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LETTER TO THE EDITOR

TRANSFUSION MEDICINE WILEY

ABO-incompatible convalescent plasma transfusion: Yes, you can

Dear Sir,

On the basis of interventional studies published to date, transfusion of convalescent plasma (CP) is hypothesized as an effective treatment in nonmechanically ventilated severe COVID-19 patients.[1] This modality continues to be pursued worldwide, and randomised clinical trials are underway to test the hypothesis.

Because the vast majority of COVID-19 cases are asymptomatic or paucisymptomatic, generating neutralising antibody (nAb) titres which are too low, the number of suitable donors of CP is limited. Repeat plasmapheresis is currently the standard of collection in westernised countries. Several studies indicate that group AB patients have greater disease severity,[2] and are hence less likely to fully recover and become CP donors before the nAb titre declines to levels which are therapeutically useless.[1] In small-scale CP programs, this and other biases have led to a patient-donor imbalance, often leaving group AB and B (and more rarely group A) patients devoid of ABO-matched CP units.

Three approaches can theoretically be implemented to address this deficiency:

1. Repeat plasma donations from the suitable donors. This is of limited scaling up, as the nAb titre can drop rapidly over the timeframe needed to harvest a useful number of donations in a large part of donors, and that is the reason why the nAb titre has to be reassessed at every donation.
2. Sourcing units from different geographic areas. This will not obviate the aforementioned imbalance as these will occur within as well as across borders.
3. ABO-incompatible (ABOi) CP transfusion. ABOi plasma transfusion has long been used under emergency setting, and no major immediate intravascular haemolytic transfusion reactions (IHTR) occurs when isoagglutinin titres are below 1:64.[3] According to the AABB Technical Manual, ABOi plasma transfusion in group AB patients should be attempted with group A before group B in order to minimise haemolysis. Group A units are generally more abundant and less likely to introduce additional unbalance within the pool of available donors. Anti-B isoagglutinin titration can be performed using high-throughput automated platforms, and, when discordance occurs between platforms, the highest signal should be prudentially used as output reported in the validation label.[4] Blood group O remains the last choice for ABOi plasma transfusion in recipients of group A, B and AB.

ABOi CP transfusion has been successfully implemented in at least one case in South Korea.[5] In the COVID-19 setting, the typical therapeutic dose under investigation is 200–400 ml, which is considerably lower than in the massive plasma transfusion setting where a larger volume of transfused ABOi plasma may pose a risk, but we reasonably expect a high degree of hesitancy from non-transfusion specialists who finally are legally responsible for patient treatment.

The issue of incompatible recipients has been accommodated by the US FDA, whose emergence investigational new drug (eIND) approach has never mandated ABO-compatibility for COVID-19 CP. Similarly, the expanded access program (EAP) led by Mayo Clinic has amended its initial protocol to state that *"ABO compatible convalescent plasma units will be transfused preferentially. If ABO compatible convalescent plasma is not available, investigators may follow their institution's guidelines for administration of incompatible plasma with respect to ABO mismatch, titer, and volume limits"* (https://www.uscovidplasma.org/pdf/COVID-19%20Plasma%20EAP.pdf).

The use of ABOi CP transfusion should be discussed in COVID-19 guidelines and included in medical education programs.

CONFLICT OF INTEREST

The authors have no competing interests.

AUTHOR CONTRIBUTIONS

Focosi Daniele: designed the manuscript and wrote the first draft. Farrugia Albert: critically revised the manuscript.

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