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.

Journal of Global Antimicrobial Resistance 24 (2021) 246–248

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar

Short Communication

Convalescent plasma: Alternative or promising therapy?

Fahmida Begum Mina[a,1], Mutasim Billah[b,1,*], Md. Siddikur Rahman[a], Sabuj Das[a], Sumon Karmakar[a], Uzzal Kumar Acharjee[b], Md. Faruk Hasan[a,b,*]

[a] Department of Genetic Engineering and Biotechnology, University of Rajshahi, Rajshahi 6205, Bangladesh
[b] Professor Joarder DNA & Chromosome Research Laboratory, University of Rajshahi, Rajshahi 6205, Bangladesh

ARTICLE INFO

Article history:
Received 15 May 2020
Received in revised form 5 November 2020
Accepted 11 January 2021
Available online 18 January 2021

In the context of an infectious disease epidemic for which there is neither a cure nor a vaccine, such as the recent COVID-19 (coronavirus disease 2019) pandemic, treatment with convalescent plasma, in which health professionals transfer the antibody-rich blood plasma of recently recovered patients to those critically ill, can provide humoral immunity in the short to medium term by quickly strengthening a person's passive immune system against a virus. The use of convalescent plasma dates back to the 1900s but has more recent precedents, which indicate its efficacy as a relatively effective stopgap measure against evolving viral infections. From H1N1 influenza to Ebola virus disease to the foremost predecessor of COVID-19, namely severe acute respiratory syndrome (SARS), medical practitioners have constantly switched to this specific type of passive immune therapy and documented encouraging decreases in mortality and viral load in many cases. Following the emergence of the COVID-19 pandemic, some researchers proposed convalescent plasma treatment as a possible therapeutic, as the use of plasma from patients several days or weeks after recovering from COVID-19 has the potential advantage of supplying appropriate virus-neutralising antibodies before structured therapies can be developed [1]. When a patient makes a complete recovery from COVID-19, immunoglobulin G (IgG) antibodies will maintain a memory of the disease for at least couple of months, ready to combat the infection.

Although immunoglobulin M (IgM) antibodies, the largest and first to be formed, disappear shortly after their role as the initial line of defence has been performed, IgG antibodies in all body fluids persist abundantly, ready to jump into action if the virus ever returns. Whereas convalescent serum is manufactured and distributed through a network of hospitals and securitisations, the preparation of hyperimmune globulins requires a proper manufacturing base, particularly on a commercial scale. Hyperimmune globulins have already been produced and prepared for SARS and for diseases such as cytomegalovirus, H1N1 influenza and hepatitis, and numerous plasma manufacturers are attempting to develop hyperimmune sera specific to SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), the causative agent of COVID-19, e.g. TAK-888 by Takeda and anti-COVID19 IgG by Kamada.

The goal is to identify and measure strongly neutralising antibodies, those best suited to battle the virus, and to concentrate them into a solution of clinical quality. Combined with recent clinical trials of COVID-19 patients, the data are sufficiently positive for convalescent plasma transfers, which were licensed by the US Food and Drug Administration (FDA) in the USA for emergency situations as of March 2020 [2].

Many trials use plasma from non-infected patients as the placebo arm of the study to verify that all of the observed effects are truly unique to antibodies to SARS-CoV-2. Viral release in survivors can occur for as long as 37 days, requiring screening for SARS-CoV-2 RNA in convalescent plasma donors. A Chinese randomised trial of 10 critically ill patients demonstrated that a single dose of 200 mL of convalescent plasma with neutralising antibody titres >1:640 resulted in undetectable viral load (7/10; 70%) and radiological and clinical progress [3]. Elsewhere, in another clinical trial in China, five mechanically ventilated patients (four with no underlying health conditions) with enzyme-linked immunosorbent assay (ELISA) IgG titre >1:1000 and a neutralisation titre >40 before transfusion received convalescent plasma transfusion 10–22 days after admission [4]. Acute respiratory

* Corresponding authors.
E-mail addresses: mutasimbillahshazu@gmail.com (M. Billah), faruk_geb@yahoo.com (M. F. Hasan).
[1] The two authors contributed equally to this article.

http://dx.doi.org/10.1016/j.jgar.2021.01.001

Table 1
Ongoing clinical trials of plasma-based therapies in COVID-19 (coronavirus disease 2019) listed in the International Clinical Trials Registry Platform (ICTRP) database.

Clinical trial ID no. (registry)	Intervention to prevent infection	Population size	Schedule	Status/indication	Country
ChiCTR2000030702 (ICTRP)	Arm A: convalescent plasma therapy Arm B: standard treatment	50	NA	Severe or critically ill patients	China
ChiCTR2000030046 (ICTRP)	Arm A: anti-2019-nCoV inactivated convalescent plasma	10	NA	Non-critically ill patients	China
ChiCTR2000030381 (ICTRP)	Arm A: anti-SARS-CoV-2 inactivated convalescent plasma Arm B: ordinary plasma	40	NA	Severe or critically ill patients	China
ChiCTR2000030010 (ICTRP)	Arm A: anti-SARS-CoV-2 inactivated plasmaArm B: ordinary plasma	100	NA	All patients	China
ChiCTR2000030841 (ICTRP)	Arm A: convalescent immunoglobulin Arm B: gamma globulin	10	NA	Non-critically ill patients	China
NCT04264858 (ClinicalTrials.gov)	Arm A: convalescent immunoglobulin Arm B: gamma globulin	10	NA	Non-critically ill patients	China
ChiCTR2000030039 (ICTRP)	Arm A: convalescent plasmaArm B: standard treatment	90	2 units of plasma (200–500 mL/24 h) vs. BSC	Recruiting	China
ChiCTR2000029850 (ICTRP)	Arm A: convalescent plasmaArm B: standard treatment	20	NA	Recruiting	China
ChiCTR2000030627 (ICTRP)	Arm A: convalescent plasma therapy Arm B: standard treatment	30	NA	Recruiting	China
ChiCTR2000029757 (ICTRP)	Arm A: convalescent plasma therapy Arm B: standard treatment	200	NA	All patients	China
ChiCTR2000030929 (ICTRP)	Arm A: convalescent plasma therapy Arm B: control plasma	60	NA	Not recruiting	China
ChiCTR2000030179 (ICTRP)	Arm A: plasma treatmentArm B: standard treatment	100	NA	All patients with COVID-19	China
NCT04321421 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	49	3 units of plasma (250–300 mL/48 h)	Moderate to severe ARDS under mechanical ventilation	Italy
NCT04323800 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	150	1 unit of plasma (~200–250 mL)	Exposed to the contagion (within 96 h of enrolment and 120 h of receipt of plasma)	USA
NCT04325672 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	20	1–2 units of plasma (300–600 mL/24 h)	Severe or critically ill patients	USA
NCT04333251 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	115	1–2 units of plasma (250 mL/24 h) vs. BSC	All patients with COVID-19	USA
NCT04333256 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	30	1–2 units of plasma (200–250 mL/24 h)	Critically ill patients	USA
NCT04332380 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	10	2 units of plasma (250 mL/24 h)	Non-critically ill patients	Colombia
NCT04332835 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	40	2 units of plasma (250 mL/24 h) vs. BSC	Non-critically ill patients	Colombia
NCT04327349 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	30	NA	Non-critically ill patients	Iran
NCT04333355 (ClinicalTrials.gov)	Arm A: convalescent plasma therapy Arm B: standard treatment	20	1–2 units of plasma (250 mL/24 h)	Severe or critically ill patients	Mexico

Sources: https://clinicaltrials.gov/; https://www.who.int/ictrp/en/.
NA, not available; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2 [formerly 2019 novel coronavirus (2019-nCoV)]; BSC, best supportive care; ARDS, acute respiratory distress syndrome.

distress syndrome (ARDS) resolved 12 days following plasma transfusion in four patients, and three patients were weaned from mechanical ventilation within 2 weeks of therapy. Johns Hopkins University (Baltimore, MD, USA) has been leading convalescent plasma trials in the USA for post-exposure prophylaxis and treatment of non-critically ill patients with antibody titres >1:64. There are currently 21 registered trials to investigate convalescent plasma or immunoglobulins in COVID-19 (Table 1).

In addition, a study was performed to evaluate the efficacy of convalescent plasma in COVID-19 patients. The findings showed that infusion of convalescent plasma could reduce mortality in critical patients and increase neutralising antibody titres and the absence of SARS-CoV-2 RNA in nearly all patients after treatment, as well as a decrease in clinical features. Based on the findings of this study, although the details are minimal, convalescent plasma therapy seems healthy, clinically successful and decreases mortality in COVID-19 patients [4]. Threats of established plasma transfusion include inadvertent contact with contagious pathogens, such as with any blood component, and patients with other immunodeficiencies or lung-related co-morbidities, such as transfusion-related circulatory overload (TACO) and transfusion-related acute lung injury (TRALI), who are among the most vulnerable to COVID-19, may not qualify for convalescent plasma treatment [5]. With so many lives at risk and with so few medical options, these risks may be worthwhile taking in the fight against the SARS-CoV-2 pandemic.

Funding

None.

Competing interests

None declared.

Ethical approval

Not required.

Acknowledgments

The authors express their deepest gratitude and thanks to almighty, our parents, families, teachers, and all those who helped and supported us along the way.

References

[1] Liu STH, Lin H, Baine I, Wajnberg A, Gumprecht JP, Rahman F, et al. Convalescent plasma treatment of severe COVID-19: a propensity score-matched control study. Nat Med 2020;26:1709–13, doi:http://dx.doi.org/10.1038/s41591-020-1088-9.

[2] Tanne JH. COVID-19: FDA approves use of convalescent plasma to treat critically ill patients. BMJ 2020;368:m1256, doi:http://dx.doi.org/10.1136/bmj.m1256.

[3] Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad U S A 2020;117:9490–6, doi:http://dx.doi.org/10.1073/pnas.2004168117.

[4] Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA 2020;323:1582–9, doi:http://dx.doi.org/10.1001/jama.2020.4783.

[5] Roback JD, Guarner J. Convalescent plasma to treat COVID-19: possibilities and challenges. JAMA 2020;323:1561–2, doi:http://dx.doi.org/10.1001/jama.2020.4940.