Commentary

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Commentary on Therapeutic Plasma Exchange to Treat COVID-19

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Abstract

Severe acute respiratory syndrome coronavirus 2, the causative agent of coronavirus disease 2019, is capable of causing severe respiratory distress syndrome, cytokine release syndrome, multi-organ failure, and has been associated with many neurologic complications. No treatment has proven to be very effective. Therapeutic plasma exchange has been proposed and used. To date, randomized controlled trials have not been completed to show therapeutic benefit.

Keywords: Severe acute respiratory syndrome; Coronavirus; SARS-CoV-2

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Description

This March marked the one-year anniversary of the coronavirus disease 2019 (COVID-19) pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [1]. Infection by SARS-CoV-2 may be asymptomatic or can cause severe disease affecting multiple organs including the lung, kidney, cardiovascular system, and gastrointestinal tract leading to Acute Respiratory Distress Syndrome (ARDS), Multi-Organ Failure (MOF), septic shock, and death [2]. In addition, SARS-CoV-2 has been associated with hypercoagulability, thromboembolic disease, Cytokine Release Syndrome (CRS), and a multitude of neurologic disorders.

Therapeutic Plasma Exchange (TPE) involves the removal of whole blood, its separation into components, with removal of plasma and return of non-plasma components along with replacement fluid (e.g., 5% albumin, Fresh Frozen Plasma [FFP]). There has been precedence for the use of TPE as adjunctive therapy in patients with viral infections who have failed conventional antiviral therapy alone [3]. For example, patients with ARDS due to avian influenza A (Hemagglutinin 7 Neuraminidases 9 [H7N9]) were treated with TPE and tandem continuous veno-venous hemofiltration. Patients with hemophagocytic lymphohistiocytosis and neurologic conditions thought to be triggered by H1N1 have also received TPE. Overall, outcome data after TPE in viral infections is sparse, variable, and inconclusive. The role of TPE in the treatment of neurologic complications associated with viral infection has not been established and lacks consensus guidelines. The only notable exceptions are in Guillain Barre Syndrome (GBS) and acute Myathenia Gravis (MG) exacerbation. TPE is accepted as a first line therapy (category I indications) for both GBS and acute MG according to the 2019 American Society for Apheresis (ASFA) guidelines [4].

Otherwise, it is unclear that TPE is beneficial in the management of other neurological complications associated with SARS-CoV-2 infection and no high-quality data to show that TPE is helpful in COVID-19 related sepsis, MOF, and CRS. Nonetheless, TPE has been tried during the search for optimal management of patients with severe and complicated COVID-19. The theoretical rational for TPE includes:

1. Attenuation of pro-inflammatory cytokines
2. Stabilization of the endothelial membrane
3. Normalization of hyperviscosity
4. Correction of aberrations in the coagulation pathway
5. Reduction of antifibrinolytic mediators
6. Fibrin degradation products
7. SARS-CoV-2 virus

These mechanisms, however, remain to be proven. In part because given the novel nature of SARS-CoV-2, much of the pathogenic pathways that lead to the complications of COVID-19 are not well understood. A final consideration is that TPE removes plasma constituents non-selectively. Therefore, removal of protective host defense proteins, anti-inflammatory mediators, anti-SARS-CoV-2 neutralizing antibodies, and potentially effective drugs (e.g, antivirals, anti-inflammatory) may actually hamper resolution of the infection [5-12].

The case reports and case series published on the use of TPE as adjunctive therapy for COVID-19 are inherently limited in their study design [12-15]. No prospective randomized controlled trials have been completed to establish that TPE is effective

therapy for COVID-19. While generally safe and well tolerated, as with any medical intervention, TPE is not without risk. Routine complications of TPE associated with central line placement, line infection, and hypocalcemia apply for COVID-19 patients. While complications of severe hypocalcemia (hypotension, arrythmia, and QT prolongation) are rare, they are of particular concern in critically ill patients with preexisting septic shock and MOF. Replacement without plasma can cause hypokalemia and decreased coagulation factors. Replacement with plasma puts patients at risk of adverse events associated with transfusion. An additional consideration is the risk of clotting during the procedure which may prematurely interrupt the procedure and lead to acute blood loss in very sick patients.

If TPE is to be performed in patients with COVID-19, it should be done as part of one of the registered clinical trials. Completion of these trials is the only way to determine the safety and efficacy of TPE in COVID-19.

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