Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Transfusion Clinique et Biologique 28 (2021) 225–227

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Editorial

Convalescent Covid-19 plasma: Back-to-basics and ethics, and next steps

The SARS-CoV-2 infection is worldwide; the virus mutates fast, speeding the spreading of the infection and subsequent disease (Covid-19) due to numerous consecutive emerging variants, each more infectious than the previous one. Efficient vaccines have been made available against the first viral strains within an amazingly short period of time [1]. Despite this tremendous achievement, too few people can get full vaccination schedule to successfully stop the virus progression, and many places in the world are currently struggling to fight both the virus transmission and the disease especially in the most vulnerable populations [2]. Vaccination is recognized as the sole protective measure that can be set in place readily to limit the pandemics and to eventually allow coming back to normal life. Convalescent plasma therapy has swiftly been tested for its safety and efficacy to limit Covid-19 pathology in the sickest [3,4], as has been the case when several past viral infections have threatened public health during the last century [5]. A year back, points to consider and questions were raised about applicability [6,7], logistic issue, impact, safety and usefulness of plasma passive immunotherapy in Covid-19 patients [8,9]; other issues dealing with ethics of plasma collection and allocation [10–13], and best protocol scaling have been addressed, and some of these questions have been resolved. Large cohorts of treated patients versus controls have been scrutinized and results on efficacy were not as straightforward as initially expected [14–18]. An innumerable number of studies have been proposed for publication in journals of different specialties; as could have been anticipated, studies coming from almost unknown teams experienced difficulties to be published, contrary to the ones led by key opinion leaders. *Transfusion Clinique et Biologique* made a considerable effort to emphasize experiences from countries reporting struggles to raise sustainable plasma therapy while facing organizational, financial, and networking difficulties [19–27]; the Journal's goal has been to assist teams from countries facing similar situations and to disseminate valuable experiences. As the vaccine programs develop—especially in high-income countries—reports on convalescent plasma therapy decrease reciprocally. For the time being, good evidence exists that antibodies raised post natural infection and/or using vaccines licensed by recognized regulatory agencies (i.e. the U.S. Food and Drug Administration and the European Medicines Agency) efficiently block the virus variant entry into people's respiratory cells. One may however question whether stepping back from convalescent plasma therapy programs is justified and wise. Several reasons argue against such a position. 1) Several clinical studies suggest that early passive immunotherapy using high-titre plasma can save patients if administered within three days of disease onset and prior to active seroconversion [28,29]; 2) Convalescent plasma therapy has been demonstrated beneficial in treatment of Covid-19 patients with various causes of immunodeficiency [30]; 3) Convalescent plasma may thus well still be a justified therapeutic option, if used wisely, in certain countries that cannot afford expensive biologicals (such as monoclonal antibodies) to limit pathological hyper-inflammation; 4) Novel SARS-CoV-2 variants may eventually be loosely targeted by the immunity procured by current vaccines (at least until vaccine production is adapted and the ad hoc shots given to exposed populations) [31]; 5) If interrupted, it would take time, effort and considerable organization to re-initiate plasma collection and therapy, when needed (as may be the case if no other suitable therapeutic option is available for any reason, or if supply of vaccines or monoclonal antibodies is interrupted). It must be kept in mind that an efficient plasma therapy program relies primarily on voluntary blood donors who must not be demotivated. For example, the experience acquired from the recent Ebola virus infection, where convalescent plasma collection was initiated and then discontinued when the epidemics resolved, has not been maintained, forcing many teams to rescale convalescent plasma collection, quality control and transfusion procedures, thereby delaying the implementation of Covid-19 convalescent plasma therapy. Some may claim that it is unethical to collect therapeutic plasma not immediately intended for direct clinical use. Still, as the SARS-CoV-2 progression goes on, international assistance programs could be put in place —i.e. with a special derogation from e.g. the European regulatory authorities—to supply safe pathogen-reduced therapeutic plasma to resource-constrained countries facing slow vaccine programs and a lack of intensive care facilities. Effort has been made to elaborate safety and quality programs designed for low and medium-income countries regarding plasma collection, pro-

https://doi.org/10.1016/j.tracli.2021.07.005

cessing, and use [32–35]. Thus, we urge public health authorities at global level, including in low- and middle-income countries, to consider maintaining the expertise and infrastructure for convalescent plasma collection. Besides, an ad hoc continuous influx and availability of therapeutic Covid-19 plasma as a safeguard and contingency for possibly urgent clinical use under the optimized therapeutic conditions known to-date (i.e. high titre and early clinical use) should be ensured. This would avoid the risk of becoming the hostage of an unethical plasma collection system put in place in case of an emergency situation [36].

Disclosure of interest

The authors declare that they have no competing interest.

The opinions expressed by the authors in this editorial do not necessarily reflect those for employers and chaired organizations.

Acknowledgements

OG is the Chairman of the European and Mediterranean Initiative in Transfusion Medicine (EMITm). TB is the Secretary of the Working Party on Global Blood Safety and a member of the working group on COVID-19 convalescent plasma of the International Society of Blood Transfusion.

References

[1] Wu T, Kang S, Peng W, Zuo C, Zhu Y, Pan L, et al. Original Hosts, clinical features, transmission routes, and vaccine development for coronavirus Disease (COVID-19). Front Med (Lausanne) 2021;8:702066.
[2] She Q, Chen B, Liu W, Li M, Zhao W, Wu J. Frailty Pathogenesis, assessment, and management in older adults with COVID-19. Front Med (Lausanne) 2021;8:694367.
[3] Farrugia A. Plasma from donors convalescent from SARS-CoV-2 infection-A matter of priorities. Transfus Clin Biol 2020;27:167–8.
[4] Garraud O, Lacombe K, Tiberghien P. A look-back at convalescent plasma to treat COVID-19. Transfus Apher Sci 2021;60:103063.
[5] Garraud O, Heshmati F, Pozzetto B, Lefrere F, Girot R, Saillol A, et al. Plasma therapy against infectious pathogens, as of yesterday, today and tomorrow. Transfus Clin Biol 2016;23:39–44.
[6] Garraud O. Passive immunotherapy with convalescent plasma against COVID-19? What about the evidence base and clinical trials? Transfus Apher Sci 2020;59:102858.
[7] Epstein J, Burnouf T. Points to consider in the preparation and transfusion of COVID-19 convalescent plasma. Vox Sang 2020;115:485–7.
[8] Al-Riyami AZ, Burnouf T, Yazer M, Triulzi D, Kumaş LT, Sağdur L, et al. ISBT Convalescent Plasma Group. International forum on the collection and use of COVID-19 convalescent plasma: protocols, challenges and lessons learned: summary. Vox Sang 2021, http://dx.doi.org/10.1111/vox.13113.
[9] Wendel S, Land K, Devine DV, Daly J, Bazin R, Tiberghien P, et al. Lessons learned in the collection of convalescent plasma during the COVID-19 pandemic. Vox Sang 2021, http://dx.doi.org/10.1111/vox.13096.
[10] Vlachogianni G, Hassapopoulou-Matamis H, Politis C, Fylaki E, Mentis A. A case of COVID-19 Convalescent plasma donation in Greece: directed donation for compassionate use in the donor's critically ill father. Transfus Clin Biol 2020;27:269–70.
[11] Vuk T, Hećimović A, Jukić I, Ravlić S, Kurtović T, Rnjak D, et al. COVID-19 convalescent plasma therapy for immunodeficient patients-weighing up risks and benefits. Transfus Clin Biol 2021 [S1246-7820(21)00083-5].
[12] Munir MA, Tandiabang PA, Setyawati T, Basry A, Cyio AD, Rahman N. Bioethical perspective of convalescent plasma therapy for COVID-19: a systematic review. Transfus Clin Biol 2021 [S1246-7820(21)00043-4].
[13] Agrawal S, Agarwal A, Jain Y. Convalescent plasma, political narrative, and public health ethics in the Covid-19 pandemic. Indian J Med Ethics 2021;VI:1–7.
[14] Tiberghien P, Toussirot E, Richard P, Morel P, Garraud O. Convalescent plasma to treat COVID-19: following the Argentinian lead. Transfus Apher Sci 2021;60:103161.
[15] Gupta T, Kannan S, Kalra B, Thakkar P. Systematic review and meta-analysis of randomised controlled trials testing the safety and efficacy of convalescent plasma in the treatment of coronavirus disease 2019 (COVID-19): evidence-base for practise and implications for research. Transfus Med 2021, http://dx.doi.org/10.1111/tme.12803.
[16] Klassen SA, Senefeld JW, Senese KA, Johnson PW, Wiggins CC, Baker SE, et al. Convalescent Plasma therapy for COVID-19: a graphical mosaic of the worldwide evidence. Front Med (Lausanne) 2021;8:684151.
[17] Senefeld JW, Klassen SA, Ford SK, Senese KA, Wiggins CC, Bostrom BC, et al. Use of convalescent plasma in COVID-19 patients with immunosuppression. Transfusion 2021, http://dx.doi.org/10.1111/trf.16525.
[18] Piechotta V, Iannizzi C, Chai KL, Valk SJ, Kimber C, Dorando E, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. Cochrane Database Syst Rev 2021;5:CD013600.
[19] Bansal N, Raturi M, Bansal Y. Covid-19 convalescent plasma therapy: analyzing the factors that led to its failure in India. Transfus Clin Biol 2021 [S1246-7820(21)00080-X].
[20] Mungmunpuntipantip R, Wiwanitkit V. COVID-19 convalescent plasma therapy and immunodeficiency. Transfus Clin Biol 2021 [S1246-7820(21)00078-1].
[21] Mahapatra S, Rattan R, Mohanty CBK. Convalescent Plasma Therapy in the management of COVID-19 patients-The newer dimensions. Transfus Clin Biol 2021 [S1246-7820(21)00070-7].
[22] Raturi M, Kusum A, Kala M, Mittal G, Sharma A, Bansal N. Locally harvested Covid-19 convalescent plasma could probably help combat the geographically determined SARS-CoV-2 viral variants. Transfus Clin Biol 2021 [S1246-7820(21)00073-2].
[23] Šemnički J, Šuperba M, Hećimović A, Kurolt IC, Kurtović T, Mačak Šafranko Ž, et al. COVID-19 convalescent plasma as long-term therapy in immunodeficient patients? Transfus Clin Biol 2021 [S1246-7820(21)00065-3].
[24] Franchini M, Glingani C, Bellani A, Cicorella N, Amadini A, De Donno G, et al. Early and persistent viral clearance in COVID-19 patients treated with convalescent plasma. Transfus Clin Biol 2021 [S1246-7820(21)00064-1].
[25] Zeng J, Yin S, Du X, Song T, Lin T. What convalescent plasma in treating severe acute respiratory infections of viral aetiology can hint for COVID-19? Evidence from a meta-analysis. Transfus Clin Biol 2021 [S1246-7820(21)00042-2}.
[26] Mahapatra S, Pati S. Constraints and challenges in convalescent plasma collection amidst the Covid 19 pandemic- strategies and recommendations to overcome these. Transfus Clin Biol 2021;28:175–9.
[27] Zhu M, Hu K, Zhu Z. Use of convalescent plasma in COVID-19 patients in China. Transfus Clin Biol 2020;27:168–9.
[28] Joyner MJ, Carter RE, Senefeld JW, Klassen SA, Mills JR, Johnson PW, et al. Convalescent plasma antibody levels and the risk of death from Covid-19. N Engl J Med 2021;384:1015–27.
[29] Klassen SA, Senefeld JW, Johnson PW, Carter RE, Wiggins CC, Shoham S, et al. The effect of convalescent plasma therapy on mortality among patients with COVID-19: systematic review and meta-analysis. Mayo Clin Proc 2021;96:1262–75.
[30] Hueso T, Pouderoux C, Péré H, Beaumont AL, Raillon LA, Ader F, et al. Convalescent plasma therapy for B-cell-depleted patients with protracted COVID-19. Blood 2020;136:2290–5.
[31] Casadevall A, Henderson JP, Joyner MJ, Pirofski LA. SARS-CoV-2 variants and convalescent plasma: reality, fallacies, and opportunities. J Clin Invest 2021;131:e148832.
[32] Epstein J, Martin Smid W, Wendel S, Somuah D, Burnouf T. Plasma-based COVID-19 treatments in low-and middle-income countries and the risk of transfusion-transmitted infections. NPJ Vaccines 2020;5:103.
[33] 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. Transfus Clin Biol 2021 [S1246-7820(21)00086-0].
[34] Bloch EM, Goel R, Wendel S, Burnouf T, Al-Riyami AZ, Ang AL, et al. Guidance for the procurement of COVID-19 convalescent plasma: differences between high- and low-middle-income countries. Vox Sang 2021;116:18–35.
[35] Epstein J, Smid WM, Wendel S, Somuah D, Burnouf T. Use of COVID-19 convalescent plasma in low- and middle-income countries: a call for ethical principles and the assurance of quality and safety. Vox Sang 2021;116:13–4.

[36] Garraud O, Farrugia A, Tissot JD. Is plasma donation ethics abused? Transfus Clin Biol 2021;28:1–2.

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