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COVID-19 convalescent plasma use in the oncology and geriatric patients: Ethical aspects in transfusion medicine



Dear Sir,

We read with great interest the article entitled “Transfusion at the border of the «intention-to-treat», in the very aged person and palliative care: A debate” by Garraud. O [1]. We wish to share our thoughts related to this article. As discussed in the article [1], the ethical issues regarding blood transfusion in palliative care and geriatrics are mainly with the red blood cell and platelet transfusion and not with plasma transfusion because the latter is rarely prescribed for palliative care. However, the coronavirus disease (COVID-19) pandemic has changed this scenario, as COVID-19 convalescent plasma (CCP) has emerged as an important therapeutic option, especially in immunodeficient patients including oncology patients [2]. Herein, we discuss the important ethical aspects related to the use of CCP in the management of oncology and geriatric patients.

1. Non-maleficence

1.1. In elderly patients

Apart from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) neutralizing antibodies, CCP also contains non-neutralizing antibodies that can assist in the entry of the virus into macrophages [3]. The virus multiplies rapidly in the macrophages, thereby, producing a pro-inflammatory condition, which subsequently can result in worsening of the cytokine storm [3]. Maro-Rillo et al. reported a case of convalescent plasma transfusion induced acute respiratory distress syndrome in a patient with Ebola virus disease [4]. Moreover, elderly patients have an age-related mild inflammatory condition called “inflamm-aging” and are more susceptible to developing a cytokine storm after COVID-19 infection [5]. Before a decision of transfusing CCP is made, in an elderly patient, these aspects must be kept in mind.

1.2. In oncology patients

The majority of oncology patients belong to the geriatric age group. Additionally, they generally have an immunocompromised state, and consequently, with defective viral clearance, they are more prone to develop chronic prolonged SARS-CoV-2 infection [6]. The current evidence that CCP administration in immunocompromised patients could accelerate the generation of SARS-CoV-2 variants [7] should also be kept in mind before planning a CCP transfusion in such a cohort of patients.

2. Beneficence

As per FDA emergency use authorization, only high titer CCP can be used in the patients that too only in the early stages of COVID-19, except for immunocompromised patients, in which case CCP could be, transfused at any stage of COVID-19 [8]. In India, in many instances, CCP was being administered either without doing any antibody titration and/or late in the course of infection [9]. Eventually, due to the indiscriminate use of CCP, it proved to be non-efficacious and ultimately led to the scrapping of CCP from the management protocols for COVID-19 in India [9]. Therefore, as suggested by Garraud O in the article [1], a careful risk-benefit analysis, should be undertaken before administering CCP

in any patient. Rather, a scoring system may also be used for this purpose [10].

Ethical issues related to plasma donors should also be kept in mind. There have been reports of donors being offered financial incentives for the donation of CCP [11,12]. Blood centres should ensure that the CCP donors are non-remunerated voluntary donors. At the same time, the process of informed consent and donor confidentiality also merits consideration [13]. Finally, ethical considerations must be the front line of the transfusion debate, especially in the matter of the very aged person or in palliative care [14]. The motto should be the best possible patient outcome and based on the underlying principle of justice with a pure intent to treat.

Funding resources

None.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Garraud O. Transfusion at the border of the “intention-to-treat”, in the very aged person and in palliative care: A debate. *TransfusClin Biol* 2021;28:367–9, <http://dx.doi.org/10.1016/j.traccli.2021.08.350>.
- [2] Garraud O, Lacombe K, Tiberghien P. A look-back at convalescent plasma to treat COVID-19. *TransfusApher Sci* 2021;60:103063, <http://dx.doi.org/10.1016/j.transci.2021.103063>.
- [3] Channappanavar R, Fehr AR, Vijay R, et al., Dysregulated Type I. Interferon and inflammatory monocyte-macrophage responses cause lethal pneumonia in SARS-CoV-Infected Mice. *Cell Host Microbe* 2016;19:181–93, <http://dx.doi.org/10.1016/j.chom.2016.01.007>.
- [4] Mora-Rillo M, Arsuaga M, Ramírez-Olivencia G, et al. Acute respiratory distress syndrome after convalescent plasma use: treatment of a patient with Ebola virus disease contracted in Madrid, Spain. *Lancet Respir Med* 2015;3:554–62, [http://dx.doi.org/10.1016/S2213-2600\(15\)00180-0](http://dx.doi.org/10.1016/S2213-2600(15)00180-0).
- [5] Sanada F, Taniyama Y, Muratsu J, et al. Source of chronic inflammation in aging. *Front Cardiovasc Med* 2018;5:12, <http://dx.doi.org/10.3389/fcvm.2018.00012>. Published 2018 Feb 22.
- [6] Avanzato VA, Matson MJ, Seifert SN, et al. Case study: prolonged infectious SARS-CoV-2 shedding from an asymptomatic immunocompromised individual with cancer. *Cell* 2020;183:1901e9–12e9, <http://dx.doi.org/10.1016/j.cell.2020.10.049>.
- [7] Kemp SA, Collier DA, Datir RP, et al. SARS-CoV-2 evolution during treatment of chronic infection. *Nature* 2021;592:277–82, <http://dx.doi.org/10.1038/s41586-021-03291-y>.
- [8] Rnjak D, Ravlić S, Šola AM, et al. COVID-19 convalescent plasma as long-term therapy in immunodeficient patients? *TransfusClin Biol* 2021;28:264–70, <http://dx.doi.org/10.1016/j.traccli.2021.04.004>.
- [9] Madawi A, Bansal N, Bansal Y. Covid-19 convalescent plasma therapy: analyzing the factors that led to its failure in India. *TransfusClin Biol* 2021;28:296–8, <http://dx.doi.org/10.1016/j.traccli.2021.05.009>.
- [10] Bansal N, Raturi M, Bansal Y, Singh P. A novel scoring system for selecting the target patients of COVID-19 convalescent plasma therapy: a hypothesis [published online ahead of print, 2021 Jun 24]. *TransfusClin Biol* 2021, <http://dx.doi.org/10.1016/j.traccli.2021.06.004> [S1246-7820(21)00086-0].
- [11] Garraud O, Farrugia A, Tissot JD. Is plasma donation ethics abused? *TransfusClin Biol* 2021;28:1–2, <http://dx.doi.org/10.1016/j.traccli.2020.12.006>.
- [12] Madawi A. If the poorest Americans sell blood, the US is in serious trouble. 21-October-2020. Available from <https://www.theguardian.com/commentisfree/2020/oct/21/if-the-poorest-americans-are-selling-their-blood-the-us-is-in-serious-trouble>. [Last accessed 30-November-2021].
- [13] Raturi M, Kala M, Das K, Kusum A. Reviewing the ethical concerns of the convalescent plasma therapy in COVID-19. *J Lab Physicians* 2021;13:91–4, <http://dx.doi.org/10.1055/s-0041-1727585>.
- [14] Varkey B. Principles of clinical ethics and their application to practice. *Med Princ Pract* 2021;30:17–28, <http://dx.doi.org/10.1159/000509119>.

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Greenish colour of single donor apheresis platelet – is it bad? A tricky decision in the resource constraint situation



Dear editor,

The plasma component of blood is usually yellowish due to the presence of carotenoids, bilirubin, haemoglobin, and transferrin [1]. Unusual colour like turbid milky, dark yellow, green, pink, red, and orange due to various physiological and pathological reasons have been described [2,3]. The green colour of plasma has been attributed predominantly to elevated ceruloplasmin levels, especially in female donors using oral contraceptive pills or *Pseudomonas aeruginosa* [4,5]. The visual assessment guide of Canadian blood services advocates acceptance of light green colour plasma units for transfusion purposes. Still, the lack of such recommendations in our country makes these units unacceptable for transfusion [6,7]. The possibility of *P. aeruginosa* contamination is another reason to quarantine or discard green coloured plasma units. We are describing a single donor apheresis platelet unit from a young male donor with green colour plasma.

A 25-year-old healthy, voluntary, repeat whole blood male donor was selected for single donor apheresis platelet (SDAP) collection as per department standard operating procedure (SOP) based on national guidelines. The donor was recruited immediately after requisition received to provide SDAP to a 68-year female patient diagnosed with acute leukaemia with a platelet count of 18,000/ μ l as practiced in most of blood centre of India [8]. The donor pre-procedure haematological parameters were within normal limits (Hb = 15.2 g/dl, Hct = 45.1%, TLC = 11,400/ μ l, Platelet = 380,000/ μ l). The mandatory transfusion-transmitted infection (TTI) testing was non-reactive. The SDAP procedure was

performed with Haemonetics MCS Plus cell separator (Haemonetics, Braintree, MA, USA) using plateletpheresis protocol with a target yield of 3×10^{11} platelets. A total of 264 ml of SDAP product was collected by processing 2690 ml whole blood and utilizing 351 ml of acid citrate dextrose (ACD) anticoagulant in a ratio of 1:9 (ACD: Whole blood) for 90 minutes procedure. The colour of the SDAP product was different from the usual plasma colour and appeared green, as shown in Fig. 1.

The clinician was contacted and informed about colour of product. The immediate clinical requirement of platelets transfusion, non-availability of another blood donors due to COVID-19 pandemic and cost of apheresis kit outweighed the risk of possible adverse transfusion reaction due to green coloured SDAP. An informed clinical decision was taken to transfuse this product in view of scheduled chemotherapy of the patient after evaluating risks and benefits involved based on individualist weighing principle [9]. The transfusion was uneventful with a 24-hour corrected count increment (CCI) of 8700. The detailed medical history of the donor revealed no possible etiology, including any recent drugs intake, clinical features suggestive of rheumatoid arthritis and any food supplements.

The product yield was 3.3×10^{11} , and both aerobic and anaerobic culture of SDAP was sterile. The donor serum bilirubin was 0.4 mg/dl (Direct = 0.1, Indirect = 0.3). The donor serum copper levels were elevated (231.8 μ g/dL, reference range 70–140 μ g/dL) and ceruloplasmin was towards upper limit (28.9 mg/dL, reference range 15–30 mg/dL). The elevated serum copper level was attributed to the product's green appearance, which was transfused uneventfully to achieve desired clinical benefit.

The visual inspection of blood components is critical, including any discoloration at each step of transfusion event from

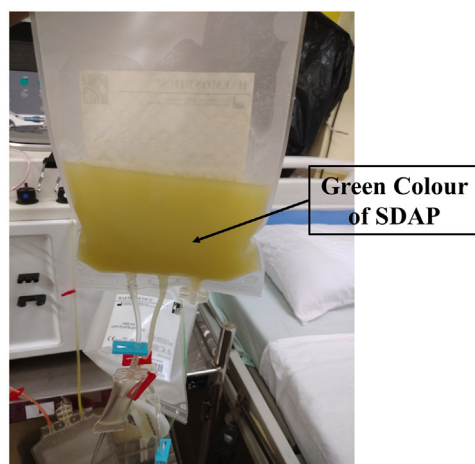


Fig. 1. Green Colour SDAP Unit.