



## Review Article

## To which extent a convalescent plasma therapy could be a benefit for COVID-19 patients?

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### Abstract

The emergence of an unprecedented pandemic SARS-CoV-2 caused perplexed in the medical community because of a high infection rate and rising mortality among COVID-19 patients. Till now, there is no particular treatment for the disease; nevertheless, there is an extensive effort from scientists to find out an immediate therapeutic plan to show how to deal with the current situation. One of the solutions currently presented is Convalescence plasma (CP). Through this narrative review, we will shed light on CP's efficiency as a therapeutic agent for COVID-19, especially there is no proven vaccine or antiviral available up to date. CP could be considered one of the therapeutic approaches, but some limitations are still considered before it is established as a therapeutic agent. Along with evaluating CP from blood donors, the plasma companies could take future steps by manufacturing a target dose of globulins that contain standardized antibody, to reach the terms of health setting administering therapy.

**Keywords:** Convalescence plasma, COVID-19, Transfusion, Neutralizing Antibodies, Sudan

### Background

In the time of COVID-19, where coronavirus disease has spread Severe respiratory distress symptoms caused by SARS-CoV-2 are considered a newly emerged beta coronavirus responsible for COVID-19. It was first reported in Wuhan, China, in December 2019, when around 81 767 cases with 3281 deaths have been recorded [1]. Later in March, the WHO proclaimed COVID-19 a pandemic disease when it appeared in approximately 195 countries [2]. The mechanism of the pathogenesis of COVID-19 infection has not been fully clarified [3]. There is no proven vaccine or therapy for COVID-19 until now. The disease's clinical management protocol recommended by WHO focuses on infection prevention, monitoring, and detection [4]. Despite the continued lack of accuracy and transparency about the COVID-19, scientists are still trying to figure out ideal strategies to develop a treatment for COVID-19. One of the promising strategies is Convalescent Plasma Therapy (CPT). Up to date, using CPT for COVID-9 patients has been demonstrated in multiple studies to reduce the mortality rate in this unprecedented pandemic situation. The investigators in these studies relied on the fact that the CPT is

not a new technique, its efficacy and safety had already been tested in other causative agents similar to SARS-CoV-2, despite the presence of a few difference between SARS-CoV-2 and other types of coronavirus, but the mechanism of CP could be the same. [5,6,7]. The issue of using the convalescent plasma has grown in importance in light of pandemic COVID-19, especially in the absence of availability of vaccine or other treatment, so in the current review, we will attempts to discuss the desired benefits and some limitation of CPT.

### Previous utilization of convalescent plasma

Convalescent plasma (CP) therapy is known for a long time and was used for many viral and bacterial diseases. Previously CP used to treat patients with various viral infections, such as treating the Spanish flu in 1918, H1N1 infection in 2009, Ebola patients in 2014, and Middle East Respiratory Syndrome (MERS) in 2015 [8,9,10]. Thereby, CP was suggested as one of the therapeutic options for COVID-19 patients [11].

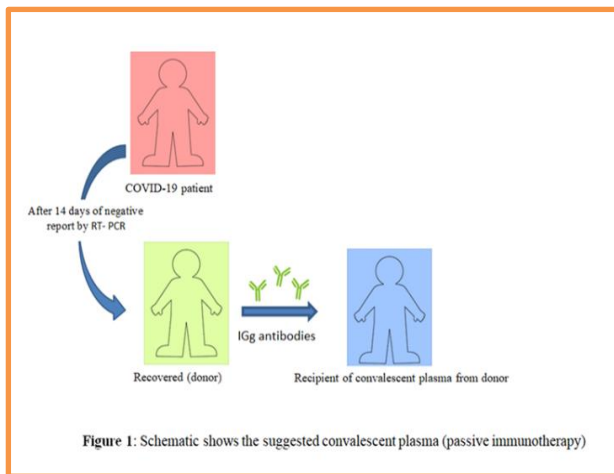
The CPT mechanism is based on plasma transfusion from recovered individuals (Who are harmful to COVID-19) to patients with COVID-19 [12,13]. This transfusion is considered as a type of passive immunity, whereas the plasma transfused from patients recovered to patients exposed to the same virus (the plasma contains a Neutralizing Antibodies (NABs)) (Figure 1) [14,15].

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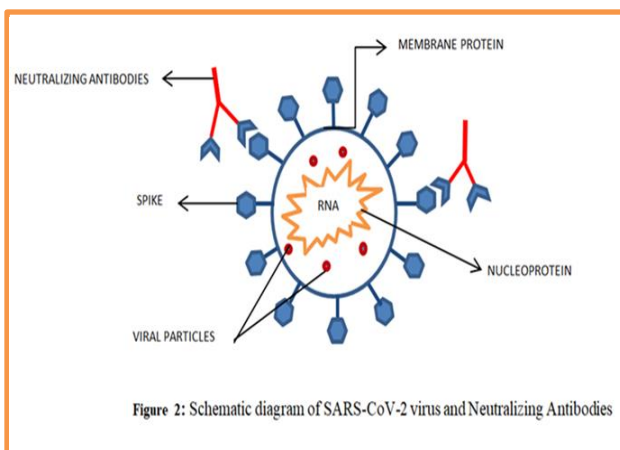
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This therapy's efficacy has been associated with the concentration of NAb in plasma from recovered donors [16]. The neutralizing antibodies against SARS-CoV-2 that has been isolated from donors may serve as a promising intervention to SARS-CoV-2 (Figure 2) [17].



## Discussion

Donors of CP should fulfill the standard eligibility requirements [18], in accordance with the National Guide on Preparation, in addition to following the recommendations from an accredited agency such as WHO. Multiple published studies have discussed CP antibodies' ability to viremia clearance, some of these studies support using CPT for COVID-19, but before starting the process of plasma transfusion, all precaution rules should be applied strictly [19,20].

For instance, Sudan is one of the developing countries that struggle against the spreading of COVID-19. One of the Sudanese studies reported the benefits of using convalescent plasma to treat COVID-19 symptomatic patients. This study has mentioned that specific criteria should be followed for both patient and donor before starting the process of transfusion. One of the CP transfusion criteria from a donor, the donor, should be free from SARS-CoV-2 infection at the time of plasma transfusion. On the other hand, one of the most important CP transfusion criteria to a patient is that the patient should have a clear symptomatic and confirmed diagnosis for COVID-19 depending on the official Sudanese therapeutic protocol for

COVID -19. Furthermore, this study recommended using CPT in COVID-19 Sudanese patients at least currently is considered an available costless therapeutic option, especially all other COVID-19 therapeutics alternatives still under investigation studies [21].

Neutralizing antibodies in donor Convalescent sera could be used for critical COVID-19 patients as recommended in one of the previous issues by the Food and Drug Administration [22,23,24]. However, the similarity between some human amino acid sequences with SARS-CoV-2 sequence could unintentionally way induce the autoimmune system [25]. Hence, a rapid vaccination strategy is needed to study interference between viral particles and human molecules to avoid an undesired self-immunity reaction, especially for those who suffer from previous medical history with autoimmune disease. Up to date, a few original practical studies used CPT for COVID-19 patients, but noteworthy still, the validation of the efficacy of CP is a controversial issue between supporters and opponents. Despite this, some reports reveal less hospitalization and a low mortality rate among patients who have been given convalescent plasma [26].

## Challenges facing the use of convalescent plasma

Dante Mário and his colleagues had mentioned that there are some challenges when we were thinking of using convalescent plasma therapy for COVID -19 patients. Some of these challenges are:-

- Is the convalescent plasma transfusion being more protective if compared with other antiviral treatments?
- Which one is more effective for patients, plasma from donors who have no symptoms or plasma from donors with symptoms?
- What is the best time to transfuse plasma to COVID-19 patients, in other words, early-stage or late-stage?

Some previous studies have also mentioned that there are expected complications accompanied by plasma transfusions, such as circulatory overload, anaphylactic reactions, and alloimmunization [27]. These are logical questions that need to be answered before starting accrediting plasma as an acceptable treatment for COVID-19.

## The current status of therapeutic efforts made with COVID-19

Until the time of writing the current manuscript, the medical Scientists are working day and night to find an effective and suitable vaccine for controlling the deadly COVID-19. Most Vaccine clinical trials platforms are done in developed countries, such as the USA, UK, Germany, Russia, and China. It seems there is an unprecedented race between these countries, which country would be the first one to produce an effective and safe COVID-19 vaccine for the entire world. Instead of racing between vaccine production companies, it would be better if there are information exchange and collaboration to help reach wisdom decision regarding COVID-19 [28].

Global cooperation will help avoid and repeat the mistakes made at the beginning of the COVID-19 crisis due to a lack of information transparency [29]. However, till that time, when the effective and trust vaccine appears and could apply confidently for patients, CPT is Considered an optimal and available option for COVID-19.

## Conclusion

To sum up, based on the previously published data, the CPT could be an efficient option, at least in the current time, to minimize the morbidity and mortality rate of patients with COVID-19. However, the extreme benefit of using CPT for COVID-19 still needs tremendous investigation. As it is recommended, it would be better if used a well-designed study such as controlled experiments with large sample size.

## Abbreviation

ARDS: Acute Respiratory Distress Syndrome; COVID-19: Corona Virus Disease of 2019; CP: Convalescence Plasma; CPT: Convalescent Plasma Therapy; FDA: Food and Drug Administration; H1N1: Influenza A virus subtype; MERS: Middle East Respiratory Syndrome; Nabs: Neutralizing Antibodies; SARS: Severe Acute Respiratory Syndrome.

## Declaration

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## Availability of data and materials

Data will be available by emailing nagiasuliman@hotmail.com

## Authors' contributions

Ahmed Abuelhassan (AA), Ebtehal Fawzi (EF), Alfatih Aboalbasher (AA), Sheima Elbasheer (SE), Nagia Suliman (NS), Alaa El-Hussein (AE), Mayada Ali (MA) have contributed equally to the study concept, design, writing of original draft. Abdelmonem Ali (AA) has reviewed and edited the manuscript. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki. However, Review Articles need no ethics committee approval.

## Consent for publication

Not applicable

## Competing interest

The author declares that he has no competing interests.

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