Critically ill COVID-19 patients and the role of Polymyxin B Hemoperfusion

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Over the last year, various works in literature have revealed the potential role of Polymyxin B Hemoperfusion in the management of non-responsive COVID-19 patients admitted to intensive care.

Patients who are undergoing long periods of hospitalization are more prone to superinfections. In addition, enteric symptoms, as well as the increasingly described 'gut-lung' interactions due to bacterial transmigration and/or their components caused by changes in the intestinal membrane (microbiotic dysbiosis), lead to the systemic circulation of endotoxin[1].

Considering Polymyxin B Hemoperfusion in the context of COVID-19 and a concomitant state of superinfection and/or endotoxemia leading to a severe clinical picture (septic shock) not responsive to standard therapy is therefore rational and pragmatic, as described in various publications [2-4].

Polymyxin B hemoperfusion has obtained IDE authorization from FDA for the treatment of COVID-19 patients with septic shock and Health Canada has authorized its use in COVID-19 patients with acute respiratory failure. Polymyxin B Hemoperfusion has reportedly been used in COVID-19 patients in Europe, Russia, Asia and the US.

We report here various case reports that have been presented as Abstracts at International Congresses and/or published in peer-reviewed journals on the use of Polymyxin B hemoperfusion in COVID-19 patients.

ABSTRACTS presented at international conferences concerning the use of PMX-HP in COVID-19 patients:

Title: **The use of Polymyxin B Hemoperfusion for COVID-19 Patients with endotoxic shock [2]**

Authors: *De Rosa S., De Cal M., Danzi V., Golino G., Pierbellini G. and Ronco C.*

Abstract: **Background**: Recent published data show how endotoxemia and bacterial DNA are frequently found in patients with COVID-19 pneumonia, indicating that loss of intestinal barrier function can contribute to the pathogenesis of COVID-19. In addition, patients who are hospitalized for extended periods in an ICU are more prone to superimposed infections.
Objectives: In this retrospective analysis we report our experience of Polymyxin B hemoperfusion (PMX-HP) as complementary therapy for unresponsive endotoxic shock management in 5 patients with COVID-19 hospitalized in our ICU ward between February and April 2020. To the best of our knowledge, there is no data published yet concerning PMX-HP use in COVID-19 patients.
Results: PMX-HP treatment was associated with rapid hemodynamic stabilization with reduction of Vasopressors Inotropic Score (VIS), reduction in blood lactate levels, rapid decrease in EA levels in a population affected by SARS-CoV-2 and endotoxic shock.
Conclusion: Endotoxic shock could be associated to SARS-CoV-2. PMX-HP can be considered for management of unresponsive endotoxic shock. In our cases, PMX-HP treatment was associated with rapid hemodynamic improvement associated with a rapid decrease in vasopressor use, blood lactates and EA levels.

Title: **Polymyxin B hemoperfusion therapy and extracorporeal CO2 removal in a patient with COVID-19: a case report [6]**

Authors: *Monastra L., Perrella A., Garzia R. and Fraganza F.*

Abstract: **Case presentation**: A 54-year-old man with a medical history of obesity and hypertension developed fever, cough and diarrhoea presented at the emergency department with fever and severe respiratory failure. The patient was asthenic and dyspnoeic and was immediately intubated and transferred to the ICU. Critical care management was initiated, including mechanical ventilation and vasopressors. A swab test for SARS-Cov-2 infection resulted positive. Tocilizumab and antibiotics therapy were initiated. Blood cultures resulted positive for multi-resistant Gram-negative infection (Acinetobacter). Endotoxic shock was suspected (endotoxin activity assay, EAA, 0.92 EU), and two treatments with Polymyxin B hemoperfusion (Toraymyxin®, Toray Medical Co., Ltd., Tokyo, Japan) were performed in 48 h. After two sessions the patient's clinical condition improved, EAA, procalcitonin, CRP and IL-6 decreased. Hemodynamic parameters also improved with increase in MAP and noradrenaline was suspended. However, a week later the patient's conditions deteriorated. The patient became hypercapnic and in order to facilitate ultraprotective ventilation, extracorporeal CO2 removal therapy was initiated and continued for 6 days resulting in improved PaCO2 and increase of pH. The patient was hospitalized in the ICU for 113 days and was then admitted to a rehabilitation facility.
Conclusion: We have presented a case of COVID-19 complicated with septic shock and ARDS who in critical moments was treated with Polymyxin B Hemoperfusion and ECCO2R.

CASE REPORTS published in international peer-reviewed journals concerning the use of PMX-HP in COVID-19 patients:

Title: **Polymyxin B haemoperfusion treatment for respiratory failure and hyperferritinaemia due to COVID-19 [7]**

Authors: *Ishiwari M., Togashi Y., Takoi H., Kikuchi R., Kono Y. and Abe S.*

Abstract: A 69-year-old man with a history of type 2 diabetes and high blood pressure was diagnosed with coronavirus disease 2019 (COVID-19). He had hyperferritinaemia and respiratory failure. Despite the initiation of favipiravir and high-dose corticosteroid and ceftriaxone, his respiratory failure progressed and serum ferritin levels increased. After polymyxin B immobilized fibre column direct haemoperfusion (PMX-DHP) therapy, there was improvement of the respiratory failure and hyperferritinaemia.
We report the first case of COVID-19-induced hyperferritinaemia and severe respiratory failure successfully treated by PMX-DHP.

Title: **Successful Recovery from COVID-19-associated Acute Respiratory Failure with Polymyxin B-immobilized Fiber Column-direct Hemoperfusion [8]**

Authors: *Kusaba Y., Izumi S., Takasaki J., Suzuki M. Katagiri D., Katsuno T., Matsumoto S., Sakamoto K., Hashimoto M., Ohmagari N., Katano H., Suzuki T., Hojo M. and Sugiyama H.*

Abstract: An 83-year-old man was hospitalized for coronavirus disease 2019 (COVID-19) after a 10-day history of a persistent fever. Chest computed tomography showed extensive non-segmental ground glass opacity. Despite the initiation of lopinavir and ritonavir, respiratory failure progressed. Two days of polymyxin B-immobilized fiber column-direct hemoperfusion (PMX-DHP) with adjunctive corticosteroid prevented his respiratory condition from worsening. For rapidly progressive COVID-19 cases, the early use of PMX-DHP may avoid the need for mechanical ventilation by suppressing local inflammation of the lung.

Title: **Continuous extracorporeal treatments in a dialysis patient with COVID-19 [9]**

Authors: *Nihei Y., Nagasawa H., Fukao Y., Kihara M., Ueda S., Gohda T. and Suzuki Y.*

Abstract: The coronavirus disease 2019 (COVID-19) pandemic is now a major global health threat. More than half a year have passed since the first discovery of severe acute respiratory syndrome coronavirus-2 (SARS-CoV2), no effective treatment has been established especially in intensive care unit. Inflammatory cytokine storm caused by SARS-CoV-2 infection has been reported to play a central role in COVID-19; therefore, treatments for suppressing cytokines, including extracorporeal treatments, are considered to be beneficial. However, until today the efficacy of removing cytokines by extracorporeal treatments in patients with COVID-19 is unclear. Herein, we report our experience with a 66-year-old male patient undergoing maintenance peritoneal dialysis who became critically ill with COVID-19 and underwent several extracorporeal treatment approaches including plasma exchange, direct hemoperfusion using a polymyxin B-immobilized fiber column and continuous hemodiafiltration. Though the patient developed acute respiratory distress syndrome (ARDS) repeatedly and subacute cerebral infarction and finally died for respiratory failure on day 30 after admission, these attempts appeared to dampen the cytokine storm based on the observed decline in serum IL-6 levels and were effective against ARDS and secondary haemophagocytic lymphohistiocytosis. This case suggests the significance of timely initiation of extracorporeal treatment approaches in critically ill patients with COVID-19.

Reference list:

1. Sirivongrangson, P., et al., Endotoxemia and circulating bacteriome in severe COVID-19 patients. medRxiv, 2020: p. 2020.05.29.20109785.
2. Ronco, C., P. Navalesi, and J.L. Vincent, Coronavirus epidemic: preparing for extracorporeal organ support in intensive care. The Lancet. Respiratory medicine, 2020: p. S2213-2600(20)30060-6.
3. Ronco, C. and T. Reis, Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol, 2020.
4. Ronco, C., T. Reis, and S. De Rosa, Coronavirus Epidemic and Extracorporeal Therapies in Intensive Care: si vis pacem para bellum. Blood Purif, 2020: p. 1-4.
5. De Rosa, S., et al., The use of Polymyxin B Hemoperfusion for COVID-19 Patients with endotoxic shock, in 38th Vicenza Course on AKI and CRRT. 2020: Virtual.
6. Monastra, L., et al., Polymyxin B hemoperfusion therapy and extracorporeal CO2 removal in a patient with COVID-19: a case report, in 38th Vicenza Course on AKI and CRRT. 2020: Virtual meeting.
7. Ishiwari, M., et al., Polymyxin B haemoperfusion treatment for respiratory failure and hyperferritinaemia due to COVID-19. Respirol Case Rep, 2020. 8(9): p. e00679.
8. Kusaba, Y., et al., Successful Recovery from COVID-19-associated Acute Respiratory Failure with Polymyxin B-immobilized Fiber Column-direct Hemoperfusion. Intern Med, 2020.
9. Nihei, Y., et al., Continuous extracorporeal treatments in a dialysis patient with COVID-19. CEN Case Rep, 2020: p. 1-6..