



CURRENT ADVANCEMENTS ON THE EFFICACY OF CONVALESCENT PLASMA AS A POTENTIAL PROMISING TREATMENT FOR COVID-19

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between both authors. Author SDNP designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors SDNP and DP managed the analyses of the study. Author SDNP managed the literature searches. Both authors read and approved the final manuscript.

Received: 15 September 2020

Accepted: 23 October 2020

Published: 21 November 2020

Systematic Review

ABSTRACT

Purpose: No sooner had COVID-19 hit the world in December, 2019 in Wuhan, China, than the emergence of tremendous developments on the therapeutic interventions for the pandemic. No therapy has been proved successful up to date regardless potentiality of several intervention that are still in clinical trials. However Convalescent plasma demonstrated some sort of interest to be potential for the treatment of COVID-19 as we are still waiting for a specific therapy or vaccine. This review discusses current developments that supported the efficacy of convalescent plasma to attract its potentiality for treating COVID-19.

Methods: A systematic search with a search term “efficacy of convalescent plasma on COVID-19” was done on PubMed, Google Scholar, Science direct, Research Gate and clinicaltrials.gov database. A search was conducted based on all the literature discussing the current advancements on the use of convalescent plasma as a potential treatment for coronavirus, however only studies that discussed its efficacy were retrieved in this review.

Results: We retrieved a total of 24 articles discussing the current developments on the use of convalescent plasma as a potential treatment for COVID-19. 70% of the articles discuss its success, 20% of the articles evaluate current ongoing clinical trials for convalescent plasma while the remaining 10% present concerns on the inappropriate administration of convalescent plasma as a COVID-19 therapy.

Conclusion: Several discussed studies demonstrated much attention on the use of convalescent plasma as a potential promising therapy for COVID-19, although this has not been proven. However, other studies expressed concerns over the inappropriate administration of the therapy where COVID-19 patients ended up developing a pro- thrombotic disease.

Keywords: Convalescent plasma; coronavirus infection; pro- thrombotic disease; pneumonia.

1. INTRODUCTION

Convalescent plasma has been identified as one of the potential promising treatments for COVID-19 since therapeutic developments commenced. This is due to its vast demonstration of precise ongoing efficacy to the treatment of SARS-CoV-2. COVID-19 convalescent plasma is an antiviral and immuno modulatory therapy option that involves collection of plasma (antibodies) from fully recovered COVID-19 patients. The antibodies are introduced in the body of severe COVID-19 patients. Several studies conducted in China and other countries globally on the efficacy of the convalescent plasma as a COVID-19 therapeutic have come up with successful outcomes. This review evaluates recent developments on the efficacy and safety of convalescent plasma.

2. METHODS

We performed a search of recently published literature on current advancements taking place globally supporting or ignoring the efficacy of convalescent plasma as a COVID-19 potential therapy. A search was conducted based on all the literature discussing the current advancements on the use of convalescent plasma as a potential treatment for coronavirus, however only studies that discussed its efficacy were retrieved in this review to achieve integrity of new evidence. We searched using one search term "efficacy of convalescent plasma on COVID-19" on PubMed, Google Scholar, Science direct, Research Gate and clinicaltrials.gov database. Retrieved literature was thoroughly analyzed to exclude duplicate, double registered and unknown studies by use of Mendeley software.

3. RESULTS

We retrieved a total of 24 articles discussing the current developments on the use of convalescent plasma as a potential treatment for COVID-19. 70% of the articles discuss its effectiveness [1-17], 20% of the articles evaluate current ongoing clinical trials for convalescent plasma (see Table 1). While the remaining 10% present concerns on the inappropriate administration of convalescent plasma as a COVID-19 therapy [18,19].

4. DISCUSSION

Several recent studies discuss that **convalescent plasma** is one of the outstanding intervention for

COVID-19 that brought much more interest regarding its ongoing efficacy [15,24,2]. All recent case studies and clinical trials on the efficacy of Convalescent plasma came up with positive results as at least all patients participated in the trials ended up with total improvements [11,5,25]. Several studies suggested that Convalescent plasma can bring a great achievement to be used in this pandemic as no specific therapy or vaccine has yet emerged [14,13,26]. Currently, the US Food and Drug Administration (FDA) has issued an Emergency Use Authorization to the use of Convalescent plasma in the United States because of its precise efficacy [27].

4.1 Mechanism of Action and Potential Side Effects

Plasma collected from a recovered COVID-19 patient contain antibodies that has the possibility of neutralizing the SARS-CoV-2 virus [7,28]. When the antibodies are introduced in the body of severe COVID-19 patient, they directly bind to the SARS-CoV-2 virus. Other factors such as Antibody-dependent complement activation, cytotoxicity, and phagocytosis also help to support the therapeutic of convalescent plasma [7]. Convalescent plasma in addition to viral clearance, it also has the possibility of reducing the disease severity by use of neutralizing and non-neutralizing antibodies hence enhancing quick recovery [29,30].

However a recently published critical care letter to the editor [18], expressed a concern on high risk of pulmonary embolism possibility in patients due to convalescent plasma. It states that since convalescent plasma contains pro-coagulant, patients end up developing a pro- thrombotic disease with high-risk of pulmonary embolism. Therefore it is advisable for the current recruiting trials to consider thoughtful administration of the plasma, following proper incident observation time frame of greater than 2 hours and specifying the plasma pre-treatment to reduce the coagulation factors.

Another recent pre-proof study [19] appreciates the efficacy of convalescent plasma, however it admits that researchers and physicians currently working on various trials should strictly commit to their ethical considerations and principles to achieve successful outcomes during this trying time.

Table 1. Convalescent plasma in patients with Coronavirus (COVID-19)

Reference	Country	Study design	Diagnosis	Individuals included	Patient outcomes	Mortality Rate
[20]	China	Case series	RT-PCR	4	Total clinical recovery	0%
[17]	China	Case series	RT-PCR	5	It resulted into increase in the number of antibodies as well as viral load improvement	0%
[21]	China	Clinical trial	RT-PCR	19	Lung imaging and improved viral load	Reduced viral load
[22]	China	Case series	RT-PCR	6	Improvement of viral load and increase of SARS-CoV-2 IgG and IgM antibodies.	Lung improvement
[23]	China	Case series	RT-PCR	2	Improvement of viral load and increase of SARS-CoV-2 IgG and IgM antibodies.	0%

Source: Authors' data

4.2 Historical Precedence

Convalescent plasma was considered a potential therapy for acute infections way back in 1900s. It was the time when Emil Adolf von Behring was awarded the first Nobel Prize in medicine for its use for the treatment of diphtheria. Until the discovery of antibiotics, convalescent plasma was found useful to treat various bacterial infections such as pneumonia, meningitis, botulism and other viral infections such as mumps, measles, polio, and influenza [6,31].

Recently, the use of convalescent plasma has also demonstrated successful outcomes in severe pandemics such as Ebola in 2013 where patients given the CP therapy ended up fully recovered. Furthermore, during the 2009–2010 H1N1 pandemic, the use of convalescent plasma was confirmed successful as it managed to improve viral clearance and cytokine reduction in severe patients [32].

4.3 Convalescent Plasma for Covid-19

Convalescent plasma is a passive immune therapy approach that involves introduction of neutralizing antibody containing plasma from fully recovered patients into severe COVID-19 patients. Several studies confirmed its efficacy as a potential COVID-19 therapy. However up to date, evidence of its effectiveness is still limited to small case series especially in China [6]. Recent clinical studies conducted in Houston, Texas, a series of 25 patients treated with CP therapy were fully recovered with improved viral clearance, cytokine decrease and oxygenation improvement. Furthermore, several

studies in China and USA have come out successful as all patients who received the treatment recovered. This greatly supported the efficacy of the Convalescent plasma as a potential therapeutic for SARS-CoV-2 regardless with no concrete evidence to be approved by the World Health Organization [33]. However the US Food and Drug Administration (FDA) allowed the use of convalescent plasma as an investigational product through 3 pathways which are Clinical trials, Expanded access program and Single-patient emergency investigational new drug (IND) application [16,34,35].

4.5 Clinical Trials of Covid-19 Convalescent Plasma

On September 5 2020, there were 144 recruiting and non-recruiting clinical trials listed on ClinicalTrials.gov of convalescent plasma for prevention and treatment of COVID-19. All preliminary results have demonstrated much improvements in COVID-19 patients [36].

5. CONCLUSION

Several discussed studies express much attention on the successful use of convalescent plasma as a potential promising therapy for COVID-19. This has greatly supported the efficacy of the Convalescent plasma as a potential therapeutic for Sars-Cov-2. However there is still no concrete evidence to be approved by the World Health Organization. Other studies expressed concerns on the inappropriate administration of the therapy that it can cause a certain harm in COVID-19 patients. For instance,

patients end up developing a pro- thrombotic disease with high-risk of pulmonary embolism due to the presence of coagulation factors in convalescent plasma.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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