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Letter to the Editor

COVID19 immune plasma donation after vaccination: pros and cons.



ARTICLE INFO

Dear Sirs,

Immune plasma is historically defined as an emergency passive immune therapeutic collected from convalescents. Nevertheless, as soon as a vaccine becomes available, collection from vaccinees is technically feasible. The latter scenario is emerging for COVID19, and health authorities are actively discussing such topic.

In a November 16, 2020 the US Food and Drug Administration (FDA) Guidance prohibited all donations of CCP after COVID vaccination. On January 15, 2021 the guidance was partially reversed (part III.B.1.d) to allow donations of convalescent plasma by vaccinated donors if they had COVID symptoms confirmed by diagnostic swab testing, were vaccinated after their illness, and were 14 days to 6 months past symptom resolution [1]. On Feb 12, 2021 the American Association of Blood Banks (AABB) updated its Toolkit accordingly [2], while the WHO has not collected this indication in its interim guidance on convalescent plasma donation dated Feb 17, 2021 [3]. The choice has been officially motivated by the FDA with the risk to provide an ineffective product, although harming the vaccinees immunity is another potential concern.

The first concern (providing an ineffective product) seems hard to sustain, given that vaccinee's plasma efficacy theoretically is superior to the one of (far more expensive and epitope-restrained) approved cocktail of anti-receptor-binding domain (RBD) monoclonal antibodies. From a virological point of view, the currently licensed vaccines are entirely based on the Spike protein (encoded either by mRNA or by viral vectors), and all of them include the RBD: the elicited immune response is hence limited to that part of SARS-CoV-2 proteome. While vaccinees plasma is more restricted in antibody specificity, not by chance it includes the most neutralizing and protective humoral activity. Historically, similar collections programs from vaccinees have been the basis of hyperimmune serum against hepatitis B, rabies or tetanus [4].

The second concern (harming the vaccinees immunity) is also hard to sustain. The geometric mean neutralizing antibody titer elicited after the full vaccine schedule largely exceeds the one observed in convalescents after natural infection. These evidences preclude the theoretical risk of significantly reducing the acquired post-vaccination protection. Paradoxically, it seems riskier to collect plasma from fragile and lower-titer convalescents.

The FDA document also says that “*administration of COVID-19 vaccines for the purpose of boosting immunity of convalescent plasma donors*

would need to be conducted within a clinical trial under IND [21 CFR Part 312.]. This is currently a topic of utmost interest, given that most countries are delivering the full (2-dose) schedule to convalescents, who are instead able to achieve protective titers (cross-reacting against variants of concern) after a single vaccine dose [5]. Romon et al. have shown that a single dose of mRNA vaccine in convalescents actually leads to Ortho Vitros antibody levels predictive of high nAb content [6]. Vickers et al. have shown that ~50 fold increases in Spike-specific antibody levels (DiaSorin) and at least a 20-fold increase in the IC₅₀ neutralizing antibody titer based on plaque reduction neutralization testing (PRNT) [7].

It has been reported that the majority of mRNA vaccine-induced antibodies did not have neutralizing activity and an original antigenic-sin like backboost to seasonal human coronaviruses OC43 and HKU1 spike proteins [8], so nAb titration before donation should remain mandatory.

Given that the vast majority of vaccinees would be healthy subjects, and eventually regular blood donors, the usage of pathogen reduction technologies could be avoided at all and the relative cost saved.

While the donor type (convalescent vs. vaccinated) should be carefully detailed and registered to allow post-hoc analyses, we feel there is no scientific rationale for denying collection of such potentially life-saving therapeutic from vaccinees.

Author contributions

D.F. designed the paper, analyzed the data, and wrote the first draft. M.F. revised the final version.

Declaration of Competing Interest

We declare we have no conflict of interests to disclose related to this manuscript.

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Abbreviations: VNT, viral neutralization test; nAb, neutralizing antibodies; CCP, COVID19 convalescent plasma.

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Daniele Focosi*

North-Western Tuscany Blood Bank, Pisa University Hospital, Pisa, Italy

Massimo Franchini

Department of Hematology and Transfusion Medicine, Carlo Poma Hospital, Mantua, Italy

* Corresponding author at: via Paradisa 2, 56124, Pisa, Italy.

E-mail address: daniele.focosi@gmail.com (D. Focosi).