

## COVID 19 – CONVALESCENT PLASMA AS A OPTIONAL TREATMENT

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### ABSTRACT

The 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new public health crises threatening the earth with the emergence. The virus originated in bats and was transmitted to humans through yet unknown intermediary animals in Wuhan, China in December 2019. No drugs are currently approved for Coronavirus Disease-2019 (COVID-19), although some are tried. This review focuses on convalescent plasma treatment to treat COVID -19. Plasma provided by COVID-19 convalescent patients may provide therapeutic relief because the number COVID-19 cases escalate steeply world-wide. The respiratory

diseases including SARS-CoV related pneumonia suggest that convalescent plasma can reduce mortality.

**KEYWORDS:** *Convalescent plasma, COVID-19, Antibody.*

### INTRODUCTION

The pneumonia induced by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is known as coronavirus disease 2019 (COVID-19).<sup>[1]</sup> Researchers first isolated a coronavirus in 1937. They found a coronavirus responsible for an infectious bronchitis virus in birds that had the power to devastate poultry stocks. The name “corona virus” is due to the crown-like projections on their surfaces.<sup>[2]</sup> In Latin “Corona” means “halo” or “crown.” Coronaviruses are enveloped single-stranded RNA viruses.<sup>[3]</sup> Coronaviruses belong to the subfamily Coronavirinae within the family Coronaviridae.

The number of cases and associated mortality has increased dramatically since the primary cases in Wuhan, China in December 2019.<sup>[4]</sup> As of April 29th, this virus had affected about

3,146,200 people worldwide and caused 218,139 deaths and 961,785 were recovered. In India, at the same date, roughly 31,332 cases were reported with 1,008 deaths and 7,747 recovered.<sup>[5]</sup> The patients appear respiratory symptoms, cough, and fever, shortness of breath and breathing difficulties. In additional severe cases, infection can cause pneumonia, severe acute respiratory syndrome, renal disorder and even death. A novel coronavirus (nCoV) is a new strain that has not been previously identified in humans and is transmitted mostly via droplets or contact. People of all ages are vulnerable to the virus.<sup>[6]</sup>

To date, no specific treatment has been confirmed to be effective for SARS-CoV-2 contamination.<sup>[7]</sup> Apart from supportive care, along with oxygen deliver in mild cases and extracorporeal membrane oxygenation for the critically ill sufferers, specific drugs for this disorder are still being researched.<sup>[8]</sup> Many drugs are tried recently within the treatment for COVID-19 that includes a low-cost antimalarial drug chloroquine and its derivative hydroxychloroquine (HCQ), together with several other antiviral drugs. Now a convalescent plasma therapy treatment enters clinical practice with serious COVID-19 patients. Even it is reported that after infusion the plasma patient's clinical signs and symptoms were improved significantly.<sup>[9]</sup>

### **Convalescent plasma therapy**

The convalescent plasma therapy is an age-old technique getting used for handling infections and was also used during the Ebola outbreak. The thought behind this therapy is that immunity is typically transferred from a healthy person to sick using convalescent plasma. Convalescent plasma refers to plasma from recovered patients. So during this therapy, blood is drawn from an individual who has recovered from the disease then the serum is separated and screened for virus-neutralising antibodies. The method for donating plasma is analogous to donating blood and takes about an hour. The method used to recover antibodies from patients had already been approved for treatment of other infectious diseases. If someone is immunodeficient and thus cannot mount an efficient immunologic response then this kind of therapy is particularly used.<sup>[10]</sup>

After the antibody serum is given, it will stay on the recipient for minimum three to four days. During that time, the diseased person will recover. If the convalescent donor has only recently recovered their plasma contains high levels of neutralising antibodies for whatever pathogen they were exposed to, so when convalescent plasma is transfused into another patient it provides an instant immunological response.<sup>[11]</sup>

Whenever a new viral outbreak takes places, there are not any drugs to treat it. Therefore, the use of convalescent serum therapy has been used during past viral epidemics. During the outbreak of 2009–2010 H1N1 influenza virus pandemic, patients with an infection requiring medical aid were used. After the treatment of passive antibody, the serum-treated person showed clinical improvement. The viral burden reduced, and thus the death rate might be lowered. The procedure was also useful during the Ebola outbreak in 2018.<sup>[12]</sup>

### **Convalescent plasma to treat viral diseases**

In terms of treatment, COVID-19 patients with mild symptoms received oseltamivir or intravenous antibiotics, while severe patients also received oxygen inhalation, mechanical ventilation. The corona virus is a new emerging virus that has not been previously identified in humans; there is no a specific drug or vaccine. Plasma from recovery patients containing corona virus specific antibodies was considered as a feasible therapeutic option. When antiviral drugs were not effective, convalescent plasma has been used as a valid option in treatment with some several infectious diseases, like (severe acute respiratory syndrome) SARS, (influenza A/H5N1) A/H5N1 flu, Ebola, etc.<sup>[13]</sup>

But the efficacy of convalescent plasma treatment for severe infectious diseases remains controversial. A meta analysis of the effectiveness of convalescent plasma therapy for SARS showed that the first treatment with plasma might be beneficial.<sup>[14]</sup> Besides, a complete of 84 Ebola virus disease patients who were treated with convalescent plasma showed no significant improvement in survival. After clinical evaluation of convalescent plasma for Ebola virus disease in Guinea, the dose of neutralizing antibodies within the donations was low and that there was no apparent association between the dose of neutralizing antibodies and human survival was shown in van Griensven, et al.<sup>[15]</sup>

Furthermore, other research showed that the convalescent plasma specimens from survivors of Ebola virus infection showed low neutralizing activity against Ebola virus.<sup>[16]</sup> This may explain why the plasma treatment for Ebola infected patients is not effective. A case report that an influenza A (H5N1) virus infected male after received convalescent plasma from a patient who had recovered from H5N1 infection, the patient's viral load was reduced during the first 8 hours and was undetectable within 32 hours.<sup>[17]</sup> Additionally with double blind, randomized, placebo controlled trials, influenza A infected adults were randomly assigned to receive standard care plus either convalescent plasma infusion or saline placebo, but when administered alongside standard care plasma treatment was not superior to placebo for adults

hospitalized with influenza A infection.<sup>[18,19]</sup> To sum up, there are still some issues to consider for the effectiveness of plasma therapy. For example, screen out potential donors with high neutralizing antibody titres; the curative rates in plasma treatment trials are going to be influenced not only by patients' risk factors but also by the specific supportive care offered by clinical hospitals.

### **Convalescent plasma to treat COVID-19 infected patients**

When people fight with the COVID-19 virus, they produce antibodies that attack the virus. Those antibodies, proteins that are secreted by immune cells known as B lymphocytes, are found in plasma, or the liquid part of blood that helps the blood to clot when needed and supports immunity. Once an individual had the virus and recovered, that person has developed antibodies that will stay in their blood waiting to fight the same virus. Those antibodies, when injected into another person with the disease, recognize the virus as something to attack.

Convalescent donors may be identified through various means and are eligible for plasma donation should be invited to undergo plasma apheresis, pending general eligibility such as an age, weight, Good health and feeling well, Have a previous diagnosis of COVID-19 and meet specific laboratory criteria, Must be symptom-free for at least 14 days prior to donation. The plasma collection not earlier than 14 to 28 days after symptoms resolved.

In particular, the quality of collected plasma could also be adapted to gender, height and weight. A mean of approximately 600 ml of plasma may undergo pathogen reduction treatment.<sup>[20]</sup> One person donation of plasma can produce two doses of the material needed for transfusions. Donors will therefore be eligible for standard blood donation. This consideration may result in questioning additional safety measures such as verifying the absence of viral RNA and pathogen reduction if not performed usually on blood products.<sup>[21]</sup> Once treated and qualified, plasma should be cryopreserved (in 200 to 250 ml units) and made available for clinical use.

### **Plasma collection in COVID-19 convalescent patients**

By using quantitative reverse transcriptase–polymerase chain reaction (qRT-PCR) (GeneoDX Co, Ltd) the laboratory confirmed COVID-19 Patients diagnosed<sup>[22]</sup>, if they fulfilled the following criteria then they was eligible to receive convalescent plasma treatment.

1. They had severe pneumonia with rapid progression and continuously high viral load despite antiviral treatment; 2. PAO<sub>2</sub> measured in mmHg and FIO<sub>2</sub> measured as fraction of inspired oxygen<sup>[23]</sup> and 3. They had been supported with mechanical ventilation.

The serum of each recipient was obtained. The one day prior to the convalescent plasma transfusion enzyme-linked immunosorbent assay (ELISA) and neutralizing antibody titers were tested. The ABO blood types of the patients were determined for Potential compatibility with the convalescent plasma donor. Each received two consecutive transfusions of 200to250mL of ABO-compatible convalescent plasma (400mL of convalescent plasma in total) on the same day it was obtained from the donor. Until the SARS-CoV-2 viral loads became negative patients received antiviral agents continuously.<sup>[24]</sup>

The age of donor who donates convalescent plasma is between the age of 18 and 60 years. The donors must be recovered from SARSCoV-2 infection and were invited to donate their convalescent plasma after written informed consent was obtained. All donors had been previously diagnosed with laboratory confirmed COVID-19 and subsequently tested negative for SARS-CoV-2 and other respiratory viruses, such as for hepatitis B virus, hepatitis C virus, HIV, and syphilis at the time of blood donation. The donors had been well for at least 10 days, with a serum SARS-CoV-2– specific ELISA antibody titer higher than 1:1000 and a neutralizing antibody titer greater than 40.<sup>[25]</sup> The 400 mL of convalescent plasma was obtained from each donor by apheresis, and on the same day plasma was immediately transfused to the recipients.

## CONCLUSION

This new virus outbreak has challenged the economic, medical and public health infrastructure of many countries. COVID-19 requires urgent development of successful curative treatment. Many treatment regimens have been explored in the treatment of COVID-19. Some of these treatments may have been tried out of desperation, and among these, some show initial promise. Convalescent plasma may be one of them. Although Convalescent plasma therapy is beneficial in absence of any other valid treatment, we believe that such treatment could be useful in the current context of pandemic COVID-19 outbreak. Administration of convalescent plasma containing neutralizing antibody was followed by improvement in the patients' clinical status. Until definitive and effective treatments are found this treatment appears to be helpful within the short term.

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