Convalescent plasma from people vaccinated after COVID-19 infection

Plasma collected from previously infected people to passively transfer antibodies to protect or treat humans (convalescent plasma), has been successfully used since the late 19th century to treat diseases such as diphtheria, hepatitis A and B, and Ebola virus disease.[1] The absence of effective treatment options for COVID-19 has led to the experimental use of convalescent plasma as a treatment to suppress the viral disease in early and advanced stages. Convalescent plasma has been widely used as a compassionate treatment for critically ill patients with COVID-19.

Despite evidence of the efficacy of convalescent plasma for treating other diseases,[2] the largest meta-analysis of convalescent plasma for COVID-19 was inconclusive about its efficacy against mortality or symptoms in patients in hospital. Subsequent studies suggested that the benefit of convalescent plasma was most apparent in patients who received plasma transfusions with high antibody titres at the early stage of the disease.[3] Currently, the US Food and Drug Administration (FDA) recommends collecting convalescent plasma from patients at least 28 days after resolving COVID-19 symptoms, or after 14 days in combination with two negative molecular tests (with ≥24 h between tests), to ensure the eradication of the virus and the development of neutralising antibodies.[4] Circulating antibody expression decays rapidly over the first 2–3 months of infection,[5] leaving a limited window of opportunity in which to collect high-titre plasma from donors. An estimate from one centre in the USA suggests that fewer than 20% of plasma donations meet the FDA high-titre criteria.[1]

In the framework of an immunogenicity study following vaccination with BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech) among health-care workers at Ziv Medical Centre, Israel,[6] IgG antibody expressions were measured 21 days after the first dose of the vaccine using the DiaSorin LIAISON assay[7] to quantify anti-COVID-19 spike IgG antibodies. Prevaccination baseline IgG was measured using an Abbott Architect SARS-CoV-2 IgG assay[7] to detect nucelocapsid antibodies with high sensitivity and specificity, and history of a previously positive PCR test was recorded. The study showed that among previously infected health-care workers (defined by either a previously positive PCR test or positive IgG serology prevaccination) IgG titres were very high, one order of magnitude higher than non-previously infected workers.[6] This difference was the case regardless of the presence of IgG antibodies at baseline and irrespective of the time interval between a positive PCR test and vaccination.[6]

Other emerging evidence from similar studies suggests that giving a boost to people previously infected with SARS-CoV-2 using one dose of RNA-based vaccine might improve protection against reinfection.[8,9] Based on these findings, antibody-rich convalescent plasma from previously infected patients vaccinated with at least one dose of the BNT162b2 vaccine might be more effective than the convalescent plasma from non-vaccinated patients that is currently being given to patients with COVID-19. Also, timing the harvesting of plasma from individuals who have a planned vaccination date is logistically easier than with individuals who are recovering from COVID-19, and can be planned to coincide with the time of highest antibody titres, vastly increasing the yield of high-titre plasma. In the Ziv Medical Centre study, serological samples were taken on the day that health-care workers came for their second dose of vaccine, taking advantage of the fact that these workers were already presenting at a vaccination site. A similar timing could be considered for plasma harvesting. This finding potentially makes harvesting antibody-rich plasma a more scalable, effective, and cost-effective approach to treating patients with COVID-19 compared with the traditional convalescent plasma currently in use. Furthermore, at least in countries in which mutant COVID-19 strains are circulating, convalescent plasma harvested from patients infected with such strains and subsequently boosted by vaccination might be effective in individuals infected with mutant strains. These findings should be confirmed in larger studies, and rigorous clinical trials of plasma therapy from previously infected vaccinated individuals should be done to determine whether these theoretical benefits translate to clinical efficacy, and for which clinical indications.

We declare no competing interests.

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