بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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Convalescent Plasma Transfusion for Treatment of Corona Virus Disease 2019 (COVID-19) Infection-: A Systematic Review

Systematic Review/Meta-Analysis

*Submitted for Partial Fulfillment of Master Degree in **Anesthesiology***

By

Ghoson Mohamed Anter Abd Elrahman

M.B.B.CH- Resident in Department of Anesthesia, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University

Under Supervision of

Prof. Dr. Sameh Michel Hakim

Professor of Anesthesia, Intensive Care and Pain Management
Faculty of Medicine, Ain Shams University

Dr: Ashraf Mahmoud Hazem Elhakim

Assistant Professor of Anesthesia, Intensive Care and Pain Management
Faculty of Medicine, Ain Shams University

Dr. Akram Mohamed Amer

Lecturer of Anesthesia, Intensive Care and Pain Management
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University

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Ghoson Mohamed Anter Abd Elrahman

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List of Abbreviations

Abb.	Full term
AE	*Adverse events*
AIDS	*Acquired immunodeficiency syndrome*
ALT	*Alanine aminotransferase*
BMI	*Body Mass Index*
CAD	*Coronary artery disease*
CD4	*Cluster of differentiation 4*
CHF	*Congestive heart failure*
CI	*Confidence interval*
CKD	*Chronic Kidney Disease*
COPD	*Chronic Obstructive Pulmonary Disease*
COVID-19	*Coronavirus disease 2019*
CP	*Convalescent plasma*
CPT	*Convalescent plasma therapy*
CRP	*C-Reactive Protein*
CT	*Computed tomography*
CVS	*Cardiovascular system*
DM	*Diabetes mellites*
ECMO	*Extracorporeal membrane oxygenation*
ECMO	*Extracorporeal membrane oxygenation*
FDA	*US Food and Drug Administration*
FiO2	*Fraction of inspired oxygen*
HFO	*High flow oxygen*
HIV	*Human immunodeficiency virus*
HR	*Hazard ratio*
HTN	*Hypertension*
ICU	*Intensive Care Unit*
IgA	*Immunoglobulin A*
IgG	*Immunoglobulin G*
IgM	*Immunoglobulin M*
IL1	*Interleukin-1*
IL6	*Interleukin-6*
IMV	*Invasive Mechanical Ventilation*
IQR	*Interquartile range*

List of Abbreviations cont...

Abb.	Full term
IQR	*Interquartile range*
LDH	*Lactate dehydrogenase*
M.V	*Mechanical ventilation*
MERS-CoV	*Middle East Respiratory Syndrome*
MV	*Mechanical Ventilation*
Nab	*Neutralizing antibodies; ab, antibodies*
NHC	*National Health Commission of the people's Republic of China*
NIV	*Non-invasive ventilation*
NRSIs	*Non randomized studies of intervension*
O_2	*Oxygen*
OSA	*Obstructive sleep apnea*
PCR	*Polymerase chain reaction*
PRISMA	*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*
RBD	*Receptor-binding domain*
RBD	*Receptor-binding domain*
RCTs	*Randomized control trials*
RCU	*Respiratory care unit*
RCUs	*Respiratory care units*
RTCI	*Recovery Time from Critical Illness*
S COV-2	*Severe acute respiratory syndrome corona virus 2*
SARS-CoV-2	*Severe acute respiratory syndrome coronavirus 2*
SD	*Standard deviation*
SD	*Standard deviation*
SOC	*Standard of care*
SOC	*Standard of care*
TRALI	*Transfusion related acute lung injury*
TRALI	*Transfusion related acute lung injury*
WHO	*World health organization;*

INTRODUCTION

The coronavirus disease 2019 (COVID-19) is a highly infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), with an outbreak originated from Wuhan, China in late 2019. COVID-19 represents a major global challenge with more than 200 million confirmed cases and over 4.5 million deaths till now.[1] Coronaviruses are a large family of viruses that cause a common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).[2]

The causative agent -SARS-CoV-2- is presented as a major challenge because, as a new virus, it has no specific therapy. Consequently, early responses focused on optimizing respiratory care, managing thrombotic and inflammatory complications with anticoagulation and corticosteroids and using existing antiviral therapies which, with the exception of remdesivir proved ineffective. Although chloroquine, hydroxychloroquine, antivirals and the antibiotic azithromycin are used for the treatment of COVID-19, no specific drug or treatment has yet proven effective.[3, 4]

Convalescent plasma seems to retain its importance as an alternative treatment method for patients with COVID-19 infection until a specific effective anti-viral agent or vaccine is found based on the concept of passive immunization.

Convalescent plasma (CP) from donors has emerged as an option for prevention and treatment of COVID-19 considering that it can rapidly be made available and theoretically, could be used for providing immediate immunity to susceptible individuals through viral neutralization.[5]

The convalescent plasma is likely to contain high levels of neutralizing antibodies against the SARS-CoV-2 virus, which when transfused to patients with acute COVID-19 infection, can provide a degree of passive immunity. Though the exact mechanism of how these antibodies in plasma clear the viral load is still not clear, multiple mechanisms including antiviral and immune modulatory actions have been hypothesized.[5]

The premise of convalescent plasma treatment is that it is most effective in patients with a high viral titer, so it is suitable for patients with rapid disease progression or who are severely or critically ill. Patients should be infused with convalescent plasma early in the course of the disease when the body has not yet produced IgG antibodies. After infusion, the body obtains high levels of IgG antibodies that neutralize the virus, decrease repeated stimulation of the immune system by killer T cells, improve the humoral immune response, prevent cytokine storms and shorten the course of disease. Theoretically, the best time to infuse patients with convalescent plasma is in the early stage of the disease, when Ig G antibodies have not been produced, the nucleic acid test is strongly positive, and the viral

load is high. Because that the antigen-antibody reaction time is approximately 24 h, 24–48 h after infusion of convalescent plasma is likely the best time to evaluate treatment efficacy.[6, 7]

The recommended minimum dose for one patient is one unit (200 mL per unit) of CP. Second unit can be administered 24-48 h following the completion of the transfusion of the first unit of convalescent plasma and can be repeated many times. Scientific rationale of this application is to avoid volume overload in these patients who are unstable in terms of cardiopulmonary functions.[6]

The risk of transfusion related adverse events is therefore likely identical to the risk associated with standard plasma, namely, transfusion-associated circulatory overload, transfusion-related acute lung injury, and allergic reactions. The incidence of adverse events is very minimal in CP therapy.[4]

The safety measures for CP transfusion such as sterility, precautionary measures for infectious disease transference such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) etc., and prevention of serum sickness type of reactions should be taken.[8]

However, evidence for therapeutic convalescent plasma efficacy still requires definitive support from large randomized clinical trials (RCTs). As a result, there remains a lack of consensus on convalescent plasma use in hospitalized COVID-

19 patients. Smaller RCTs, matched control studies, and case-series studies investigating convalescent plasma therapy for COVID19 have emerged and provided a positive efficacy signal. Most of these studies, however, lacked appropriate statistical power or were terminated early.

There is a lack of structured systematic reviews looking into the efficacy of convalescent plasma therapy for COVID-19 patients. Therefore, we have conducted this systematic review to provide an insight into the clinical effectiveness of convalescent plasma as a potential therapy for COVID-19 patients.