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Letter Open Access

Comments on: "Clinical efficacy of convalescent plasma for treatment of COVID-19 infections: Results of a multicenter clinical study" [Transfusion and Apheresis Science 59 (2020) 102875]

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Dear Editor

We read the recent work about the clinical efficacy of convalescent plasma for the treatment of COVID-19 infections by Abolghasemi et al., in Transfusion and Apheresis Science with great interest[1] and identified several concerns with the design and findings. For example, while the patients of the two groups were matched on two comorbidities- diabetes and hypertension- they were not matched on the severity of the COVID-19 progression or several other comorbidities that affect the lung, kidney and blood. Factors such as mortality, length of stay, and intubation, were included as outcomes and are affected by these confounding factors. By carefully examining the findings we determined that the p-value, estimated as 0.09, indicates that mortality does not significantly differ between the two groups. Yet, the discussion begins with a statement that mortality has improved "significantly". The discussion also states that plasma therapy reduced the length of stay from 12.88 to 9.54 days. We posit that this conclusion cannot be drawn due to the many confounding factors involved and the lack of patient matching on significant variables.

Moreover, some of the limited studies that have reported positive results of convalescent plasma therapy on COVID-19 did not use convalescent plasma therapy alone, but rather as an adjuvant therapy or in combination with standard treatments.[2]

A recent analysis of the pathophysiology of COVID-19 has shown that SARS-CoV-2 not only creates an inflammatory and hypercoagulable state, it creates a hypofibrinolytic state that is not observed in most other types of coagulopathy conditions.[3] It has also been shown that plasma taken from recovered patients of COVID-19 results in direct damage to vascular endothelial cells under laboratory conditions.[4] Detailed clinical trials following the United States Food and Drug Administration treatment protocol, show that cardiac events occurred in 88% and thrombotic events occurred in 66% of patients with COVID-19.[5] These events were not included in the Abolghasemi report[1] and therefore were not reported as side effects. In another clinical trial in India, researchers found no beneficial effects associated with plasma therapy in hospitalized patients with moderate-to-severe COVID-19. Agarwal et al., found minor beneficial decreases in shortness of breath and fatigue, but the evaluators in that study were not blind to the subject data, decreasing the reliability of their findings.[6] Similarly, in this study,[1] the evaluators were not blind, and thrombotic events and consequences were not considered as complications. In addition to the bias in the allocation of patients, Abolghasemi's study was also biased in the selection of patients and ignored the theory of plasma therapy and its

possible blood consequences, blood diseases were not matched between the two groups, and blood consequences such as coagulation were not reported in the follow-up.[1] So the claim "This clinical study provides strong evidence to support the efficacy of convalescent plasma therapy in COVID-19 patients and recommends this treatment for management of these patients. Clinical efficacy, immediate availability and potential cost effectiveness could be considered as main advantages of convalescent plasma therapy [see the conclusion][1]" cannot be made.

One point to note is that in Iran, the use of plasma therapy for patients with COVID-19 is prohibited. Several research groups examined treatment options at the beginning of the COVID-19 epidemic. One of these treatments- plasma therapy was abandoned as this therapy was found to be ineffective for patients by the World Health Organization.[7] This challenges the claim by Abolghasemi et al., of the effectiveness of plasma therapy for Iranian patients with COVID-19.[1]

High-quality clinical research must become an integral part of a coordinated international response. Low-quality research wastes scarce resources, and is inherently unethical to conduct. The findings of previous trials suggest the following recommendations to monitor the safety and effectiveness of plasma therapy. First, the possible harms of the non-immune components of plasma therapy should be carefully investigated, especially the prothrombotic risks. Second, only donor plasma with detectable neutralizing antibody titers should be given to patients in the intervention group, to ensure that intervention is useful and effective for all patients in the intervention group. Third, evaluators should be double-blind to the details of the control group. Fourth, non-immune plasma should not be used for the control group, because it may cause possible harm. Fifth, when multiple research teams require patients, triage committees should be in place to direct and allocate patients to avoid low-priority, duplicate, or low-powered studies that have little potential to yield usable findings.

Authors' contributions

The authors read and approved the final manuscript. They take responsibility for the integrity of the data and the accuracy of the data analysis.

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None.

Abbreviations

Coronavirus disease 2019: COVID-19; Severe acute respiratory syndrome coronavirus 2: SARS-CoV-2.

Competing interests

None.

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Availability of data and materials

The data used in this study are available from the corresponding author on request.

Ethics approval and consent to participate

None.

Consent for publication

By submitting this document, the authors declare their consent for the final accepted version of the manuscript to be considered for publication.

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