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The relationship between convalescent plasma therapy for patients recovering from COVID-19 and patients positive for COVID-19

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Abstract

The arrival of a pneumonia disease with severe acute respiratory syndrome called COVID-19 has taken the world by storm. It is presence has made researchers and the World Health Organization (WHO) continue to try to find the right clinical management protocol to deal with this pandemic. The use of convalescent plasma, which has been around for a long time, has been discussed recently. Convalescent plasma (CP) therapy is a classic adaptive immunotherapy that has been applied in the prevention and treatment of infectious diseases for more than a century and has been used previously in the improvement of survival in patients with SARS and many studies have shown significant improvement in the condition of patients after administration of convalescent plasm.a As virological and clinical characteristics have similarities between SARS, Middle East Respiratory Syndrome (MERS), and COVID-19, CP therapy may be a promising treatment option for COVID-19 rescue.

Keywords: Convalescent plasma; COVID-19; Immunotherapy; Infectious diseases

1. Introduction

Since December 2019, the whole world has been galvanized with a pneumonia disease with severe acute respiratory syndrome, namely coronavirus 2 (SARS-CoV-2). The disease, named coronavirus 2019 (COVID-19) by the World Health Organization (WHO), emerged in Wuhan, China. The epidemic spread rapidly around the world within 3 months and was marked as a pandemic by WHO on March 11, 2020. As of March 12, 2020, a total of 80,980 confirmed cases and 3,173 deaths have been reported in China. Meanwhile, a total of 44,377 confirmed cases and 1,446 deaths were reported in 108 countries.[1] COVID-19 has been a global pandemic since early 2020 and has infected more than 161 million people and caused nearly 3.4 million deaths worldwide as of May 18, 2021. Indonesia alone has contributed more than 1.64 million people. COVID-19 in Indonesia has caused more than 44,500 deaths. People infected with this virus will usually experience respiratory problems that can be mild, moderate, or severe infections and sometimes require specialized care. [(2)] Although there is currently a vaccine or proven therapy for COVID-19, the clinical management protocol of the disease recommended by the World Health Organization (WHO) focuses on prevention, monitoring and detection of infection. Convalescent plasma (CP) or immunoglobulin therapy has been used previously in the improvement of survival in patients with SARS. In 2014, WHO recommended the use of convalescent plasma in 2015 as an empirical treatment in several outbreaks including the SARS virus and the Middle East Respiratory Syndrome (MERS) pandemic in the Middle East. In addition, hemorrhagic fevers such as the West African Ebola outbreak in 2014, human flu-A (H1N1) in 2009, and avian flu-A (H5N1) in 2019. Many studies have shown significant improvement in the condition of patients after administration of convalescent plasma.[2]

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1.1. Convalescent Plasma Therapy

Convalescent plasma (CP) therapy is a classic adaptive immunotherapy that has been applied in the prevention and treatment of infectious diseases for more than a century. Over the past two decades, CP therapy was successfully used in the treatment of SARS, MERS, and the 2009 H1N1 pandemic with satisfactory efficacy and safety. A meta-analysis of 32 studies on SARS and severe influenza coronavirus infections showed a statistically significant reduction in the probability of death after CP therapy. As virological and clinical characteristics have similarities between SARS, Middle East Respiratory Syndrome (MERS), and COVID-19, CP therapy may be a promising treatment option for COVID-19 rescue. Patients who have recovered from COVID-19 with high neutralizing antibody titers may be a valuable source of CP donors. However, the potential clinical benefits and risks of recovery blood products in COVID-19 remain uncertain.[2] With the writing of this article review, it is hoped that it can provide information on how the relationship that occurs between convalescent plasma belonging to COVID-19 recovered patients can be a therapy for COVID-19 positive patients.

2. Methods

In writing this literature review, the method used is a literature search in the form of theories and research data related to the relationship between convalescent plasma therapy for COVID-19 recovered patients and COVID-19 positive patients through Google Scholar, Elsevier, Pubmed, and Sciencedirect. Journal searches were conducted using the keywords "Convalescent plasma in COVID-19 treatment", "Effectiveness of convalescent plasma in COVID-19 treatment", and "Convalescent plasma therapy" with a maximum publication limit of the last five years (2017-2021), in English and/or Indonesian, and in the form of research journals, clinical trials and/or article reviews. Journals selected were research journals, clinical trials, and article reviews with topics discussing the relationship of convalescent plasma therapy for patients recovering from COVID-19 to COVID-19 positive patients. Based on these inclusion criteria, ten relevant journals were obtained for discussion.

Table 1 Journal Inclusion Criteria

Criteria	Inclusion
Timeframe	2017-2021
Language	English and/or Indonesian
Journal Type	Research, Clinical trial, and/or Article review
Theme/Content	Relation of convalescent plasma therapy of COVID-19 recovered patients to COVID-19 positive patients

Journal analysis was carried out by briefly describing the contents of journals related to the relationship of convalescent plasma therapy for patients recovering from COVID-19 to positive patients with COVID-19 to find the relationship and ability of convalescent plasma therapy in the treatment of COVID-19 from each journal.

3. Discussion

Severe Acute Respiratory Syndrome Coronavirus or SARS-CoV-2 is a β-coronavirus family that is the main cause of the COVID-19 pandemic in the world. Coronavirus is a type of virus that has a single-chain RNA genome. The symptoms vary such as shortness of breath, complications, multiorgan failure, and some are even asymptomatic.[1] The virus can cause a reduction in B lymphocytes (and a reduction in IL-6) early in the disease, which can affect antibody production. Lymphocytes may continue to decrease during the course of the disease, and inflammatory cytokines increase. Therefore, therapy should focus on 1) improving the patient's immune function and 2) inhibiting the formation of inflammatory cytokine storms.[5]

Various therapies have been developed to overcome the COVID-19 outbreak, one of which is convalescent plasma therapy. Plasma from patients who have recovered from COVID-19 is thought to have a therapeutic effect because it has antibodies against SARS-CoV-2. Convalescent plasma has been FDA approved for critical COVID-19 therapy. Plasma donors must have been symptom-free for 14 days, negative on SARSCoV-2 detection test, and no contraindications to blood donation.

Convalescent Plasma (CP), obtained from recovered COVID-19 patients who have established humoral immunity to the virus, contains large amounts of antidote antibodies capable of neutralizing SARS-CoV-2 and eradicating the pathogen from the blood circulation and lung tissue. In the study, all investigated patients achieved SARS-CoV-2 RNA negative serum after CP transfusion, accompanied by increased oxygen saturation and lymphocyte count, and improved liver function and CRP. The results suggest that inflammation and overreaction of the immune system are alleviated by antibodies contained in CP.[1] Effective convalescent plasma should contain high-titer specific antibodies that bind to SARS CoV-2 and neutralize virus particles, block access to uninfected cells, and activate potent effector mechanisms.[5]

During apheresis, in addition to neutralizing antibodies (NAbs), other proteins such as anti-inflammatory cytokines, clotting factors, natural antibodies, defensins, pentraxin, and other undefined proteins are obtained from the donor. In this case, CP transfusion for infected patients may provide further benefits such as immunomodulation through amelioration of severe inflammatory responses.[6] The composition of CP varies and includes a wide variety of blood-derived components. Plasma contains a mixture of inorganic salts, organic compounds, water, and more than 1000 proteins. Also found are albumin, immunoglobulins, complement, coagulation and other antithrombotic factors. It is suspected that plasma from healthy donors exerts immunomodulatory effects through the infusion of anti-inflammatory cytokines and antibodies that block complement, inflammatory cytokines and autoantibodies. These factors may influence the immunomodulatory effects of CP in patients with COVID-19.[6]

NAbs are essential in viral clearance and have been considered important in protecting against viral diseases. Passive immunity driven by CP may provide these NAbs to resist infection. The efficacy of this therapy has been linked to the concentration of NAbs in plasma from recovered donors. In SARS-CoV and MERS it was found that NAbs bind to spike receptor-binding protein 1 (S1-RBD), S1-N and S2 terminal domains, thereby inhibiting their entry, limiting viral amplification. In addition, other antibody-mediated pathways such as complement activation, antibody-dependent cellular cytotoxicity and/or phagocytosis may also enhance the therapeutic effects of convalescent plasma.[6] Plasma obtained from a donor and transfused into a recipient on the same day causes the viral load to decrease. After transfusion of convalescent plasma, IgG and IgM titers in recipients increase in a time-dependent manner. In addition, the presence of NAbs in the recipient plays an important role in the limitation of viral infection.[6]

The risks of convalescent plasma administration are similar to those of standard plasma. Infection with other infectious disease agents (viral transmission or bacterial contamination), immunologic reactions such as serum sickness, non-hemolytic transfusion reactions (tremor, fever, urticaria), associated circulatory overload may be observed. No serious adverse events have been reported in studies of convalescent plasma therapy.[7]

In discussing the use of convalescent plasma in COVID-19 therapy, several studies have been conducted. Based on research by Zeng et al (2020), in an experiment on 8 patients with COVID-19, it was found that 5 out of 8 patients experienced an increase in IgG after receiving a convalescent plasma transfusion, and 3 of the 5 patients experienced a drastic increase. In this study, a comparison of the clinical picture between patients who received convalescent plasma transfusions at different times and with different doses was conducted. Patients who received convalescent plasma transfusions before 21 days from the onset of COVID-19 symptoms tended to show more rapid negative changes of viral nucleic acid, and had a shorter treatment period compared with patients transfused after 21 days. In addition, based on the dose of convalescent plasma, it was found that viral nucleic acid in patients transfused with 400 mL of convalescent plasma tended to deteriorate faster than in patients who received 200 mL of convalescent plasma.[8]

In the study of Abolghasemi et al (2020), it was also found that convalescent plasma therapy in patients with COVID-19 could reduce patient hospitalization time. Patients who received convalescent plasma therapy also had a higher percentage of mortality, namely 85.2% compared to patients who did not receive convalescent plasma therapy with a percentage of 75.7%.[9] In a study by Hu et al (2020), it was found that after convalescent plasma transfusion, the clinical manifestations of all patients improved, and respiratory function improved, determined based on improvements in PaO2/FIO2 and SPO2 values. No adverse effects, such as fever, allergic reactions, increased kidney or liver function, and lung damage were found in patients receiving convalescent plasma transfusion.[10]

4. Conclusion

Based on these three studies, it was found that patients who received convalescent plasma transfusion experienced an increase in survival. Therefore, convalescent plasma therapy in COVID-19 patients can be a recommended therapy for the management of COVID-19 patients.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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