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Exceptional Case

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# Treatment for severe COVID-19 with a biomimetic sorbent haemoperfusion device in patients on haemodialysis

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## ABSTRACT

Haemodialysis (HD) patients present more morbidity and mortality risk in coronavirus disease 2019 (COVID-19). In patients who may develop severe symptoms, the process called 'viral sepsis' seems to be a crucial mechanism. In those cases, the HD procedure provides an excellent tool to explore the benefit of some extracorporeal therapies. We reported the outcome of four HD patients with severe COVID-19 treated with Seraph®100 haemoperfusion (HP) device. Three of the four cases presented a good clinical response after HP. In conclusion, the treatment with Seraph®100 device may be a simultaneous treatment to improve HD patients with severe acute respiratory syndrome coronavirus 2.

**Keywords:** COVID-19, cytokine storm, haemodialysis, haemoperfusion, sepsis viral

## BACKGROUND

In-centre haemodialysis (HD) patients show a major coronavirus disease 2019 (COVID-19) incidence with a high mortality rate [1]. Among 848 prevalent HD patients in our health area, the incidence of COVID-19 was 14.3% with a mortality rate of 23%. In patients who develop severe symptoms, the process called 'viral sepsis' seems to be a crucial mechanism [2, 3]. Up to now, the management of COVID-19 infection is mainly based on supportive therapy [4]. However, the HD procedure provides an excellent tool to explore the benefit of some extracorporeal therapies aimed to reduce 'viral sepsis'.

The Extracorporeal device Seraph®100 Microbind® Affinity Blood produced by ExThera Medical (Martinez, CA, USA) is a haemoperfusion (HP) device approved by the US and European agencies for the reduction of some bacterial and viral pathogens. Moreover, on 17 April 2020, the US Food and Drug Administration granted COVID-19 emergency use authorizations for the Seraph®100. This device has ultrahigh molecular weight polyethylene beads with end point-attached heparin [5]. Herein we describe the first four cases of HD patients with severe COVID-19 treated with Seraph®100 HP.

## METHODS

The procedure consisted of two sessions of HP with Seraph®100 in parallel with standard HD performed in two consecutive days. The Seraph®100 was placed pre-dialyzer. Blood samples

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were taken to admission, at the start and the end of each HP and subsequent days of treatment until the patients were discharged. Patients selected for treatment were not candidates for intensive therapy.

## CASE REPORTS

Table 1 summarizes the main characteristics of the four patients treated with HP. All patients were very old, had some comorbidities and criteria of bad prognosis and severe pulmonary involvement. The HP was started between Days 2 and 13 after the symptomatology onset. All patients but Patient 2 showed favourable outcome and were discharged. In Patient 2, the HP was incompletely performed because of hemodynamic intolerance. Table 1 shows the evolution of some inflammatory and coagulation parameters during the HP procedure. Interestingly, comparing pre-HP with post-HP, we did not observe a significant reduction in interleukin-6, ferritin and D-dimer. The decrease of these inflammatory parameters appeared after the two-session HP protocol was completed in responder patients. The second peak increase of ferritin in Patient 4 was related to secondary bacterial pneumonia that was successfully treated with antibiotics.

## DISCUSSION

COVID-19 direct viral attack on lung epithelial cells, lung capillary endothelial cells, vascular endothelial cells with high levels of ACE2 and T lymphocytes [2, 3] may account for the severe inflammatory response, microcirculation dysfunction and prothrombotic state observed in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Theoretically, the reduction of viral load and/or some inflammatory mediators may alleviate the course of the disease. Seraph®100 is an HP device that mimics the endothelial cell glycocalyx that has an anti-thrombogenic, anti-inflammatory and pathogen immobilization effect by selective adsorption. Four hours *in vitro* perfusion provides >99% reduction of HSV-1, HSV-2, Ebola, Zika, CMV and adenoviruses [5]. Also, COVID-19 and other coronaviruses bind to heparin and so it seems feasible that COVID-19 will bind to Seraph®100 sorbent.

Patients on HD are particularly susceptible to infection by several mechanisms including deficient immune response. On the contrary, HD patients have an impaired glycocalyx barrier and sustained endothelial cell activation as mechanisms involved in viral shedding. Thus, increased viral shedding in combination with a deficient immune response may put HD

**Table 1. Clinical features, laboratory and HP parameters**

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|
| Sex | Male | Male | Female | Male |
| Age (years) | 86 | 87 | 87 | 81 |
| Barthel index (%) | 75 | 10 | 35 | 85 |
| COVID-19 | | | | |
| Symptom onset (days) upon admission | 1 | 3 | 4 | 1 |
| Treatment | Hydroxychloroquine Steroids | Hydroxychloroquine Steroids | None | Steroids |
| Pre-HP laboratory analysis | | | | |
| LDH (U/L) | 567[a]/545[b] | 328[a]/303[b] | 305[a]/308[b] | 224[a]/259[b] |
| RCP (mg/L) | 215[a]/174[b] | 19.5[a]/14.6[b] | 9.4[a]/7.4[b] | 45.9[a]/58.4[b] |
| Ferritin (μg/L) | 3235[a]/3871[b] | 1677[a]/1501[b] | 981[a]/1287[b] | 587[a]/685[b] |
| IL-6 (ng/L) | 123[a]/29[b] | 10.4[a]/11.7[b] | 56.6[a]/68.2[b] | 28.4[a]/41.2[b] |
| D-dimer (μg/L) | 537[a]/548[b] | 1197[a]/1102[b] | 490[a]/385[b] | 337[a]/405[b] |
| Post-HP laboratory analysis | | | | |
| LDH (U/L) | 635[a]/635[b] | 335[a]/335[b] | 266[a]/327[b] | 239[a]/247[b] |
| RCP (mg/L) | 239[a]/191[b] | 18.9[a]/14.5[b] | 7.7[a]/8.5[b] | 54.6[a]/59.3[b] |
| Ferritin (μg/L) | 4287[a]/5110[b] | 1687[a]/1609[b] | 1153[a]/1111[b] | 580[a]/692[b] |
| IL-6 (ng/L) | 162[a]/86[b] | 21[a]/23.6[b] | 58.8[a]/79.8[b] | 48.7[a]/27.5[b] |
| D-dimer (μg/L) | 1098[a]/902[b] | 2427[a]/2870[b] | 372[a]/499[b] | 452[a]/498[b] |
| Discharge laboratory analysis | | | | |
| LDH (U/L) | 340 | 335 | 259 | 241 |
| RCP (mg/L) | 13.4 | 14.5 | 3.1 | 53.1 |
| Ferritin (μg/L) | 1756 | 1609 | 593 | 1174 |
| IL-6 (ng/L) | 18.2 | 23.6 | 41.2 | 2.4 |
| D-,dimer (μg/L) | 484 | 2870 | 250 | 368 |
| Arterial blood gases before to start first HP | | | | |
| $FiO_2$ (%) | 60 | 21 | 21 | 50 |
| $pO_2$ (mmHg) | 150 | 64 | 45 | 74 |
| $pCO_2$ (mmHg) | 33 | 31 | 38 | 33 |
| PaO2/$FiO_2$ ratio | 250 | 304 | 214 | 148 |
| HP and haemodialysis parameters | | | | |
| HP start (days after disease onset) | 13 | 11 | 7 | 2 |
| Blood flow (mL/min) | 280[a]/300[b] | 220[a]/200[b] | 300[a]/300[b] | 350[a]/350[b] |
| Time (min) | 180[a]/240[b] | 180[a]/150[b] | 240[a]/240[b] | 240[a]/240[b] |

Conversion factor for U/L to ukat/L: 0.01667.

[a]First session HP.

[b]Second session HP.

LDH, lactate dehydrogenase; RCP, reactive C protein; IL-6, interleukin 6; $FiO_2$, inspired fraction of $O_2$; $pO_2$, O2 pressure; pCO2, CO2 pressure.

patients on the worse clinical scenario. Actually, our patients on HD with COVID-19 showed a mortality rate of 23%. However, the dialysis session brings an excellent opportunity to perform simultaneous HP. Blood passes over exclusive microbeads coated with molecular receptor sites that mimic endothelial glycocalyx before entering the haemodialyzer.

Herein, we reported the outcome of four HD patients with severe COVID-19 treated with Seraph®100. All patients had criteria of poor prognosis and were not suitable candidates to ICU management. Interestingly, we observed a good clinical response in three out of four cases. The Patient 2 had a clinical worsening with intolerance to HP, dying 24 h after second HP. As we did not observe reduction of inflammatory molecules during the 4-h HP session, our hypothesis is that the HP beneficial effect could be mainly related to the viral load reduction. In this regard, it seems advisable to perform the HP earlier in the course of the disease (in two out of the three responders HP was performed in the first week).

In conclusion, HP with Seraph®100 during the first week after the onset of the disease may be a simultaneous treatment to improve the HD patients with severe SARS-CoV-2 although further studies should be performed.

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## CONFLICT OF INTEREST STATEMENT

None declared.

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