The Effectiveness and Safety of Convalescent Plasma as a Therapy for COVID-19 Patients: A Literature Review

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Abstract

COVID-19 is a new disease caused by SARS-CoV-2 with an increasing number of cases. until now, no specific vaccine or antiviral therapy regimen has yet been found. A therapy that has been known for approximately a century ago called convalescent plasma therapy has been discussed again as an effective and safe therapy for COVID-19 patients. Conduct a literature review of scientific studies related to the effectiveness and safety of convalescent plasma as a therapy for COVID-19 patients. Convalescent plasma has proven to be effective because it can improve the clinical condition felt by patient, prevent the entry of viruses into cells and inhibit the virus replication. This therapy is also proven to have no harmful effects, so it is safe to be performed by paying attention to certain things such as conditions that must be fulfilled by the donors.

Keywords: *COVID-19, SARS-CoV-2, Convalescent Plasma, plasma, virus, therapy*

Introduction

In Wuhan (China), at the end of 2019, there was an outbreak of the corona virus that had never been identified in humans(1). WHO officially labeled this kind of virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resulting disease as coronavirus disease (COVID-19)(2). Infected by COVID-19, a person will show a number of symptoms such as fever, cough, rapid breathing and difficulty breathing. In severe cases, it causes pneumonia, severe acute respiratory syndrome and the worst possibility, death(1).

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WHO affirmed that on May 10, 2020 there were 3,925,815 people worldwide infected by COVID-19 and 274,488 people reported dead(2). COVID-19 is currently a major concern throughout the world(3). The number of infected cases keeps increasing, but specific vaccines or antiviral therapy regimens have not been found yet (4–6). Treatment only focuses on supportive care in the form of oxygen administration, ventilation, fluid therapy, low-dose corticosteroid combination therapy, antivirals and atomized inhalation of interferon (4).

Convalescent plasma therapy has been utilized since a century ago and is now re-discussed as an effective therapy for COVID-19 patients(7,8). The convalescent plasma is a blood plasma obtained from a person who has been declared cured of the infection process and has antibodies against certain pathogens. This plasma can be transfused to patients with varying degrees of severity of infection as a relative treatment(8).

Convalescent plasma has been used in a variety of previous infectious diseases, such as influenza,

cytomegalovirus infections, Middle East Respiratory Syndrome (MERS-CoV), Severe Acute Respiratory Syndrome (SARS-Cov), H1N1 - H5N1 avian flu and Ebola[9–11]. The United States Food and Drug Administration (FDA) has now approved the use of convalescent plasma as a therapy for critical COVID-19 patients. However, the use of this therapy follows the usual system of new drug investigations[12].

Based on the aforementioned issues, the main focus of this paper is to conduct a review of previous studies related to the effectiveness and safety of convalescent plasma as a therapy in COVID-19 patients.

Method

Some international journal databases such as Pubmed, Proquest and the Indonesian Scientific Journal are sources of literature search conducted through Google Scholar. The literature search aims to find a lot of information related to convalescent plasma therapy and COVID-19. It is done using the keywords "convalescent plasma" and "COVID-19".

Results and Discussion

Efforts to create the SARS-CoV-2 vaccine and COVID-19 treatment have now been carried out by many scientific laboratories. However, referring to previous therapeutic experience of infectious diseases, a convalescent plasma therapy might be an effective therapeutic option in the treatment of COVID-19[6].

A good result of convalescent plasma therapy has been demonstrated by a study conducted at Wuhan Huoshenshan Hospital on 6 patients who were confirmed to be positive for COVID-19 with different clinical, laboratory and radiological symptoms. The study was carried out based on the results of a Reverse Transcription-Polymerase Chain Reaction (RT-PCR) throat swab in male and female patients with an age range of 28 - 75 years who had confirmed COVID-19. They had a variety of main conditions ranging from fever, shortness of breath, recurrent infections of COVID-19, to those with comorbidities with Sjogren's Syndrome. Convalescent therapy was given to each patient after more than 4 weeks from the initial complaint that appeared. The therapy was given 1-3 times with a dose of 200 ml for 30 minutes each time of transfusion. Evaluation results showed that this therapy could reduce the clinical symptoms felt by the patient, improve lung conditions evidenced by a gradual reduction in consolidation and ground glass opacity occured in the lungs, clear SARS-CoV-2 which could lead to a double increase in titers of IgM and IgG antibodies against SARS-CoV-2 in patients receiving the therapy[13].

Another study was conducted on 4 male and female patients who were critically ill due to SARS-Cov-2 infection with an age range of 31-73 years. Each patient had comorbidities including hypertension, chronic obstructive pulmonary disease (COPD), chronic kidney disease and pregnancy. Patients obtained treatment in the ICU, experienced acute respiratory distress syndrome (ARDS), respiratory failure, septic shock and dysfunction and even multiple organ failure. Each patient was given 1-8 times convalescent plasma therapy with a volume of 200-400 ml each. The results indicated that the convalescent plasma therapy had a good effect on the patients' condition. This therapy improved their clinical condition, radiological picture and laboratory picture by which they no longer needed therapy for COVID-19 management. The duration required between administration of convalescent plasma therapy with a negative RT-PCR throat swab was in the range of 3 to 22 days[14].

There was also a research conducted at Shenzhen Third People's Hospital in China on the use of convalescent plasma therapy for COVID-19 patients. The study was conducted in 5 critical patients who were characterized by the following conditions: respiratory failure requiring mechanical ventilation, shock identified by vasopressor therapy and elevated lactate levels (> 2 mmol/L) despite adequate fluid resuscitation, or organ failure. The amount of plasma given to each patient was two consecutive transfusions of 200 - 250 ml with a total plasma of 400 ml. After conducting the convalescent plasma therapy, the patients' clinical condition improved, which was indicated by a decrease in body temperature, an increase in PAO_2/FIO_2 and chest radiology results showed a gradual improvement. Laboratory results showed a decrease in the number of viruses; some viruses become negative and there was a decrease in the number of inflammatory biomarkers (C-reactive protein, procalcitonin and IL-6). Four patients who had received mechanical ventilation and ECMO no longer needed 9-day respiratory assistance after the plasma transfusion [15].

Similar study was also carried out in three different hospitals in Wuhan on 10 patients with severe COVID-19. Each patient received a 200 ml convalescent plasma

therapy which was transfused within 4 hours. This therapy had a good effect on COVID-19. All symptoms in these 10 patients, especially fever, cough, shortness of breath and chest pain disappeared or, in other words, most of their condition improved within 1 to 3 days after the transfusion was performed. Antibody titer against SARS-CoV-2 increased in 5 patients and had a constant level in 4 other patients. The amount of SARS-CoV-2 RNA in each patient decreased and was not detected after 2-6 days of convalescent plasma therapy[16].

In Korea, a study on the effectiveness of convalescent plasma therapy was also conducted in two COVID-19 patients with acute respiratory distress syndrome (ARDS). The study was conducted on days 7 and 22 after the initial appearance of symptoms in each patient. Positive effects were shown after the administration of the therapy including improvement of clinical conditions, chest X-ray results accompanied by an increase in PaO_2/FiO_2, reduction in the number of inflammatory biomarkers and SARS-CoV-2 RNA showing negative results on days 20 and 26 after administration of therapy[17].

In addition, a study conducted on 21 COVID-19 patients obtaining intensive care in Henan Province of China showed that 6 patients given 300 ml convalescent plasma therapy had viral clearance and a longer survival rate than patients without plasma therapy[18].

Based on the aforementioned results of studies, the convalescent plasma therapy was effective for COVID-19 patients. It has been mentioned in the literature that antibodies mediated by the humoral response are very important for preventing or treating viral infections. Some parts of the antibody reduce the amount of virus by binding the epitope to the external surface of the virus particle, thus it prevents the entry of the virus into the cell and also prevents the replication of the virus[19].

The research stated that no harmful effects appeared after the plasma therapy was carried out[16,20]. However, one of the patients showed reddish spots on the face that easily disappeared after getting the therapy[20]. To avoid the harmful effects of therapy, it must be ensured that the plasma donor has completely healed. Here are some conditions that have to be fulfilled by the donors: 1) Free of fever for at least three days; 2) Reduction of respiratory symptoms; 3) Negative SARS-CoV-2 RT-PCR in two consecutive tests (one day interval between tests); 4) Anti-SARS-CoV-2 is positive, while HIV, HBV, HCV and other respiratory viruses are negative; and 5) Plasma should be taken after three weeks of disease onset[13,15,20].

Conclusion

This study established a conclusion based on the results of the research that had been carried out in various places with clinical symptoms, the results of radiological examinations and the results of various laboratory examinations. It concluded that therapy using convalescent plasma was proven effective since it could minimize the clinical symptoms felt by patients, prevent the entry of viruses into cells and inhibit viral replication. This therapy was also proven to have no harmful effects by which it was safe to do by paying attention to certain things such as conditions that needed to be fulfilled by donors.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Indonesia.

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