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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Short communication

A novel scoring system for selecting the target patients of COVID-19 convalescent plasma therapy: A hypothesis

Naveen Bansal a, Manish Raturi b,∗, Yashik Bansal c, Pushpendra Singh d

a Department of Transfusion Medicine, VCSG Government Institute of Medical Science and Research, Srinagar, Uttarakhand, India
b Department of Immunohematology and Blood Transfusion, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Jolly Grant, Dehradun, Uttarakhand, India
c Department of Microbiology and Immunology, VCSG Government Institute of Medical Science and Research, Srinagar, Uttarakhand, India
d Department of Forensic Medicine and Toxicology, VCSG Government Institute of Medical Science and Research, Srinagar, Uttarakhand, India

A R T I C L E   I N F O

Article history:
Available online 24 June 2021

Keywords:
COVID-19
Early convalescent plasma therapy
Scoring system
Disease severity
Cytokine storm

A B S T R A C T

The primary cause of mortality in patients of coronavirus disease 2019 (COVID-19) is the cytokine storm and not directly due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Therefore, it is being stressed by transfusion medicine specialists to use COVID-19 convalescent plasma (CCP) therapy early in the course of the disease, preferably within 72 h of diagnosis. The authors herein, propose a scoring system for the rapid assessment of the patients who have tested positive for SARS-CoV-2. Therefore, a systematic approach may be followed where the patients are categorised into two groups, namely, the low-risk group [LRG; score ≤ 5] and the high-risk group [HRG; score ≥ 5] based on this scoring system. Those classified as an HRG should be administered CCP therapy within 72 h of a confirmed diagnosis of COVID-19 to neutralise the SARS-CoV-2 virus and prevent the occurrence of the cytokine storm. This in turn could help reduce the overall mortality in the recipients.

© 2021 Société française de transfusion sanguine (SFTS). Published by Elsevier Masson SAS. All rights reserved.

1. Introduction

With the evolving understanding of coronavirus disease 2019 (COVID-19) [1], the COVID-19 convalescent plasma (CCP) therapy has emerged as an important investigational therapy being used in the management of the same [2]. It is now well established that the mortality in COVID-19 patients is due to the SARS-CoV-2 virus-induced cytokine storm and systemic inflammatory response syndrome and not directly due to the SARS-CoV-2 virus [3]. The autopsy findings in patients with COVID-19 have confirmed the presence of cytokine release syndrome (CRS) characterized by hypercytokinemia and multi-organ damage [4]. Furthermore, there is a window of opportunity of few days between the entry of SARS-CoV-2 inside the body and the development of CRS [5]. Therefore, early CCP therapy can result in SARS-CoV-2 neutralisation and prevent the occurrence of cytokine storm [6]. However, practically it has been observed that clinicians have been using CCP even in

severe COVID-19 patients as a compassionate therapy and in whom the CRS has already occurred. Therefore, it is highly unlikely that CCP will be effective in such cases [7]. The authors have conceptualised a novel scoring system for identifying the high-risk patients who are likely to develop severe COVID-19 and remain ideal candidates for early CCP therapy. However, even before the authors could test the hypothesis, the CCP therapy was dropped from the treatment protocol for COVID-19 patients in India largely due to the unscientific and indiscriminate use of CCP in the country [8].

2. Proposing the hypothesis

The authors herein propose a novel Rapid CCP [RCCP] scoring system for the early assessment of patients who have tested positive for SARS-CoV-2. The scoring system has a total of twelve parameters and can be used to identify those who are at a high risk of developing severe COVID-19 infection (Table 1). The parameters selected are based on the conditions which have been found to have a significant co-relation of developing severe COVID-19 infection based on the published research [9–15]. Therefore, a systematic approach may be followed and the patients can be categorised into two groups, namely, the low-risk group [LRG; score ≤ 5] and the high-risk group [HRG; score ≥ 5] based on this scoring system.

https://doi.org/10.1016/j.traci.2021.06.004
1246-7820/© 2021 Société française de transfusion sanguine (SFTS). Published by Elsevier Masson SAS. All rights reserved.
Table 1
Rapid COVID-19 convalescent plasma therapy (RCCP) scoring system.

| Parameter                                                                 | Score          |
|---------------------------------------------------------------------------|----------------|
|                                                                           | 0              |
|                                                                           | 1              |
| Age                                                                       | <60 years      | ≥60 years     |
| Core body temperature > 37°C                                              | No             | Yes           |
| Cough                                                                     | No             | Yes           |
| Smoking history                                                           | No             | Yes           |
| Hypertension                                                              | No             | Yes           |
| Diabetes                                                                  | No             | Yes           |
| Cardiovascular disease                                                    | No             | Yes           |
| Hematological and/or non-hematological malignancies                       | No             | Yes           |
| Chronic liver diseases                                                    | No             | Yes           |
| Chronic renal diseases                                                    | No             | Yes           |
| Breathlessness                                                            | No             | Yes           |
| Oxygen saturation                                                        | > 94%          | ≤ 94%         |

Total score
Score 0–4: No intervention [Baseline standard care & hospital management]
Score ≥5: Early convalescent plasma therapy preferably within 72 h

![Diagram of CCP therapy using RCCP scoring system](image)

**Fig. 1.** CCP therapy using RCCP scoring system (CCP: COVID-19 convalescent plasma; RCCP: Rapid COVID-19 convalescent plasma therapy; LRG: Low-risk group; HRG: High-risk group).

(Fig. 1). Those classified as an HRG should be administered CCP therapy within 72 h of a confirmed diagnosis of COVID-19 to neutralise the SARS-CoV-2 virus and prevent the occurrence of the CRS. This in turn could help reduce the overall mortality in the recipients.

3. Support for the hypothesis

CCP therapy as an experimental treatment is being used as early as January 2020 [16]. Initial studies gave conflicting results about its safety and efficacy in the treatment of COVID-19. The majority of this data was either case reports or institutional experiences [17–19]. In fact, the PLACID trial [a multi centre clinical trial] from India concluded that the CCP was successfully able to neutralise the SARS-CoV-2 virus, however, it did not result in a decreased patient mortality [20]. This result could be explained by the fact that the primary cause of mortality in patients of COVID-19 is a SARS-CoV-2 virus-induced cytokine storm and not the SARS-CoV-2 virus itself. The most probable reason for the ineffectiveness of CCP therapy in reducing the patient mortality could be attributed to the transfusion of CCP in patients who had already developed severe COVID-19 symptoms compounded with a CRS. Moreover, the convalescent plasma contains non-neutralising antibodies which can assist the virus to gain entry into the macrophages. The virus undergoes rapid proliferation in the macrophages, establishing a pro-inflammatory environment, resulting in the aggravation of the cytokine storm [21]. This was observed in a case report wherein, the use of the convalescent plasma therapy in a patient with Ebola virus disease resulted in acute respiratory distress syndrome (ARDS) [22]. Therefore, in patients having severe COVID-19 infection, where cytokine storm has already occurred, the use of the CCP therapy is not only unjustified rather it merits a clinical reconsideration.

If the CCP therapy is given within the first few days of the diagnosis, the passive IgG anti-SARS-CoV-2 antibodies can neutralise the virus and prevent the occurrence of this CRS in the patients. Early treatment with CCP had resulted in a better outcome in patients having severe symptoms during the 2002–04 SARS epidemic [23,24]. In a recent study, early administration of convalescent plasma (i.e. within 72 h of the onset of mild COVID-19
4. Conclusion

CCP therapy must be used judiciously in a specific patient population where it is likely to be effective. The HRG patients can be identified by using the proposed RCP-CCP scoring system which could be easily utilised in hospital settings and or screening centres. Multicentre prospective interventional studies need to be done to be able to understand the effectiveness of CCP therapy in reducing the mortality rate when administered within the first 72 h of diagnosis especially in those susceptible to develop severe COVID-19 infection.

Author contributions

| S.No. | Category of contribution | Author 1 | Author 2 | Author 3 | Author 4 |
|-------|--------------------------|---------|---------|---------|---------|
| 1.    | Conceptual design        | Yes     | No      | No      | No      |
| 2.    | Literature search        | Yes     | Yes     | Yes     | No      |
| 3.    | Data compilation         | Yes     | Yes     | Yes     | Yes     |
| 4.    | Manuscript preparation and editing | Yes | Yes | Yes | Yes |
| 5.    | Manuscript review and final approval | Yes | Yes | Yes | Yes |
| 6.    | Final guarantor of the entire manuscript | No | No | No | No |

Source of funding

None.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Raturi M, Kala M, Das K, Kusum A. Reviewing the ethical concerns of the convalescent plasma therapy in COVID-19. J Lab Phys 2021;13:91–4.
[2] Garraud O, Lacombe K, Tiberghien P. A look-back at convalescent plasma to treat COVID-19. Transfus Apher Sci 2021;60:103063, http://dx.doi.org/10.1016/j.transci.2021.103063.
[3] Melo Silva Júnior ML, Souza LMA, Dutra REMC, Valente RGM, Melo TS. Review on therapeutic targets for COVID-19: insights from cytokine storm. Postgrad Med J 2020, http://dx.doi.org/10.1136/postgradmedj-2020-138791, postgradmedj-2020-138791 [published online ahead of print, 2020 Oct 2].
[4] Núñez-Torráon C, Ferrer-Gómez A, Moreno Moreno E, et al. Secondary haemophagocytic lymphohistiocytosis in COVID-19: correlation of the autopsy findings of bone marrow haemophagocytosis with HScore. J Clin Pathol 2021, http://dx.doi.org/10.1136/jclinpath-2020-207337, jclinpath-2020-207337 [published online ahead of print, 2021 Mar 15].
[5] Sun X, Wang T, Cai D, et al. Cytokine storm intervention in the early stages of COVID-19 with convalescent plasma. Front Vet Res 2020;5:38–42, http://dx.doi.org/10.3389/fvets.2020.00002.
[6] Tiberghien P, Toussiot E, Richard P, Morel P, Garraud O. Commentary: Convalescent plasma to treat COVID-19: following the Argentinian lead. Transfus Apher Sci 2021;103:161, http://dx.doi.org/10.1016/j.transci.2021.103161 [published online ahead of print, 2021 May 23].
[7] Katz LM. (A Little) Clarity on convalescent plasma for Covid-19. N Engl J Med 2021;384:666–8, http://dx.doi.org/10.1056/NEJM20210526.
[8] Bansal N, Raturi M, Bansal Y. Covid-19 convalescent plasma therapy: analyzing factors that led to its failure in India. Transfus Clin Biol 2021, http://dx.doi.org/10.1016/j.trac.2021.05.009, S1246-7820(21)00008-X [published online ahead of print, 2021 June 9].
[9] Motta LP, Silva PPF, Borgezau BM, et al. An emergency system for monitoring pulse oximetry, peak expiratory flow, and body temperature of patients with COVID-19 at home: Development and preliminary application. PLoS One 2021;16, http://dx.doi.org/10.1371/journal.pone.0247635, e0247635, Published 2021 Mar 26.
[10] Du RH, Liang LR, Yang CQ, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J 2020;55:200024, http://dx.doi.org/10.1183/13993003.00524-2020, Published 2020 May 7 [published correction appears in Eur Respir J 2020;56(3)].
[11] de Almeida-Pittito B, Dualith PM, Zajdender L, et al. Severity and mortality of COVID-19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. Diabetol Metab Syndr 2020;12, http://dx.doi.org/10.1186/s13098-020-00586-4, Published 2020 Aug 31.
[12] Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. J Am Med Dir Assoc 2020;21:915–8, http://dx.doi.org/10.1016/j.jamdd.2020.05.045.
[13] Hosseinzadeh R, Goharzadeh MAB, Bahardoust M, et al. Should all patients with hypertension be worried about developing severe coronavirus disease 2019 (COVID-19)? Clin Hypertens 2021;27:3, http://dx.doi.org/10.1111/cih.12085-021-00161-7, Published 2021 Jan 15.
[14] Xue J, Cassovius N, Fan Z, et al. Association between hypoxemia and mortality in patients with COVID-19. Mayo Clin Proc 2020;95:1138–47, http://dx.doi.org/10.1016/j.mayocp.2020.04.006.
[15] Gütken A, Yigitbas BA, Uslu B, Dörmann D, Kiloni O. The effect of smoking on COVID-19 symptom severity: systematic review and meta-analysis. Pulm Med 2020;2020, http://dx.doi.org/10.1155/2020/7590207, 7590207, Published 2020 Sep 8.
[16] Shen C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA 2020;323:1582–9, http://dx.doi.org/10.1001/jama.2020.4783.
[17] Zeng QL, Yu ZJ, Gou JJ, et al. Effect of convalescent plasma therapy on viral shedding and survival in patients with coronavirus disease 2019. J Infect Dis 2020;222:38–43, http://dx.doi.org/10.1093/infdis/jiaa228.
[18] Ye M, Fu D, Ren Y, et al. Treatment with convalescent plasma for COVID-19 patients in Wuhan, China. J Med Virol 2020;92:1890–901, http://dx.doi.org/10.1002/jmv.25982.
[19] Zhang L, Pang R, Xue X, Bao J, Ye S, Dai Y, et al. Anti SARS-CoV-2 virus antibody levels in convalescent plasma of six donors who have recovered from COVID-19. Aging (Albany NY) 2020;12:6536–42, http://dx.doi.org/10.18632/aging.103102.
[20] Agarwal A, Mukherjee A, Kumar G, et al. Convalescent plasma in the management of moderate COVID-19 in adults in India: open label phase II multicenter randomised controlled trial (PLACID Trial). BMJ 2020;371, http://dx.doi.org/10.1136/bmj.m3939, m3939. Published 2020 Oct 22 [published correction appears in BMJ 2020;371:i4322].
[21] 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.
[22] Mora-Rillo M, Arsuaga M, Ramírez-Olivescia 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.
[23] Cheng Y, Wong R, Soo YOV, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. Eur J Clin Microbiol Infect Dis 2005;24:44–6, http://dx.doi.org/10.1007/s10026-004-0127-9.
[24] Soo YO, Cheng Y, Wong R, et al. Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients. Clin Microbiol Infect 2004;10:676–8, http://dx.doi.org/10.1111/j.1469-0691.2004.00956.x.
[25] Libster R, Pérez Marc G, Wappner D, et al. Early high-titer plasma therapy to prevent severe covid-19 in older adults. N Engl J Med 2021;384:610–8, http://dx.doi.org/10.1056/NEJMoa2033700.
[26] Hegerova L, Gooley TA, Sweerus KA, et al. Use of convalescent plasma in hospitalized patients with COVID-19 case series. Blood 2020;136:759–62, http://dx.doi.org/10.1182/blood.2020006564.