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Convalescent plasma as additional therapies in COVID-19 patients

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ABSTRACT

Corona Virus 2 (SARS-CoV-2) is a new virus who can make an infectious disease that we called Corona Virus Disease 2019 (COVID-19). The main symptoms manifest in the respiratory tract such as fever, cough, and shortness of breath. This disease spread very fast to various continents in a short time. The use of convalescent plasma as additional therapy for COVID-19 patients based on the previous cases like SARS, Ebola, MERS. A lot of research has been done to find the good therapy for patients. One of the approved treatments by WHO is the administration of COVID convalescent plasma (CCP), as additional therapy, to prevent cytokine storms and to increase life expectancy at COVID-19 patients in Indonesia. Plasma from healthy patients after having cured from COVID-19 infection, who has many Immunoglobulin G, processed by plasmapheresis. This review explained 299 plasma convalescent donors in the Jakarta Blood Center, Red Cross Indonesia. While for the efficacy of patients in the hospital there is no data that we can report. Some clinicians suggest that convalescent plasma should be administered immediately after infection, before the seventh day.

Keywords: COVID-19, convalescent plasma, additional therapy.
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INTRODUCTION

The first occurrence of an unexplained pneumonia was reported in December 2019 in Wuhan, Hubei province. Though the initial case was linked to a seafood market in Wuhan, the source of the transmission was unknown. Five individuals were treated between December 18 and December 29, 2019, with ARDS as their diagnosis.[1] The samples under investigation revealed Coronavirus as the etiology. The condition was once referred to as 2019 novel coronavirus (2019-nCov).[2] The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) induced Coronavirus Disease (COVID-19) was given a new designation by the World Health Organization (WHO) on February 11th, 2020. This virus, which may be communicated from person to person, has spread significantly around the world, including China and more than 190 other nations. The WHO classified COVID as a pandemic on March 12, 2020. On March 2, 2020, the first COVID-19 case in Indonesia was reported. In Indonesia, there were 320,564 positive confirmed cases of COVID-19 as of October 9, 2020, with 11,580 instances of deaths (CFR 3.6%). The highest mortality were observed in patients with an age range of 55-64 years.[3]

Common symptoms of COVID-19 include fever, cough, headache, and shortness of breath. Laboratory examinations show a white blood cell count below normal, lymphopenia, hypoxemia, impaired liver function, and kidney function.[4] Currently supportive therapy for existing symptoms, but specific antiviral has been recommended for the treatment of COVID-19. Many antiviral therapies have been developed during this pandemic, but their efficacy for severe disease caused by SARS-CoV-2 remain unclear.[5]

Immunotherapy with specific viral antibodies in convalescent plasma has been performed as an effective therapy to maintain life expectancy in patients with pre-existing viral infections with different viral causes including severe acute respiratory syndrome coronavirus, middle east respiratory syndrome, Ebola virus, pandemic influenza A, and avian-origin influenza A. Previous studies on SARS patients treated with convalescent plasma from recovered patients showed a decrease in the number of hospitalized patients and reduced patient mortality.[6] The aim of this study is to review the convalescent plasma as an additional therapy for COVID-19 which is currently being used by clinicians in Indonesia.

METHOD

This study is a review of the literature. The PubMed and Google Scholar databases were chosen as the primary literature sources. A systematic, explicit, and repeatable procedure known as a literature review can be used to identify, evaluate, and synthesize research works as well as the opinions of academics and practitioners. The literature review includes a synopsis of the theory, research findings, and additional research materials acquired from reference materials that will operate as the basis for research efforts.

RESULTS AND DISCUSSION

Therapy of Convalescent Plasma

Prevention and Management of COVID-19

The key to prevention includes breaking the chain of transmission through isolation, early detection, and universal precautions. The Ministry of Health recommends the universal precautions consist of regular washing hands with alcohol or soap and water, social distancing, practicing coughing or sneezing etiquette, and seeking for treatment when such signs are exist.[7]

The main treatment for patients is supportive therapy according to the patient's condition, adequate fluid therapy as needed, and oxygen therapy according to the degree of disease. If a secondary infection is suspected, broad-spectrum antibiotics are given. If there is a clinical deterioration or a decrease in consciousness, the patient will be treated in the intensive isolation room (ICU) at the hospital.[8]

Plasma from patients who recovered from COVID-19 is assumed to have therapeutic effect because it has antibodies against SARS-CoV-2. Shen C et al reported five case series of critically ill COVID-19 patients who received this plasma therapy. All patients showed clinical improvement, three of whom have been discharged. Studies for convalescent plasma are currently small and uncontrolled, but the Food and Drug Administration (FDA) has approved convalescent plasma for critical COVID-19 therapy. Plasma donors must have been symptom-free for 14 days negative for SARS-CoV-2 detection, and there are no contraindications to blood donation.[9,10]

Convalescent Plasma as an Additional Therapy for COVID-19

Convalescent plasma is plasma from patients who have recovered from COVID-19, assumed to have a therapeutic effect because it has antibodies against SARS-CoV-2.[11] The convalescent plasma from patients recovered from COVID-19 containing antibodies then transfused to patients infected with COVID-19 for a faster recovery.[12]

Convalescent plasma has been used in infectious diseases since the early 20th century and has played a role in reducing mortality in the 1918 influenza pandemic, 2003 SARS, and 2009 H1N1 influenza.[9,12] A study was conducted at Prince of Wales Hospital, Hong Kong in 2003 used convalescent plasma therapy combined with anti-viral and anti-inflammatory drugs in 80 patients who were confirmed positive for SARS before the 14th day since clinical symptoms appeared. The results were 66.7% of the PCRs turned into negative.[13] A retrospective study comparing convalescent plasma therapy and high-dose methylprednisolone in the treatment of SARS patients in combination with antiviral drugs was performed in 2004 to determine the effectiveness of adjunctive therapy with convalescent plasma.[14] Currently, convalescent plasma is an option for prevention and treatment of COVID -19 that can be obtained from a number of recovered patients who can become convalescent plasma donors.[15]

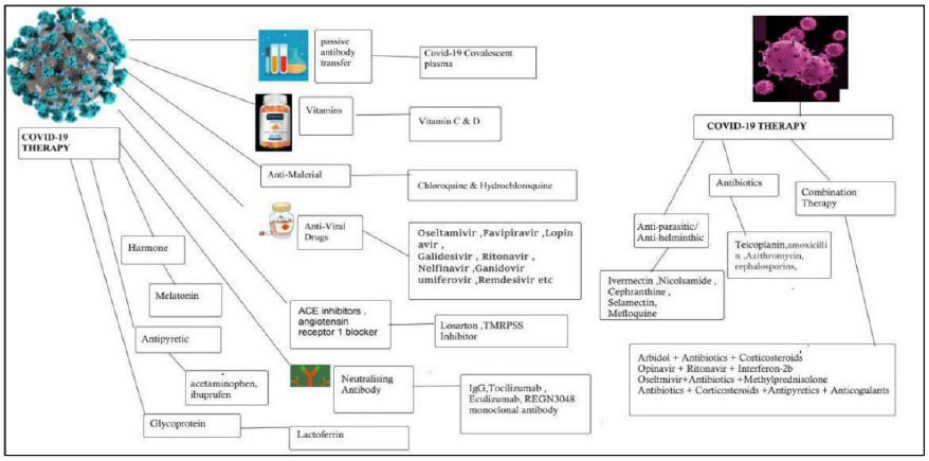

Figure 1. Medications for patients with COVID-19.[9]

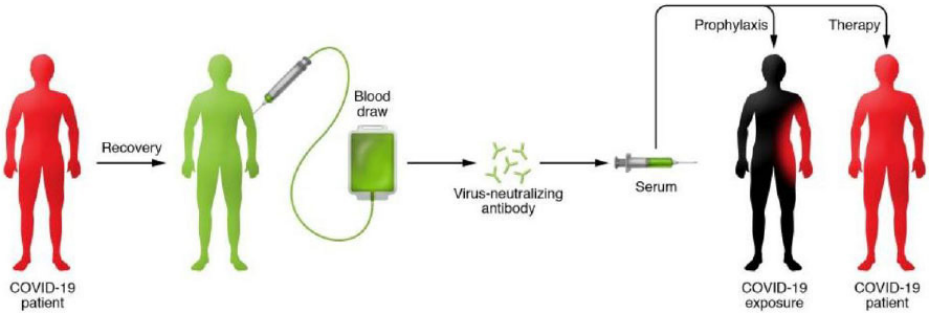

Figure 2. Schematic of the use of convalescent plasma for covid-19.[15]

Convalescent Plasma Preparation

Preparation of convalescent plasma is critical. It starts with the recruitment and selection of donors to the provision of convalescent plasma to patients. All steps must be carefully regulated and ensure that convalescent plasma products are

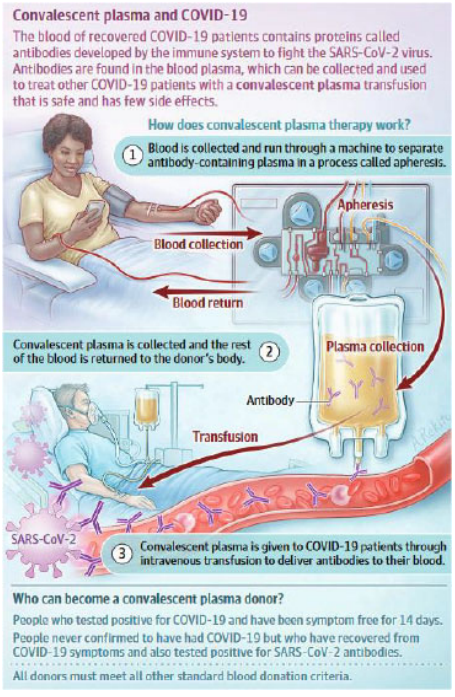

Figure 3. Illustration of convalescent plasma from a donor to a COVID-19 patient.[17]

Table 1. Criteria and composition of convalescent plasma providers in Red Cross Transfusion Unit, Jakarta[22]

Criteria	Composition	Amount
Sex	Male	274
	Female	25
Methods	Plasmapheresis	299
Blood type	O	100
	A	84
	B	86
	AB	29
Rhesus	Positive	296
	Negative	3
IMLTD: CLIA / ELISA	Positive	0
	Negative	299
IMLTD: NAT	Positive	0
	Negative	299
Antibody screening and blood type confirmation	Positive	0
	Negative	299
Component	Liquid plasma	0
	FFP	299
HLA antibody	Positive	12
	Negative	13

of good quality and safe in accordance with the GMP from National Agency of Drug and Food Control.[16] Convalescent plasma is blood plasma from patients who have recovered from COVID 19, will have antibodies against SARS-CoV-2. Antibodies in plasma will be obtained from donors through the apheresis or through conventional blood donors. Convalescent plasma from recovered patients is expected to increase the ability of COVID-19 patients to fight the SARS-CoV-2 virus.[17]

The eligibility for patients who recovered from COVID-19 to be able to donate convalescent plasma that donors must be voluntary and meet the general requirements according to service standards that has been determined by National Agency of Drug and Food Control, Ministry of Health and Indonesian Red Cross.[16,18,19] Convalescent plasma from donors can be obtained by plasma apheresis. Plasma collection by apheresis results in 400-500 mL plasma (maximum 600-800 mL depending on the weight of the donor). To maintain quality and ensure safety until transfusion to the patient, convalescent plasma collection is carried out by a blood transfusion unit that already has a license or certificate for plasma collection from the regulator that handles it.[20] Female donors who have a history of pregnancy must be screened for HLA, HPA, and HNA antibodies to prevent the occurrence of Transfusion Related Acute Lung Injury (TRALI). All steps carried out in the preparation of convalescent plasma must comply with the rules, in Indonesia the license is Good Manufacturing Practice (GMP) certification or CPOB from the Food and Drug Administration. Donor blood samples will be given the same label as the blood bag, which is used for examination: ABO and Rhesus antibody screening, serological screening for Infections Transmitted by Blood Transfusion including Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) and Syphilis. The examination is conducted by two methods, namely the Chemiluminescent Assay (CHLIA) and the Nucleic Acid Test (NAT) which run in parallel, hematological examination, specific antibody titers against SARS-CoV-2, viral neutralization test (Plaque Reduction Neutralization Test/PRNT method). The convalescent plasma that has been obtained will be processed in a closed system into two or three plasma bags. Plasma in liquid form is stored at a temperature of 2°- 6°C and has an expiration date of 24 hours. If plasma is not yet to be used, it can be stored in frozen or cryoprecipitate form. Frozen plasma stored at a temperature of -30° to -39°C have a shelf life of up to 1 year. Labeling for ready release is given if all screening results are in accordance with standards, and the product is ready to be stored or distributed to patients in hospitals.[16,18]

Convalescent Plasma in the Jakarta Blood Center

In Indonesia, convalescent plasma has been an additional therapy selected by clinicians for the treatment of COVID-19 patients. Currently, the Ministry of Health is conducting clinical trials of convalescent plasma as a supporting therapy for COVID-19, with the Coordinator from Health Research and Development. This clinical trial involved 33 hospitals throughout Indonesia and 13 convalescent plasma providers that have been certified by GMP. Data from the Indonesian Red Cross report as of October 2, 2020, there were 407 convalescent plasma donors from 13 units of convalescent plasma providers. System of regionalization, sub regionalization and consolidation of technical activities are implemented to support the distribution of convalescent plasma in hospitals throughout Indonesia.[21] The Red Cross Blood Transfusion Unit of Jakarta Province from June 14 to October 14, 2020 reported as many as 299 plasma donors with the composition in the table above.

The provision of convalescent plasma in Transfusion Unit Jakarta has been conducted for five months and to date there have been no reports of severe transfusion reactions in patients receiving convalescent plasma transfusions. Likewise, the research team in clinical trials of convalescent plasma administration as a supporting therapy for COVID-19 reported that most of the patients were recovered.[21]

CONCLUSION

Convalescent plasma is blood plasma obtained from COVID-19 patients who have been declared cured of COVID-19 infection with negative RT-PCR swab and no relevant symptoms within 14 days after being declared cured. Convalescent plasma therapy is the administration of plasma from recovered COVID-19 patients. Convalescent plasma containing polyclonal antibodies transfused into COVID-19 patients is a passive immune

therapy that is currently used as an adjunctive therapy for patients in critical condition in hospitals. As an additional therapy that brings new hope for the recovery of COVID-19 patients, the preparation of convalescent plasma from recruitment to distribution must meet existing standards to maintain quality assurance. Further clinical trials of convalescent plasma are needed to assess the risk, efficacy of administration, and protocol of administration. To obtain detailed clinical test results, it takes time until the research is completed so that it can provide results that can be scientifically justified and can provide benefits to the world of medicine and science about blood transfusions.

DISCLOSURES

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Author Contribution

All authors similarly contribute to the think about from the investigate concepts, information acquisitions, information investigation, factual investigations, changing the paper, until detailing the consider comes about through publication.

Ethical Consideration

None.

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