



# The effect of hemoperfusion on the recovery of COVID-19 in hospitalized patients; case series and review study

Sepideh Hajian<sup>1</sup> , Nafiseh Rastgoo<sup>2\*</sup> 

<sup>1</sup>Department of Nephrology, Velayat Hospital, Qazvin University of Medical Sciences, Qazvin, Iran

<sup>2</sup>Student Research Committee, Qazvin University of Medical Sciences, Qazvin, Iran

## \*Correspondence to

Nafiseh Rastgoo, Email:  
nafis.rastgoo.20@gmail.com

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## Abstract

Hemoperfusion is an effective modality in removing certain toxins from the blood, especially those that bind to proteins in the body. Hemoperfusion has shown a therapeutic effect on COVID-19 patients. In this case series, we report four patients without effective results following the use of hemoperfusion on the recovery of COVID-19 patients. This study is a case series which carried out on four patients referred to COVID-19 ward of Velayat hospital in Qazvin, Iran. The mean age of the COVID-19 patients was  $52.75 \pm 18$  years. The mean stay at the hospital was  $21.5 \pm 15.15$  days. This study showed that hemoperfusion cannot show a significant therapeutic effect on COVID-19.

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## Introduction

On March 11, 2020, a pandemic of COVID-19 was announced by the World Health Organization (WHO) as an infectious disease of the century with many detrimental effects on public health (1). The effect of COVID-19 on various organs including the lungs and kidneys is life-threatening, because several factors affect the frequency and severity of the consequences. Despite the use of various drugs including antivirals, there are no acceptable results (2). While there is no effective anti-virus drug or vaccine for COVID-19, there is a strong need for new treatment measures such as hemoperfusion to improve the prognosis of this group of patients (3). Hemoperfusion is a treatment in which a large amount of the patient's blood is transferred to an adsorbent to remove toxins from the blood. Absorption is the process in which the molecules or particles of a substance are absorbed to the surface of a solid and stored there (4, 5). Hemoperfusion is more effective than other treatments in removing certain toxins from the blood, especially those that bind to proteins in the body or those that are difficult to dissolve. Hemoperfusion is used to treat overdose of drugs such as barbiturates, carbamazepine, methotrexate, and acetaminophen, as well as to treat paraquat poisoning (6-8). Severe

## Key point

In patients with COVID-19, relying only on hemoperfusion does not guarantee a significant therapeutic effect. Therefore, alternative therapeutic modalities should be considered too.

infection and septic shock are common causes of death in hospitalized patients. Sepsis often occurs after infection, in which the body responds by producing chemicals that cause massive inflammation throughout the body. This inflammation can lead to failure of organs such as the kidneys, heart, circulation or lungs. This organ failure, which is caused by inflammation, leads to a high rate of infection-related death (9-11). In hemoperfusion, after the blood is removed, its toxins are removed through a filter. The clean blood is then returned to the patient through a catheter. This method requires particular specialized equipment and additional training (12, 13). Approximately 67% of critically ill COVID-19 patients develop multi-organ failure which is due to cytokines released into the blood (14). We report four patients with effective results following the use of hemoperfusion on the recovery of COVID-19 patients.

### Case Presentation 1

The first patient was a 62-year-old man who has been hospitalized for 15 days and was intubated on the 4<sup>th</sup> day. In the course of treatment, the patient underwent five times hemoperfusion with HA330 and HA280 filters. The patient weighed 86 kg and was 174 cm tall. The patient did not have comorbidity, and the symptoms of the disease were dry cough, shortness of breath, anorexia, weakness, and lethargy. The polymerase chain reaction (PCR) test was positive. At admission, blood pressure was 108/74 mm Hg; respiratory rate and heart rate were 17 breathes per minute and 82 beats per minute, respectively. The body temperature was 37°C and the oxygen saturation was 89%. The drugs prescribed for the patient were naproxen, ceftriaxone, vancomycin, azithromycin, heparin, pantoprazole, dopamine, dexamethasone, meropenem, Kaletra, and fresh frozen plasma. Changes in pH, HCO<sub>3</sub>, and PCO<sub>2</sub> in venous blood gas with white blood cells (WBC), poly, lymphocytes, monocytes, red blood cell (RBC), hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), Blood urea nitrogen (BUN), creatinine, sodium, potassium, magnesium, phosphate, calcium, C-reaction protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, lactate dehydrogenase (LDH), D dimer, uric acid, bilirubin direct, bilirubin total, alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate aminotransferase (AST), platelet was recorded on the first, third, and the last time before being expired. Finally, the patient died due to severe respiratory failure.

### Case Presentation 2

The second patient was a 35-year-old man who has been hospitalized for 20 days and was intubated on the 3<sup>rd</sup> day. The patient was under a mechanical ventilator for eight days. In the course of treatment, the patient underwent three times hemoperfusion with HA230 and HA280 filters. The patient weighed 112 kg and was 176 cm tall. The patient did not have comorbidity, while the symptoms of the disease included dry cough, shortness of breath, fever and myalgia. The PCR test was positive. At admission, blood pressure was 128/76 mm Hg, respiratory rate and heart rate were 40 breathes per minute and 135 beats per minute, respectively. The body temperature was 38.3 °C and the oxygen saturation was 94%. The drugs prescribed for the patient were naproxen, ceftriaxone, diphenhydramine, azithromycin, heparin, hydroxychloroquine, dexamethasone, meropenem, Kaletra, and intravenous immunoglobulin (IVIG). Changes of paraclinical parameters were recorded as the same for the first patient at the first, third, and the last day of hospitalization. Finally, the patient discharged with normal blood oxygen saturation levels (SpO<sub>2</sub>) of 97%.

### Case Presentation 3

The second patient was a 41-year-old man who has been

hospitalized for 43 days and was intubated on the 16<sup>th</sup> day. The patient was under a mechanical ventilator for 39 days. In the course of treatment, the patient underwent three times hemoperfusion with HA330 filter. The patient weighed 73 kg and was 173 cm height. The patient did not receive IVIG, and the symptoms of the disease included productive cough, headache, fever and lethargy. The patient suffered from hypertension and had a history of splenectomy 17 years ago due to car accident. The PCR test was positive. At admission, blood pressure was 150/90 mm Hg, respiratory rate and heart rate were 24 breathes per minute and 126 beats per minute, respectively. The body temperature was 39°C and the oxygen saturation was 93%. The drugs prescribed for the patient were naproxen, ceftriaxone, diphenhydramine, azithromycin, enoxaparin, atorvastatin, losartan, methylprednisolone, hydroxychloroquine, dexamethasone, meropenem, Kaletra, and IVIG. Changes of paraclinical parameters were recorded as the same for the other patients at the first, third, and the last time before being expired. Finally, the patient died due to severe respiratory failure.

### Case Presentation 4

The fourth patient was a 74-year-old man who has been hospitalized for seven days and was intubated on the 2<sup>nd</sup> day. In the course of treatment, the patient underwent one time hemoperfusion with HA230 filter. The patient weighed 84 kg and was 173 cm height. The patient received IVIG, and the symptoms of the disease included productive cough, shivering and shortness of breath. The patient suffered from hypertension and had a history of nephrolithiasis and coronary artery bypass grafting. The PCR test was positive. At admission, blood pressure was 120/80 mmHg; respiratory rate and heart rate were 25 breathes per minute and 80 beats per minute, respectively. The body temperature was 37.2°C and the oxygen saturation was 84%. The drugs prescribed for the patient were ceftriaxone, hydroxychloroquine, dexamethasone, atorvastatin, aspirin, vancomycin, meropenem, dopamine, and heparin. Changes of paraclinical parameters were recorded as the same for the other patients at the first, third, and the last time before being expired. Finally, the patient was expired. [Tables 1](#) and [2](#) present the non-paraclinical and paraclinical information of four patients with COVID-19.

### Discussion

In a Cochrane review conducted by Borthwick et al, high-volume haemofiltration (HVHF) improved outcomes in critically ill adults who referred to the intensive care unit (ICU) with severe infection or septic shock. The authors reported that the relative risk of death in 28 days with HVHF was 0.89. One study with 137 participants reported a reduction in the length of hospital stay in the ICU. The results of this meta-analysis show that very little research has been conducted on the use of

**Table 1.** Non-paraclinical information of four patients with COVID-19

Variable	Minimum	Maximum	Mean	SD
Age (year)	35.00	74.00	52.75	18.00
Stay (day)	8.00	43.00	21.50	15.15
Weight (kg)	73.00	112.00	86.25	18.154
Height (cm)	173.00	176.00	174.00	1.41
Temperature (°C)	37.00	39.00	37.87	0.94
Pulse rate (beat/minute)	80.00	135.00	105.75	28.82
Respiratory rate (breath/min)	17.00	40.00	26.50	9.67
SBP (mm Hg)	108.00	150.00	126.50	17.69
DBP (mm Hg)	74.00	90.00	80.00	7.11

Abbreviations: SBP, Systolic blood pressure; DBP, Diastolic blood pressure.

**Table 2.** Paraclinical information of four patients with COVID-19

Variable	Min.	Max.	Mean	SD
pH 1	7.21	7.48	7.3850	0.12124
pH 2	7.44	7.51	7.4725	0.03304
pH 3	7.30	7.46	7.3775	0.07500
HCO3 1 (mEq/L)	14.30	24.30	20.8250	4.47763
HCO3 2 (mEq/L)	21.50	28.50	25.1500	3.05341
HCO3 3(mEq/L)	21.40	28.90	25.2500	3.06649
PCO2 1 (mm Hg)	30.10	35.50	32.5500	2.27669
PCO2 2 (mm Hg)	30.70	38.00	33.9000	3.34564
PCO2 3 (mm Hg)	35.10	53.10	41.8750	7.82320
White blood cell 1 (%)	5.20	17.10	12.8500	5.52600
White blood cell 2 (%)	11.60	23.20	15.5750	5.18355
White blood cell 3(%)	9.80	21.90	17.3000	5.23514
PMN 1 (10 <sup>9</sup> /L)	8.00	89.00	66.7500	39.24602
PMN 2 (10 <sup>9</sup> /L)	90.00	94.00	92.0000	2.30940
PMN 3 (10 <sup>9</sup> /L)	76.00	88.00	82.7500	5.12348
Lymphocyte 1 (%)	5.00	14.00	9.0000	3.74166
Lymphocyte 2 (%)	3.00	7.00	4.0000	2.00000
Lymphocyte 3 (%)	2.00	16.00	8.0000	6.32456
Bilirubin total 1 (mg/dL)	0.25	2.60	1.1050	1.05976
Bilirubin total 2 (mg/dL)	0.39	1.60	.7475	.57355
Bilirubin total 3 (mg/dL)	0.39	2.00	.8650	.76029
Uric acid 1 (mg/mL)	2.00	2.00	2.0000	-
Uric acid 2(mg/mL)	2.30	2.30	2.3000	-
Uric acid 3(mg/mL)	2.00	2.00	2.0000	-
BUN 1 (mg/dL)	15.00	20.00	17.2500	2.62996
BUN 2 (mg/dL)	13.00	34.00	23.0000	10.09950
BUN 3(mg/dL)	13.00	35.00	21.7500	9.77667
Creatinine 1 (mg/dL)	.60	1.20	.9450	0.29456
Creatinine 2 (mg/dL)	.80	1.40	1.1250	0.25000
Creatinine 3 (mg/dL)	.50	1.10	.8750	0.28723
Potassium 1 (mEq/L)	3.60	4.30	3.9750	0.29861
Potassium 2 (mEq/L)	3.60	4.00	3.8600	0.18903
Potassium 3 (mEq/L)	3.20	4.60	3.8750	0.57373
Calcium 1 (mg/dL)	7.70	9.90	8.9750	0.99121
Calcium 2 (mg/dL)	7.90	9.50	8.4667	0.89629
Calcium 3 (mg/dL)	8.10	8.70	8.4000	0.30000
CRP 1 (mg/L)	18.00	45.00	33.0000	14.07125
CRP 2 (mg/L)	9.00	42.00	25.5000	23.33452
CRP 3 (mg/L)	36.00	48.00	42.0000	6.00000
LDH 1 (U/L)	796.00	1022.00	897.3333	114.79257
LDH 2 (U/L)	723.00	1165.00	892.6667	238.21489
LDH 3 (U/L)	458.00	1154.00	747.3333	362.53184
Ferritin 1 (ng/mL)	859.00	1000.00	964.7500	70.50000
Ferritin 2 (ng/mL)	1000.00	1000.00	1000.0000	0.00000
Ferritin 3 (ng/mL)	889.00	1000.00	944.5000	78.48885
Monocyte 1 (%)	1.00	4.00	2.2500	1.25831
Monocyte 2 (%)	2.00	3.00	2.2500	0.50000
Monocyte 3 (%)	1.00	4.00	2.2500	1.25831
RBC 1 (%)	4.56	5.14	4.8625	0.27693

**Table 2.** Continued

Variable	Min.	Max.	Mean	SD
RBC 2 (%)	3.78	5.10	4.5675	0.58807
RBC 3 (%)	3.28	4.30	3.6400	0.45986
Hemoglobin 1 (g/dL)	13.30	15.30	14.5750	0.88459
Hemoglobin 2 (g/dL)	11.00	15.50	13.8000	1.95448
Hemoglobin 3 (g/dL)	9.70	14.10	11.1000	2.03470
Platelet 1 (10 <sup>9</sup> /L)	87.00	441.00	262.2500	145.50000
Platelet 2(10 <sup>9</sup> /L)	94.00	271.00	199.5000	79.17281
Platelet 3(10 <sup>9</sup> /L)	82.00	278.00	159.7500	85.19145
AST 1 (IU/L)	36.00	111.00	69.0000	34.18577
AST 2 (IU/L)	58.00	79.00	65.0000	9.69536
AST 3 (IU/L)	22.00	107.00	67.7500	42.64094
ALT 1(IU/L)	19.00	201.00	79.5000	83.52844
ALT 2 (IU/L)	28.00	157.00	79.2500	56.19238
ALT 3 (IU/L)	65.00	152.00	89.0000	42.15052
ALP 1 (IU/L)	131.00	201.00	161.7500	32.32517
ALP 2 (IU/L)	167.00	231.00	185.5000	30.43572
ALP 3(IU/L)	141	251	214	51.6
Bilirubin direct 1 (mg/dL)	0.40	2.90	1.3850	1.08054
Bilirubin direct 2 (mg/dL)	0.89	1.20	1.0225	0.15283
Bilirubin direct 3 (mg/dL)	0.90	1.12	1.0300	0.10132
MCV 1 (fL)	82.10	89.60	85.9000	3.31361
MCV 2 (fL)	82.40	92.40	86.7250	4.26097
MCV 3 (fL)	84.90	91.40	88.6000	2.95184
MCH 1 (pg)	29.20	31.30	30.0000	.90554
MCH 2 (pg)	29.10	31.50	30.1750	1.03078
MCH 3(pg)	28.70	32.80	30.0500	1.86994
Na 1 (mEq/L)	34.00	136.00	108.7500	49.87568
Na 2 (mEq/L)	131.00	136.00	133.3750	2.28674
Na 3 (mEq/L)	131.00	141.00	135.2500	4.19325
Magnesium 1 (mg/dL)	2.00	2.50	2.2250	0.22174
Magnesium 2 (mg/dL)	2.20	2.80	2.4000	0.28284
Magnesium 3 (mg/dL)	1.80	2.30	2.0750	0.20616
Phosphate 1 (mg/dL)	2.40	5.90	3.8750	1.49972
Phosphate 2 (mg/dL)	3.40	4.50	3.9500	0.77782
Phosphate 3 (mg/dL)	2.30	4.50	3.4000	1.55563
D-dimer 1 (ng/mL)	1179.00	10000.00	3681.5000	4235.45200
D-dimer 2 (ng/mL)	2058.00	2867.00	2462.5000	572.04939
D-dimer 1 (ng/mL)	6061.00	10000.00	8030.5000	2785.29361
ESR 1 (mm/h)	26.00	84.00	54.0000	29.05168
ESR 2 (mm/h)	12.00	79.00	45.5000	47.37615
ESR 3 (mm/h)	20.00	90.00	55.0000	49.49747

Abbreviations: PMN, Polymorphonuclear leukocyte; RBC, red blood cell; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; BUN, blood urea nitrogen; CRP, C-reaction protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase.

HVHF in critically ill patients with severe infection (four studies; 201 participants). Researchers should consider large, multi-centered randomized, controlled trials that have clinically relevant outcomes. The cost-effectiveness of HVHF should also be studied (15). In a case study conducted in 2020 by Dastan et al for the treatment of COVID-19 patients, the hemoperfusion method with a single load cartridge was used. A 54-year-old patient was admitted to Niayesh hospital in Tehran with symptoms of fever, dyspnea, cough and fever above 38 degrees, along with 90% of SpO<sub>2</sub>. A clinical finding indicated a positive CRP with severe acidosis. The PCR test was positive. Hemoperfusion was performed at 35 mL/kg/h. After 6 hours, the cartridge was changed. After three sessions of perfusion, the lung involvement was over and the patient

was transferred to the ward. Hemoperfusion was cleared after beneficial effects. The cytokines of the patient were reduced in patients who discontinued treatment for acute respiratory distress syndrome (16).

The mean age of patients in our study was 52.75 years with the mean stay at hospital of 21.5 days. These issues can confound the therapeutic effect of hemoperfusion.

In a study in China by Fu et al, a patient with hemodialysis showed promising effects on treatment. A 75-year-old male patient with chronic renal failure who had recently been admitted for COVID-19 with symptoms of cough and shortness of breath since two weeks ago was hospitalized due to positive PCR test. The patient's heart rate and respiratory rate were 100 beats and 23 breathes per minute, and the patient's blood oxygen level was 90%. Some laboratory tests were also evaluated in the laboratory (serum creatinine:1,432.3  $\mu\text{mol/L}$ , BUN: 40  $\mu\text{mol/L}$ , K:4.63  $\text{mmol/L}$ , and uric acid:760  $\mu\text{mol/L}$ ). The patient underwent continuous renal replacement therapy (CRRT). In total, the patient underwent CRRT for 51 hours (blood flow:120 mL/min; effluent flow rate: 1000 mL/h; ultrafiltration rate:150–200 mL/h). CRRT had an effective role to treat the patient by eliminating blood toxins and stabilizing hemodynamic status and metabolites. Nitrogen levels in blood urea, creatinine, CRP, and potassium normalized. The symptoms improved faster and cleared up with a negative PCR test (17).

### Conclusion

According to our observation contrary to the results of others, hemoperfusion cannot show a significant therapeutic effect among COVID-19 patients with severe conditions.

### Conflicts of interest

The authors declare that there is no conflict of interest in this study.

### Authors' contribution

SH and NR conceived the idea of this study. NR performed the data collection. SH and NR contributed to the literature review, data analysis, and review of the article for final publication.

### Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. Informed consent was obtained from the patients for publication of this report.

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