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Therapeutic Apheresis and Dialysis

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LETTER TO THE EDITOR

When should polymyxin B-immobilized polystyrene column be introduced to improve COVID-19 prognosis?

Dear Editor

Increased cytokine levels are involved in severe COVID-19. Moreover, apheresis is used to prevent or alleviate organ damage in moderate to severe COVID-19 patients. In particular, targets for removal are circulating mediators, including cytokines and damage-associated molecular patterns (DAMPs). Direct hemoperfusion using a polymyxin B-immobilized polystyrene column (PMX-DHP) selectively adsorbs endotoxins and various endogenous substances. We previously evaluated the efficacy and safety of PMX-DHP in COVID-19 patients that required oxygen support ($N = 12$) [1]. On Day 14 after the first treatment, disease severity decreased in 58.3% of patients. Additionally, the P/F ratio increased on Days 4 and 8. Cytokine measurements before and after PMX-DHP revealed decreased IL-6 levels.

In which stage of COVID-19 should we start PMX treatment? In our observational study, seven patients were on ventilator or extracorporeal membrane oxygenation (ECMO) at the time of PMX treatment, and five of them (71.4%) survived. Furthermore, out of five patients receiving oxygen at the time of PMX treatment, four of them (80.0%) survived. Unfortunately, three patients died. The COVID-19 Clinical Practice Guide in Japan (6th Edition) [2] states that PMX-DHP treatment should be considered in certain cases due to its suppression of excessive inflammatory reactions in the "early stage before multiple organ failure progresses." Remarkably, PMX-DHP improves prognosis in sepsis patients with sequential organ failure assessment (SOFA) scores of 7–9, 10–12. However, PMX-DHP does not affect prognosis in sepsis patients with SOFA 0–6, 13–15, 16–24 [3]. Therefore, we believe that PMX-DHP should be considered in patients with moderate disease II when oxygen demand appears (Figure 1).

Finally, it is unclear if PMX is effective in patients with severe COVID-19. In this stage, multiple infections are a major problem and endotoxin removal plays an important role. De Rosa et al. performed PMX-DHP in 12 COVID-19 patients on invasive mechanical ventilation. In COVID-19 patients with sepsis, the SOFA score was improved at 120 h after the procedure, and the endotoxin activity assay (EAA) decreased from 0.78 to 0.60 [4]. Recently, we measured EAA before and after PMX-DHP in COVID-19 patients at our hospital;

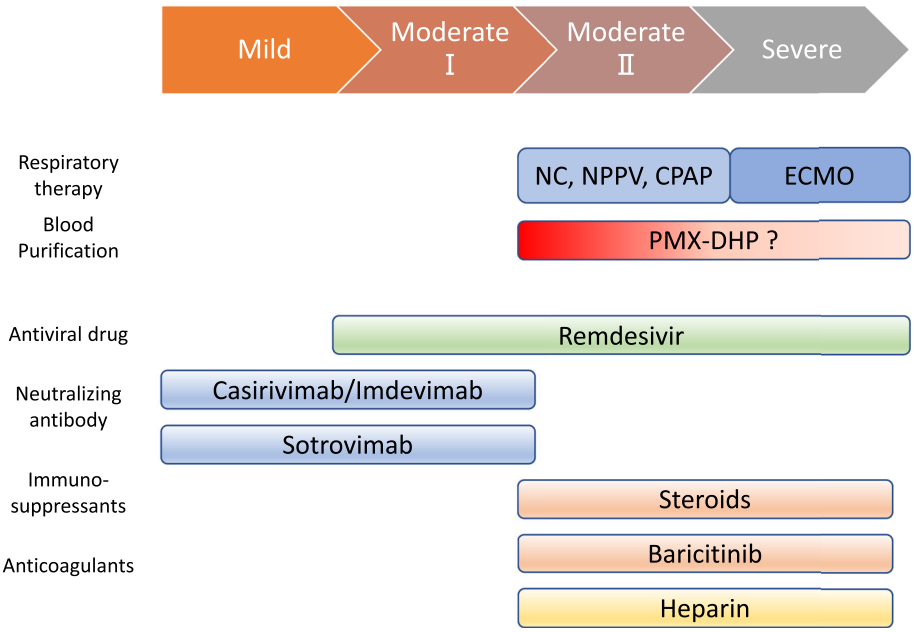

FIGURE 1 A suggestion on when to introduce PMX to COVID-19. Introduction of PMX at the time when oxygen demand starts is expected to be the best for improving prognosis, but even in the case of multiple organ failure, there is a role for endotoxin adsorption. Quoted with some modifications from Reference [2]

EAA in patients with high EAA tended to decrease after PMX treatment (unpublished data). Proposed mechanisms of action of PMX-DHP on COVID-19 include cytokine regulation, oxygenation enhancement by removal of activated neutrophils, and adsorption and removal of endotoxins.

In addition to the vaccines, antiviral drugs, immunosuppressive agents, and neutralizing antibody therapies that are being applied clinically. However, certain cases may become severe. Subsequently, we initiated a prospective multicenter study. This study is ongoing and we hope to obtain valuable results to provide insight on the apt time to implement.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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