

Micro-Thrombosis,
Perfusion Defects, and
Worsening
Oxygenation in
COVID-19 Patients: A
Word of Caution on the
Use of Convalescent
Plasma



To the Editor: Joyner et al¹ recently provided a safety update on the use of convalescent plasma (CP) in a population of 20,000 patients with coronavirus disease-19 (COVID-19). The results on the safety aspects, elegantly presented by the authors, may seem encouraging from many perspectives. However, we would like to comment on an extremely important aspect when considering the use of CP.

Most of the attention on safety issues during administration of CP has been directed toward adverse effects unrelated to the clinical settings (ie, infection, transfusion-related acute lung injury, or transfusion associated circulatory overload) and “disease-specific” (eg, viral enhancement). However, clinicians should bear in mind that CP contains procoagulant factors and in common clinical practice plasma is administered in patients with coagulopathies or hemorrhage, or both. Thus, administering CP to patients with COVID-19 means introducing procoagulant factors into their bloodstream. This may be troublesome when considering that COVID-19 patients stand at the other side of hemostasis disorders and that their tendency to develop a prothrombotic disease has been reported.² This prothrombotic state causes perfusion abnormalities at the pulmonary

level, contributing to the peculiar phenotype of respiratory failure in patients with COVID-19.³

In this context, it is worth noting the results of a recent study investigating the pulmonary abnormalities in COVID-19. Indeed, Patel et al⁴ recently showed significant alterations in the pulmonary vasculature in patients with severe COVID-19. The authors presented a combination of physiologic data, findings of high-resolution imaging, and hematologic results; they showed an activation of both inflammatory and coagulation pathways playing a pivotal role in the development of respiratory failure and compromising oxygenation in patients with severe COVID-19. Of note, hypercoagulability and reduction in the fibrinolytic activity in the pulmonary vasculature resulted in pulmonary perfusion abnormalities.

Although Joyner et al¹ reported a low incidence of thromboembolic or thrombotic events at 7-day follow-up (n = 113; <1%), when considering the administration of CP to COVID-19 patients, clinicians should bear in mind that even small quantities of coagulation factors contained in the CP can enhance the coagulation cascade. Such an event might represent a serious harm for patients with severe COVID-19; indeed, enhancing microthrombosis and the consequential perfusion abnormalities at the pulmonary level might ultimately lead to worsening oxygenation and increased risk of clinical deterioration.

In consideration of this risk, it would be interesting to access data on the ratio between partial pressure of oxygen in arterial blood and the fraction of inspired oxygen (PaO₂/FiO₂) before and after CP administration. Meanwhile, we would like to

express a word of caution on the use of CP in severe COVID-19 patients.

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In Reply — Micro-Thrombosis, Perfusion Defects, and Worsening Oxygenation in COVID-19 Patients: A Word of Caution on the Use of Convalescent Plasma



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