

## ■ Review Article

# The Convalescent Serum for Treatment of COVID-19 Infection: Review

Sadeq Kadhim Hachim<sup>1\*</sup> 

<sup>1</sup> Ministry of Higher Education, Middle Technical University, Iraq

\* Corresponding author: Sadeq Kadhim Hachim E-mail: [sadeq.kadhim2016@yahoo.com](mailto:sadeq.kadhim2016@yahoo.com) ORCID: 0000-0001-6469-7669

Received: 18 April 2020 Accepted: 21 April 2020

## ABSTRACT

In the early of 2020, people are challenging a pandemic in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 causes coronavirus disease, abbreviated as COVID-19. At the time of this writing, SARS-CoV-2 is spreading in multiple countries worldwide. There are above two million cases in different region of world. This virus appears to be a new human pathogen. Currently there are no vaccines, monoclonal antibodies (mAbs), or drugs available for SARS-CoV-2, though many are in rapid development and some may be accessible in a short time. This aim of this review that human convalescent serum is an option for stoppage and treatment of COVID-19 disease. Explain main advantage of convalescent serum, in addition to disadvantage of this method.

**Keywords:** COVID-19, convalescent serum, treatment, antibody

## INTRODUCTION

The pneumonia related with severe acute respiratory syndrome coronavirus 2(SARS-COV-2) which then named as Coronavirus disease 2019 (COVID-19) by World Health Organization (WHO), appeared in Wuhan, China since December 2019 [1]. The corona virus 2019 spread rapidly in different region of World in 3 months was categorized as pandemic by WHO on March 11, 2020. By way of March 12, 2020, an overall of 80,980 confirmed cases and 3,137 deaths had been stated in China. The total of 44,377 definite cases and 1,446 deaths was informed in another 108 countries or regions, however the total number of cases reported in different region of World reach to over 2,000,000 cases. There is no official specific antiviral drug against the novel virus, however some antiviral drugs still under investigation as remdesivir and lopinavir in addition to antimalarial drug

(chloroquine) also was suggested. Convalescent plasma (CP) therapy, a classic adaptive immunotherapy, has been useful.

To the prevention and treatment of numerous infectious diseases for over than one century. The CP treatment was used in the past two decades as in treatment of SARS, MERS, in addition to 2009 H1N1 pandemic with satisfactory efficacy and safety [2,3]. The result from study on SARS coronavirus infection in addition to sever influenza virus explained a statistically significant decrease in the in the pooled odds of death after CP therapy, when compared with placebo and no therapy (odd ratio, 0.25; 95% CI) [4]. Conversely, the CP therapy was incapable to significantly improve the period of survival for the Ebola virus diseases, possibly because of the absence of information and data about neutralizing antibody level for stratified examination [5]. The Middle East Respiratory Syndrome (MERS) and COVID-19 was shared

virological and clinical feature [6], so the CP therapy might be favorable treatment option for COVID-19 save [7]. Patients who have improved from COVID-19 with elevated level of neutralized antibody titer may be an appreciated donor source of CP. However, the prospective clinical benefit and danger of convalescent blood component in COVID-19 remain uncertain. Therefore, the aim of this mini review is to concern on role of CP in treatment of COVID-19 patients and advantage or disadvantage of this method.

### **SELECTION OF DONOR**

The donors must be recovered from SARS-CoV-19 infection to request for donation. The donor must be written informed consent. The donor must be previously diagnosed with COVID-19 and successively laboratory test is negative for COVID-19 in addition to other respiratory virus, as well as for Hepatitis B virus, Hepatitis C virus, HIV, and syphilis at period of blood donation. The donor must be asymptomatic for at least 10 days, with serum SARS-COV-19 specific ELISA antibody level more than 1:1000 and a neutralizing antibody titer above than 40. The amount of serum approximately 400 ml of convalescent plasma was obtained by apheresis, then plasma must be immediately transfused to the recipient on the same day was taken [8].

### **PLASMA PREPARATION PROCEDURE AND QUALITY CONTROL**

Apheresis must be performed by using cell separator (Baxter Cs 300). A 200-400 ml ABO compatible plasma sample harvested from donor depending on age and body weight, then plasma samples divided and stored as 200 ml aliquots at 4°C devoid of detergent or heat treatment. The CP was then treated with methylene blue and light treatment for 30 minutes by using virus inactivation cabinet.

### **EXPERIMENT ON USE OF CONVALESCENT PLASMA TO TREAT COVID-19**

Viral load dropped within days of treatment with CP, and the clinical conditions of these patients treated by plasma will be better, this indicated by lowering of body temperature, improving of  $PAO_2/FIO_2$ , in addition to chest imaging. The largest study included the treatment of 80 patients with SARS in Hong Kong [9]. Patients treated before day 14 had enhanced prognosis distinct by discharge from hospital before day 22, reliable with the concept that earlier administration is more likely to be active [9]. Additionally, those who were PCR positive and seronegative for coronavirus at the interval of therapy had better prognosis [9]. There is also some circumstantial evidence on the use of

convalescent serum in extremely ill individuals. Three patients with SARS in Taiwan were treated with 500 mL CP, resultant in a decrease in serum virus titer, and each survived [10]. Three patients with MERS in South Korea were treated with CP, but then only two of the recipients had neutralizing antibody in their serum [11]. The latter study places of interest a challenge in using convalescent sera, namely, that some who recover from viral disease may not have high titers of neutralizing antibody [12]. Constant with this point, an analysis of 99 samples of convalescent sera from patients with SARS indicated that 87 had neutralizing antibody, with a geometric mean titer of 1:61 [13]. This submits that antibody declines with time and/or that few patients make high-titer comebacks. It is also potential that non-neutralizing antibodies are produced that contribute to shelter and recovery, as described for other viral diseases [14-16].

In the recent study, SARS-CoV-2 was remain detectable in all 5 patients in spite of antiviral treatment have been introduced for about 10 days, even though viral titer lowered and became unnoticeable soon after CP treatment which determined by ELISA. The plasma from the donors had high titer of IgM and IgG titer [8].

The neutralizing antibody titers of 5 patients elevated and four patients stay at the same equal level after CP transfusion. SARS-COV-19 RNA, measured by RT-PCR, which positive in 7 patients and negative in three patients on next 3 days, in addition to one patient on day followed CP therapy. These data are in support of neutralizing consequence of CP on serum SARS-COV19 [17]. The study by Arturo and Liiseanne The convalescent serum is an selection for prevention and treatment of COVID-19 disease that could be speedily available when there are enough numbers of persons who have recovered and can donate the serum which contain on immunoglobulin [18].

### **BENEFIT AND RISK**

The advantage of convalescent serum administration is that it can protect from infection and subsequent disease in individuals who are at high risk for disease, such as vulnerable individuals with underlying medical circumstances, health care suppliers, and those with exposure to confirmed cases of COVID-19. Passive antibody administration to prevent disease is previously used in clinical practice. Based on the historical familiarity with antibody administration, it can be predicted that antibody administration would be more active in preventing disease than in the treatment of well-known disease [19].

Risks of passive direction of convalescent sera fall into two classifications, known and theoretical. Well-known risks are those related with transfer of blood constituents, which contain accidental infection with another infectious disease agent and reactions to serum constituents component, including immunological reactions such as serum sickness. With current blood banking techniques that monitor for blood-borne pathogens and match the blood type of donors and recipients, the danger of unintentionally transferring known infectious agents or initiating transfusion reactions are low. Nevertheless, convalescent sera used in a therapeutic method would likely be directed to individuals with pulmonary disease, in whom plasma infusion carries some risk for transfusion-related acute lung injury (TRALI) [19].

## CONCLUSION

Convalescent plasma transfusion may be cooperative in the treatment of critically infected patients with COVID-19, in addition this sera can be easily obtained and prepared in adequate amount especially when there is wide spread of pandemic in some region of world. The convalescent plasma can give us promise as a method for treatment of COVID-19 until effective antiviral drugs and vaccine are discovered.

## DECLARATION OF CONFLICT OF INTEREST

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

## REFERENCES

1. Zhou P, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020; 579: 270-3.
2. Chen N, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *Lancet* 2020; 395: 507-13.
3. World Health Organization, Coronavirus disease (COVID-19) Pandemic. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019> (Accessed 11 March 2020).
4. Mair-Jenkins J, et al. Convalescent Plasma Study Group, The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: A systematic review and exploratory metanalysis. *J. Infect. Dis* 2015; 211: 80-90.
5. van Griensven J, et al. Ebola-Tx Consortium, Evaluation of convalescent plasma for Ebola virus disease in Guinea. *N. Engl. Med.* 2016; 347: 33-42.
6. Lee PI, Hsueh PR. Emerging threats from zoonotic coronaviruses-from SARS and MERS to 2019-nCoV. *J. Microbiol. Immunol. Infect.*, in press 2020.
7. Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect. Dis.* 2020; 20: 398-400.
8. Shen C, Wang Z, Zhao F, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. *American Medical association*; March 27: 2020.
9. Cheng Y, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur J Clin Microbiol Infect Dis.* 2005; 24(1): 44-6.
10. Yeh KM, et al. Experience of using convalescent plasma for severe acute respiratory syndrome among healthcare workers in a Taiwan hospital. *J Antimicrob Chemother.* 2005; 56(5): 919-22.
11. Ko JH, et al. Challenges of convalescent plasma infusion therapy in Middle East respiratory coronavirus infection: a single centre experience. *Antivir Ther (Lond).* 2018; 23(7): 617-22.
12. Arabi YM, et al. Feasibility of using convalescent plasma immunotherapy for MERS-CoV infection, Saudi Arabia. *Emerging Infect Dis.* 2016; 22(9): 1554-61.
13. Zhang JS, et al. A serological survey on neutralizing antibody titer of SARS convalescent sera. *J Med Virol.* 2005; 77(2): 147-50.
14. van Erp EA, Luytjes W, Ferwerda G, van Kasteren PB. Fc-mediated antibody effector functions during respiratory syncytial virus infection and disease. *Front Immunol.* 2019; 10: 548.
15. Jenks JA, Goodwin ML, Permar SR. The roles of host and viral antibody Fc receptors in herpes simplex virus (HSV) and human cytomegalovirus (HCMV) infections and immunity. *Front Immunol.* 2019; 10: 2110.
16. Gunn BM, et al. A role for Fc function in therapeutic monoclonal antibody-mediated protection against ebola virus. *Cell Host Microbe.* 2018; 24(2): 221-233.e5.
17. Duana K, Liuc B, Lid C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19. *PNAS* 2020: 1-7.

18. Casadevall A, Pirofski L-A. The convalescent sera option for containing COVID-19. *J Clin Invest.* 2020; 130(4): 1545-8.
19. Luke TC, Casadevall A, Watowich SJ, Hoffman SL, Beigel JH, Burgess TH. Hark back: passive immunotherapy for influenza and other serious infections. *Crit Care Med.* 2010; 38(4 suppl): e66-e73.

