Commentary on "Convalescent Plasma Therapy in Late-State, Severe COVID-19 Infection"

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In this issue of the *Southern Medical Journal*, Kumar et al report on the use of convalescent plasma in late-stage, severe coronavirus disease 2019 (COVID-19) infection.[1] In this case series, convalescent plasma use improved Sequential Organ Failure Assessment scores without increasing adverse events. This commentary provides some historical context for using plasma to treat viral pandemics.

Since the Spanish flu pandemic of the early 20th century, medical professionals have used transfusion of convalescent blood products to mitigate the impact of viral infectious diseases. Transfusion gained increased notice while managing the Ebola virus, West Nile virus, Middle East respiratory syndrome coronavirus, severe acute respiratory syndrome-coronavirus-1, and H1N1 pandemics. In response to the COVID-19 pandemic, convalescent plasma use during the early stages of the disease was one strategy to help manage patients during this unprecedented outbreak.[2]

Convalescent plasma has been lauded as a relatively safe option for treatment in patients, given its association with minimal and transient adverse effects ranging from transfusion reactions to fever, hypotension, and tachycardia while showing improvement in clinical parameters.[3] It has been suggested that convalescent plasma can provide passive immunity when vaccines and other treatment options are not yet widely available when pandemics and outbreaks occur.[2]

Although the use of convalescent plasma is not novel, there has been a lack of robust studies to identify which variables in treating viral infections with plasma can affect patient care outcomes. Some studies have already demonstrated that variables in timing, volume, dosing administration, and concomitant use of antivirals, steroids, and other medications may influence patient outcomes. For example, Ortigoza et al propose that high-titer administration of plasma before using remdesivir and corticosteroids may benefit the treatment of COVID-19.[3] In another study of critically ill adults with confirmed COVID-19, treatment with two units of high-titer, ABO-compatible convalescent plasma had a low likelihood of improving the number of organ support-free days. Still, it may have shown some benefit in immunodeficient subgroups and those early in the illness.[4] Other studies have shown that changing patient characteristics, such as age and exposure to steroids and remdesivir, had varying effects on symptom duration and mortality outcomes.[3]

The data surrounding sex, age, ethnicity, race, comorbidities, and socioeconomic level remain poorly explored. Previous narrative reviews of convalescent plasma use focus on hospital settings, specifically severely ill medical inpatients or intensive care unit patients. Information surrounding medical outpatients and minoritized patient populations is lacking in most studies involving plasma use, limiting clinical certainty as to which patients benefit most from this treatment.[5]

To make convalescent plasma a relatively applicable and viable treatment option, investigators should prioritize understanding the subgroups of patients most likely to benefit, resources to scale up production during pandemics, and systemic barriers to care that may affect the use of plasma. Just in regard to setting up a system that can support the requirements of such a treatment option, one must consider that convalescent plasma use would require prophylaxis and therapeutic protocols for administration, blood processing facilities that would need to be adjusted, testing capabilities with sufficient screening assays, and the ability to standardize dosing. Failure to address these barriers can limit the use of this therapy for a broad audience of patients. Although convalescent plasma shows some promise, more questions and optimization are needed to make this treatment applicable and beneficial for diverse and unique communities.

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