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## Commentary

### Plasmapheresis: A new strategy in the treatment of COVID-19

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**Running Title:** Covid-19 and Plasmapheresis

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In early December 2019, the initial pneumonia cases of severe acute respiratory syndrome coronavirus (SARS-COV-2) were identified in Wuhan city, China. World Health Organization (WHO) named the disease as coronavirus disease 2019 (COVID-19) and recognized as a pandemic on 11 March 2020. As of July 09, 2020; there were 11669259 confirmed infected cases and 539906 deaths of people in the world.<sup>1</sup>

COVID-19 can be asymptomatic and these cases need no treatment. However, infected cases possibly have pneumonia and respiratory distress syndrome. As the treatment, antiviral, antibacterial, and immunomodulatory drugs [ hydroxychloroquine, Interleukin-1(IL-1), IL-6 antagonists] can be used, and studies related to vaccine development are ongoing. Angiotensin-Converting Enzyme-2 and Transmembrane protease serine-2 (TMPRSS) negative stem cells in mesenchymal stem cell (MSC) transplantation can benefit in COVID-19. The transplantation of MSCs improved the outcome of patients, possibly due to regulating inflammatory response and promoting tissue repair and regeneration. Besides these, there are other treatment approaches such as convalescent plasma infusion (CPI) and successful results have been reported for viral infections.<sup>2-3</sup> It is difficult to evaluate the outcomes of CPI due to the limited number and application of simultaneous other Covid-19 therapies. These data support that passive immunization by CPI can be beneficial among Covid-19 cases.<sup>4-5</sup>

Interleukin-1, IL-2, IL-7, granulocyte colony-stimulating factor, IL-6, IL-8, IFN- $\gamma$ , tumor necrosis factor are inflammatory cytokines in COVID-19.<sup>6</sup> IL-6 is the main cytokine of acute-phase inflammatory responses and also significantly increases in chronic inflammation. Janus kinase (JAK) system is also responsible for inflammation and cellular entry in COVID-19. It is hypothesized that JAK inhibitors such as pacritinib and tofacitinib as well as IL-6 inhibitors as tocilizumab and siltuximab can be treatment options for COVID-19.<sup>7-9</sup>

TPE is the separation of plasma from other blood components. TPE can remove antibodies, immune complexes, lipoproteins, and macromolecules, toxic and inflammatory molecules from plasma. Viral diseases are generally not recommended for TPE; but for

autoimmune conditions such as systemic lupus erythematosus [Category (C) 2, grade (GR) 2C], hemophagocytic lymphohistiocytosis in which cytokine Storm is common (CIII, GR2C), catastrophic antiphospholipid syndrome (CI, GR2C) and sepsis (CIII, GR2B); TPE can be an option although evidence level is weak due to Recommendations for Therapeutic Apheresis Guidelines.<sup>10-11</sup>

TPE is an adjunctive approach in addition to antiviral therapy in hepatitis C(HCV) patients, contributing to a decrease in the viral load. Double-Filtration Plasmapheresis (DFPP) is found to be beneficial to obtain rapid virologic response among HCV patients resistant to Peg-interferon and ribavirin.<sup>12</sup> Among patients with active rheumatoid arthritis, TPE seems to be beneficial to decrease clinical symptoms and the inflammatory marker levels such as C-reactive protein and erythrocyte sedimentation rate. These two examples support the effectiveness of TPE to decrease viral burden and inflammation in these groups.<sup>13</sup> Among these patients; immune adsorption and DFPP are used due to the effective removal of particles larger than 55-60 nm. DFPP removes pathogenic substances from separated plasma based on molecular weight and three-dimensional configuration (such as auto antibodies, immune complexes, lipoproteins, etc.), by using plasma filters with different pore sizes. SARS-COV-2 can be removed from circulation with DFPP because of being large enough as 60-140 nm size. And also TPE can be beneficial in addition to conventional treatment to reduce mortality in patients with septic shock.<sup>14-15</sup> Recently, the United States Food Drug Agency has approved the use of investigational device exemption (IDE) for toraymyxin (PMX) in the treatment of Covid-19 patients suffering from septic shock.<sup>16-18</sup>

The level of hypercytokinemia and viral load is the most important parameter to determine the clinical picture for Covid-19. The absence of satisfactory and specific treatments for Covid-19 obligates the need for new research for investigational therapies. TPE seems to be a reasonable approach possibly to decrease the viral burden and especially to remove

circulating cytokines. Convalescent plasma as a replacement fluid during the TPE procedure can be the most beneficial among the Covid-19 patients.

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#### **AUTHORS CONTRIBUTION**

**P.K.** Conceptualization; Data curation; writing- original draft, **M.I.A.** Visualization; review & editing. **S.S.** Writing- review & editing.

#### **CONFLICTS OF INTEREST**

None

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