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COVID-19 vaccination: The impact on the selection criteria of the convalescent plasma donors



Sir,

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected in Wuhan [1]. Subsequently, the worldwide spread of SARS-CoV-2 has resulted in a COVID-19 pandemic. Clinical management protocols for COVID-19 are evolving rapidly as more information about the epidemiology and pathophysiological changes in COVID-19 become available [2]. However, no definite treatment of COVID-19 has been found to date. The COVID-19 convalescent plasma (CCP) therapy has emerged as an important investigational therapy in the management of COVID-19 patients [3]. Historically, CCP therapy has been used in various infectious diseases, such as influenza, EBOLA and SARS viruses [4]. Therefore, several clinical trials were undertaken in different parts of the world to study the efficacy and safety of CCP therapy in the COVID-19 patients [5]. While few studies concluded that CCP therapy resulted in decreased mortality [6–9], others found no clinical benefit from the use of CCP therapy in COVID-19 patients [10,11]. This is probably due to the inconsistencies in defining the appropriate selection criteria of the intervention subject, the timing of intervention, antibody titre levels in the harvested CCP and clear demarcation of the primary as well as the secondary outcomes [3]. Emphasis is now being given to the early administration of CCP containing high titre IgG anti-SARS-CoV-2 antibodies for the therapy to be effective [12]. Further, we believe that there might be a lot of paranoia, uncertainty and false assumptions in the minds of donors about whole blood donation [WBD] as well as CCP donation amid this pandemic [13]. The efforts to develop an effective vaccine started as soon as February 2020. In fact, as of 20th April 2021, a total of six vaccines have been given emergency use authorization [EUA] by the World Health Organization recognized stringent regulatory authorities. Also, mass immunization programs against SARS-CoV-2 are currently going on in various countries throughout the globe. Therefore, there are now two types of seroconverted individuals:

- those as a result of natural infection with the SARS-CoV-2 virus and;
- those as a result of vaccination against SARS-CoV-2.

Additionally, with the overtly visible role of a transfusion medicine specialist [TMS] in the community these days [14], the scientific community is bound to ask them the following three queries.

Query1: whether individuals who have seroconverted as a result of COVID-19 vaccination are eligible to donate their immune plasma?

Discussion: The convalescent plasma obtained from an individual who was naturally infected by SARS-CoV-2 contains antibodies directed against the spike protein, the nucleocapsid protein and the receptor-binding domain [RBD] of the virus. Moreover, the plasma obtained from a seroconverted donor as a result of natural SARS-CoV-2 infection is polyclonal in nature and therefore carries antibodies having paratopes against the different epitopes of a pathogen. Also quantitatively, these are sufficient to be effective against the original virus and then randomly derived viral variants [15]. In contrast, the immune plasma obtained from vaccinated individuals has a high level of IgG antibody titres against the SARS-CoV-2 spike protein only. Therefore, despite providing immunity to the individual vaccinated, it will not be completely effective when used as a CCP in the COVID-19 sufferers. Further, according to United States Food and Drug Administration (US-FDA) guidelines, individuals who have never been infected with SARS-CoV-2 and have received a jab of COVID-19 vaccine are ineligible to donate their immune plasma in the configuration of a CCP [16]. However, other agencies, including the Indian regulatory agencies have not yet issued any interim recommendations in this regard.

Query 2: what are the CCP donation eligibility criteria for the COVID-19 recovered individuals who have also received a vaccination?

Discussion: For those who had been naturally infected with SARS-CoV-2, the US-FDA has recommended a deferral period of 14 days after the resolution of COVID-19 symptoms before the CCP donation. Further, the FDA has recommended a deferral period of 14 days after receiving a live vaccine and no deferral period for receiving an inactivated or killed vaccine [16]. While, few regulatory agencies have issued guidelines for donor deferral towards WBD following COVID-19 vaccination [17], others have largely remained silent on defining an appropriate deferral period for CCP donation in such vaccinated individuals. Furthermore, it has also been seen that previously infected individuals are producing very high titre SARS-CoV-2 specific neutralizing antibodies following vaccination [18]. Therefore, the CCP obtained from these individuals may be more effective in the COVID-19 treatment than the CCP obtained from non-vaccinated COVID-19 recovered patients alone.

Query 3: CCP donor eligibility for the COVID-19 recovered individuals who themselves received CCP therapy during their hospital stay?

Discussion: All the donors who wish to make either a WBD or CCP donation must meet the allogeneic blood donor criteria, including the three-month deferral from the date of CCP administration or the transfusion of any other blood component [16].

To conclude, the regulatory agencies, in particular, the Indian blood transfusion council must release some interim recommendations on the CCP donor eligibility in the aforementioned situations. Additional clinical trials are needed to know the efficacy of the CCP harvested from COVID-19 recovered individuals who have been vaccinated against those COVID-19 recovered individuals who who are not vaccinated at all.

Research involving human participants and/or animals

Human participants.

Informed consent

As per our department policy an informed consent is obtained from all the donors prior to their convalescent plasma harvest in accordance to our standard operating protocol.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Contribution

Naveen Bansal contributed to the literature search, data compilation, manuscript preparation, editing and review, while Yashik Bansal contributed to the manuscript editing and review. Manish Raturi contributed to the conceptual design, literature search, manuscript preparation, editing, review as well as being the guarantor who takes the complete responsibility for the integrity of the work done as the whole, right from its inception to the published article.

Disclosure of interest

The authors declare that they have no competing interest.

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Early and persistent viral clearance in COVID-19 patients treated with convalescent plasma



Passive immune therapy by means of transfusion of hyper-immune plasma from recovered donors was utilized in many viral epidemics in the past century and has recently been re-discovered for the treatment of patients with coronavirus disease 2019 (COVID-19). Several trials evaluating the potential beneficial effects of convalescent plasma (CP) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are ongoing or have been published [1]. Although mostly inconclusive, recent evidence does suggest that CP is clinically effective when administered early (within 72 h of hospital admission), with a high titer of anti-SARS-CoV-2 neutralizing antibodies (> 1:160 as determined using the plaque reduction neutralization test) and in COVID-19 patients with an inadequate antibody virus response, such as elderly subjects and immunocompromised patients [2,3]. The initial rate, timing and temporal duration of the viral clearance in COVID-19 patients receiving CP are poorly understood, mostly because of the lack of studies with an adequate follow-up. With the aim of elucidating these issues, we followed 54 consecutive patients with severe COVID-19 treated with CP for compassionate use between April 1 and April 30, 2020. Their demographic, clinical and treatment characteristics are summarized in Table 1. Overall, 81 CP units, each of 300 mL, were transfused to the 54 COVID-19 patients (median: 1 CP unit per patient, range 1–3 units). The median neutralizing anti-SARS-CoV-2 antibody titer per CP unit was 1:160 (range 1:80–1:640, measured using the standard plaque reduction neutralizing test). The molecular test for SARS-CoV-2 became negative in 85.2% of patients already 72 h after CP infusion and by day 7, all patients resulted negative. The viral clearance persisted at the end of follow-up (median: 9 months).

In conclusion, the results of this study document the short- and long-term SARS-CoV-2 suppression by CP therapy. While the high efficacy of passive immune therapy in rapidly eradicating SARS-CoV-2 is in accordance with previously published data [4], the sustained virus eradication by CP infusion is reported here for the first time. The latter finding enables us to make some important