning from the ventilator was implemented. One week was considered necessary for weaning. Before and after hemoperfusion, changes in patients' hemodynamics, improvement in consciousness level, oxygen saturation, hypercapnia, initiating spontaneous breathing, and changes in lung involvement were assessed. The collected variables for each patient were sex, age, disease history, mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), saturation of peripheral oxygen (SpO_2), positive end-expiratory pressure (PEEP), ratio of arterial oxygen partial pressure to fractional inspired oxygen (P/F ratio), plateau pressure, compliance, spontaneous ventilation, number of hemoperfusion treatments, complications of hemoperfusion, duration of hospitalization, duration of intubation, APACHE II score, outcome, and the cause of death (if any).

The data were analyzed using SPSS V.25 (SPSS, RRID:SCR_002865). Quantitative data were presented as average and standard deviation (SD),

Table 1: Patient characteristics by outcome

Parameters	Outcome		P-value
	Successfully weaned	death	
Age	44.1 ± 15.6	50.6 ± 10.2	0.017
Gender			
• Male	8 (42.1)	5 (45.5)	0.858
• Female	11 (57.9)	6 (54.4)	
Disease history			
• Yes	13 (68.4)	11 (100)	0.061
• No	6 (31.6)	0	
Hospitalization duration	30.3 ± 19.1	28.1 ± 13.2	0.776
Hemoperfusion treatments	1.56 ± 0.50	1.71 ± 0.48	0.499

Data presented as n (%) or mean ± SD

while categorical data were described in terms of frequency and percentage. The normality of data distribution was evaluated using the Kolmogorov-Smirnov test. Independent t-test, Mann-Whitney U test, paired t-test, and Wilcoxon test, were used for data analysis. A $P < 0.05$ was deemed to be statistically significant.

3. RESULTS

The patients average age was 48.38 (SD =15.04) years. Seventeen (56.7%) patients were female, and thirteen (43.3%) were male. Twenty-four (80%) patients had a history of underlying diseases. The mean duration of hospitalization and intubation for patients were 28.60 ± 17.08 and 22.56 ± 19.14 days, respectively. The APACHE II score for patients was 32.20 ± 20.86. Complications of hemoperfusion were observed in 5 (16.7%) patients (gastrointestinal bleeding in 13.3% and kidney gangrene in 13.3% of the patients). Twenty-three (76.7%) patients had successful weaning, while eleven (36.7%) patients lost their lives. The causes of death were unsuccessful weaning (23.3%), renal failure (6.7%), deteriorated consciousness (3.3%), and cardiac complications (3.3%).

The outcome of patients showed a significant relationship with age ($P = 0.017$) and spontaneous ventilation ($P = 0.001$) but no statistically meaningful association with gender ($P = 0.858$), disease history ($P = 0.061$), duration of hospitalization ($P = 0.776$), and number of hemoperfusion treatments ($P = 0.499$) (Table 1).

The post-hemoperfusion values of P/F ratio ($P < 0.001$), MAP ($P = 0.003$), HR ($P < 0.001$), PEEP ($P < 0.001$), and SpO_2 ($P < 0.001$) were significantly different compared to their pre-hemoperfusion values. However, no statistically meaningful differences were noted in pre- and post-hemoperfusion values of RR ($P = 0.086$), plateau pressure ($P = 0.709$), and compliance ($P = 0.563$) (Table 2).

Table 2: Hemodynamic parameters of patients before and after hemoperfusion

Parameter	Before hemoperfusion	After hemoperfusion	P-value
SpO_2 (%)	90.7 ± 1.6	95.2 ± 2.0	< 0.001
MAP (mmHg)	73.4 ± 3.1	76.5 ± 3.7	0.003
RR (per min)	12.9 ± 1.6	11.9 ± 2.3	0.086
HR (per min)	99.0 ± 9.2	85.0 ± 7.3	< 0.001
P/F ratio	74.1 ± 12.2	149.2 ± 17.3	< 0.001
PEEP (cmH_2O)	9.4 ± 1.6	7.3 ± 1.1	< 0.001
Platue pressure	23.1 ± 3.1	21.7 ± 3.2	0.709
Compliance	30.2 ± 5.4	32.1 ± 4.6	0.563

Data presented as mean ± SD

4. DISCUSSION

With the global emergence and spread of COVID-19 and the failure of healthcare systems to control it, various approaches for managing and treating patients with this disease, particularly critically ill patients, have been proposed. Impaired immunoregulation plays a significant role in the pathogenesis of acute respiratory distress syndrome and multiorgan failure observed in critically ill COVID-19 patients.[15] Numerous cytokines are involved in this pathway, which could potentially be eliminated from the patient's circulation via a technique known as hemoperfusion.[3] Hemoperfusion involves the use of specialized devices that selectively remove molecules such as endotoxins or provide broad adsorption of pro-inflammatory mediators. Despite being utilized for many years, hemoperfusion has shown varying results in clinical practice.[16] In this research, we examined the effect of hemoperfusion on the weaning of difficult-to-wean patients who had failed to be weaned off the ventilator for seven days after the initial attempt due to unexplained reasons.

The results of our study presented evidence supporting the efficacy of hemoperfusion in COVID-19 patients with difficult weaning. Of 30 ICU-hospitalized corona patients undergoing mechanical ventilation

who experienced difficulty weaning from the ventilator, 19 (63%) were successfully weaned off the ventilator after hemoperfusion.

In the current study, the deceased patients had a significantly higher age compared to those who were successfully weaned from the ventilator and survived (P = 0.017). Advanced age is identified as a significant contributing factor for mortality in COVID-19, and our results are consistent with previous findings. The reason is that aging contributes to immune dysfunction in older people due to immune-senescence and inflammations. In addition, the prevalence of underlying diseases, which are strongly associated with COVID-19-related mortality, is higher in elderly patients.[17,18] These factors play a role in the higher severity of the disease and, consequently, the higher mortality in elderly patients with COVID-19. Moreover, they may compromise the expected effectiveness of various therapeutic interventions and increase the mortality in this age group despite treatment intervention.

The present study indicated a tendency towards a significant association between underlying diseases and successful weaning from the ventilator, with lower rates of successful weaning in patients with underlying diseases (P = 0.061). Our finding aligns with previous studies demonstrating a strong association between underlying diseases and death rate among individuals with COVID-19.[19]

The frequency of death among the patients was 36.7% in our study, which is much higher than the overall mortality reported by the World Health Organization (WHO) for COVID-19 patients.[20] The high mortality rate in corona patients in the current study can be explained by the fact that they were all critically ill and mechanically ventilated in the ICU. In a recent systematic review and meta-analysis (2021) on 33 studies, including 13398 COVID-19 patients, the mortality rate of hospitalized coronal patients was estimated as 17.1%[21] and ranged from 11.5 to 40.5% depending on the disease severity. The frequency of death in our patients is within the same range and close to the upper bound.

Several other studies have also examined the therapeutic effect of hemoperfusion on COVID-19 patients. In a study by Dastan et al.,[11] SpO_2 levels increased following hemoperfusion. Their result is consistent with our finding regarding the improvement of vital signs of patients with severe COVID-19 disease after hemoperfusion. Asgharpour et al.[12] reported improvement in 60% of COVID-19 patients after hemoperfusion, which is close to our reported rate of 63.3%. Similarly, a study by Mikaeili et al.[13] found that hemoperfusion led to a notable improvement in symptoms and a decrease in mortality rates among patients with severe COVID-19. In line with our finding, Abbasi et al.[14] discovered that patients undergoing early perfusion were less likely to require mechanical ventilation and had a significantly reduced duration of mechanical ventilation than those who did not receive hemoperfusion.

Conversely, Soleimani et al.[22] reported that hemoperfusion did not affect mortality in corona patients and that there was no notable disparity in mortality rate between hemoperfusion and control groups. Following treatment with hemoperfusion, improvement in ventilation and respiratory status has been reported in ARDS cases, in addition to hemodynamic improvement.[23] Consistently, in our study, post-perfusion SpO_2 level significantly increased compared to its pre-perfusion value. In the study by Dastan et al., the SpO_2 level increased considerably in a COVID-19 patient following hemoperfusion, and his clinical status improved.[11] In another study by Kozohiro et al. hemoperfusion improved hypoxemia in patients with severe ARDS and under mechanical ventilation.[24]

5. LIMITATIONS

The main limitations of this study include its single-center design, small sample size, and the lack of a control group.

6. CONCLUSION

In conclusion, our study findings support the use of hemoperfusion in ICU-hospitalized COVID-19 patients experiencing difficulty in weaning from mechanical ventilation. Hemoperfusion demonstrated significant improvements in vital signs for the majority of patients and was associated with a successful weaning and survival rate of 63.3%. While these results are promising, further evidence is needed to consider hemoperfusion as a routine clinical approach. Future large-sample multicenter studies are warranted to corroborate and elucidate our observations.

7. Conflicts of interest

No conflicts of interests declared by the authors.

8. Data availability

Numerical data generated in this study is available with the corresponding author, and can be provided on request.

9. Author Contributions

SF, SM, AV, MS: Conception and design

SF, SM, AV: Administrative support

SF, SM, AV, MH, MY: Provision of study materials or patients

All authors took part in collection and assembly of data, data analysis and interpretation, manuscript writing and final approval of the manuscript

10. REFERENCES

1. Parisi N, Janier-Dubry A, Ponzetto E, Pavlopoulos C, Bakalli G, Molina R, et al. Non-applicability of a validated predictive model for intensive care admission and death of COVID-19 patients in a secondary care hospital in Belgium. J Emerg Crit Care Med. 2021;5:1-13. DOI: 10.21037/jeccm-20-173
2. Abidin NHZ, Lee CK, Zakaria SA, Ramaiah Y, Hilmi ZS, Maule SS. Clinical course and outcomes of ventilated critically ill COVID-19 patients in Selangor state, Malaysia. J Emerg Crit Care Med. 2021;5(6):1-7. DOI: 10.21037/jeccm-20-82
3. Darif D, Hammi I, Kihel A, Saik IEI, Guessous F, Akarid K. The pro-inflammatory cytokines in COVID-19 pathogenesis: What goes wrong? Microb Pathog. 2021;153:104799. [PubMed]
4. Anand D, Ray S, Bhargava S, Das S, Garg A, Taneja S, et al. Proinflammatory versus anti-inflammatory response in sepsis patients: looking at the cytokines. Crit Care. 2014;18(Suppl 2):P13. [PMC] DOI: 10.1186/cc14016
5. Hu B, Huang S, Yin L. The cytokine storm and COVID-19. J Med Virol. 2021;93:250-6. doi: 10.1002/jmv.26232. [PubMed] DOI: 10.1002/jmv.26232
6. Monard C, Rimmele T, Ronco C. Extracorporeal blood purification therapies for sepsis. Blood Purif. 2019;47(Suppl 3):2-15. [PubMed] DOI: 10.1159/000499520
7. Ronco C, Bellomo R. Hemoperfusion: technical aspects and state of the art. Crit Care. 2022;26(1):1-12. DOI: 10.1186/s13054-022-04009-w [PubMed]
8. Ke J, Wei Y, Chen B. Application of hemoperfusion in the treatment of acute poisoning. Blood Purif. 2024;53(1):49-60. DOI: 10.1159/000532050 [PubMed]
9. Binh NG, Manabe T, Co DX, Tuan ND, Thach PT, Kudo K. Polymyxin-B-immobilized-fiber column hemoperfusion with oseltamivir treatment for ARDS due to influenza H1N1/09. Respirol Case Rep. 2015;3(2):57-60. DOI: 10.1002/rcr2.100 [PubMed]
10. Takeda S, Munakata R, Abe S, Mii S, Suzuki M, Kashiwada T, et al. Hypercytokinemia with 2009 pandemic H1N1 (pH1N1) influenza successfully treated with polymyxin B-immobilized fiber column hemoperfusion. Intensive Care Med. 2010;36:906-7. DOI: 10.1007/s00134-010-1830-8 [PubMed]
11. Dastan F, Saffaei A, Mortazavi SM, Jamaati H, Adnani N, Samiee Roudi S, et al. Continues renal replacement therapy (CRRT) with disposable hemoperfusion cartridge: a promising option for severe COVID-19. J Glob Antimicrob Resist. 2020;21:340-1. DOI: 10.1016/j.jgar.2020.04.024 [PubMed]
12. Asgharpour M, Mehdinezhad H, Bayani M, Zavareh MSH, Hamidi SH, Akbari R, et al. Effectiveness of extracorporeal blood purification (hemoadsorption) in patients with severe coronavirus disease 2019 (COVID-19). BMC Nephrol. 2020;21(1):1-10. DOI: 10.1186/s12882-020-02020-3 [PubMed]
13. Mikaeili H, Taghizadieh A, Nazemiyeh M, Rezaeifar P, Zununi Vahed S, Safiri S, et al. The early start of hemoperfusion decreases the mortality rate among severe COVID-19 patients: A preliminary study. Hemodial Int. 2022;26(2):176-82. DOI: 10.1111/hdi.12982 [PubMed]
14. Abbasi S, Naderi Z, Amra B, Atapour A, Dadkhahi SA, Eslami MJ, et al. Hemoperfusion in patients with severe COVID-19 respiratory failure, lifesaving or not? J Res Med Sci. 2021;26(1):34. DOI: 10.4103/jrms.JRMS_1122_20 [PubMed]
15. Tsang HF, Chan LWC, Cho WCS, Yu ACS, Yim AKY, Chan AKC, et al. An update on COVID-19 pandemic: the epidemiology, pathogenesis, prevention and treatment strategies. Expert Rev Anti Infect Ther. 2021;19(7):877-88. DOI: 10.1080/14787210.2021.1863146 [PubMed]
16. Ricci Z, Romagnoli S, Reis T, Bellomo R, Ronco C. Hemoperfusion in the intensive care unit. Intensive Care Med. 2022;48(10):1397-408. DOI: 10.1007/s00134-022-06810-1 [PubMed]
17. Goshayeshi L, Akbari Rad M, Bergquist R, Allahyari A, Hashemzadeh K, Hoseini B. Demographic and clinical characteristics of severe COVID-19 infections: a cross-sectional study from Mashhad University of Medical Sciences, Iran. BMC Infect Dis. 2021;21:1-8. DOI: 10.1186/s12879-021-06363-6 [PubMed]
18. Eid RA, Attia AM, Hassan M, Shaker MA, Kamal MA. Demographic, clinical, and laboratory characteristics of patients with COVID-19 during the second and third waves of the pandemic in Egypt. Infect Public Health. 2021;14(10):1358-66. DOI: 10.1016/j.jiph.2021.08.009 [PubMed]
19. Choi WY. Mortality rate of patients with COVID-19 based on underlying health conditions. Disaster Med Public Health Prep. 2022;16(6):2480-5. DOI: 10.1017/dmp.2021.139 [PubMed]

20. Organization WH. WHO Coronavirus (COVID-19) Dashboard. Available from: https://covid19.who.int/

21. Macedo A, Goncalves N, Febra C. COVID-19 fatality rates in hospitalized patients: systematic review and meta-analysis. Ann Epidemiol. 2021;57:14-21. DOI: 10.1016/j.annepidem.2021.02.012 [PubMed]

22. Soleimani A, Taba SM, Taheri SH, Loghman AH, Shayestehpour M. The effect of hemoperfusion on the outcome, clinical and laboratory findings of patients with severe COVID-19: a retrospective study. New Microbes New Infect. 2021;44:100937. DOI: 10.1016/j.nmni.2021.100937 [PubMed]

23. Kogelmann K, Jarczak D, Scheller M, Drüner M. Hemoadsorption by CytoSorb in septic patients: a case series. Crit Care. 2017;21(1):1-10. DOI: 10.1186/s13054-017-1662-9 [PubMed]

24. Kazuhiro Y, Yamasaki K, Kawanami T, Tokuyama S, Ogoshi T, Kouzaki M, et al. A case of successful treatment with polymyxin B-immobilized fiber column direct hemoperfusion in acute respiratory distress syndrome after influenza A infection. Intern Med. 2011;50(6):601-5. DOI: 10.2169/internalmedicine.50.4604 [PubMed]

