ORIGINAL RESEARCH PAPER
Volume-9 | Issue-5 | May-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PLASMA THERAPY IN COVID-19 PATIENTS

General Medicine

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ABSTRACT

Since the starting of COVID-19 pandemic neither specific therapy is discovered which can cure the patient nor any vaccine which can prevent the disease. So only one therapy, convalescent plasma from recently recovered virus negative patient may be effective in treating the critically ill patient which can possibly recover the patient if can be administered within 10 – 15 days of; onset of disease.

KEYWORDS

INTRODUCTION

In last part of December, 2019, there was COVID-19 outbreak started in Wuhan, China, which ultimately spreaded in more or less all the countries worldwide within 3 months and declared as "Pandemic" by WHO on 11th march, 2020. In March 12th, 80980 and 44377 confirmed cases were reported in China and other 108 countries respectively with reported death of 3173 in China and 1446 in other countries. So it needs urgent intervention in the form of definite drug or administration of passive immunization.

Concept:

Concept of convalescent plasma therapy started nearly one century back when in 1890, German Physiologist, Emil Von Behring demonstrated that sera obtained from a rabbit infected with diphtheria effectively prevented diphtheria infection and for that he received Nobel prize in the subject of Medicine in the year of 1901. After that in 1918 diphtheria outbreak, in 1930 flesh-0eatting bacteria epidemic it failed to demonstrate its effectivity, on the other hand, large number of side-effects. After several years, antibody fraction was separated but unintended antibodies present in the convalescent plasma produces side-effects still now.

Different reviews:

Till date after the outbreak of COVID-19 from Wuhan in China to become pandemic no specific therapy is proven effective worldwide in this disease other than supportive therapy, like oxygen therapy, fluid balance in mildly symptomatic therapy or invasive ventilation or extracorporeal membrane oxygenation in case critically ill patients, only lots of researches are going on throughout the World to get any specific drug against this virus. In United States of America first affected patients was treated with intravenous Remdesivir along with intravenous hydration, patient recovered and discharged enhancing the researcher to do further research on the efficacy and any adverse effect in the body[1]. So randomised controlled trial is very urgent on this drug. Those patients who deteriorate in spite of giving providing all the supportive therapies, and intravenous pulse methyl prednisolone, convalcent plasma containing immunoglobulin were given as a last resort to save their life. Later on several studies demonstrated the usefulness of giving plasma therapy as it reduces the hospital stay, it increases the immunity and lower mortality of the affected patients[2,3,4]. In the 2014 Ebola outbreak the plasma was collected from the patients recovered from Ebola virus and was recommended by World Health Organization (WHO) to give it to all empirically in outbreak[5]. A prospective cohort study of Chinese researchers in 2009 demonstrated the reduction of mortality in pandemic of H1NI (H1N1pdn09) by administration of convalescent plasma[6]. It reduced the viral load within 7 days of plasma administration without any complication or adverse effects. Similarly, in 2015 convalescent plasma against Middle East respiratory syndrome coronavirus[7]. Later on, meta-analysis was also done and it was shown that administration of convalescent plasma reduced viral load without any adverse effect of its administration[8]. Again, another meta-analysis based eight studies demonstrated that on administration of human convalescent plasma of patients recovered from influenza in various dosages to 1703 patients suffering from influenza-pneumonia from 1918 to 1923 reduced the crude overall case fatality rate by 21% ($p<0.0001$) in those patients[9]. Possible explanation for this effective therapy was based upon the fact that antibodies present in that plasma reduced the viremia has been recommended to by WHO in any coronavirus infection. In Wuhan, China in COVID-19 pandemic, plasma therapy was tried in 10 severely ill COVID-19 patients with median age of 53.4 years receiving many antiviral therapies, 4 with chronic morbid illness and 3 in mechanical ventilators[10]. Most of the patients, within 3 days of administration of convalescent plasma demonstrated following features:

A. Improvement of clinical symptoms.
B. Increased lymphocyte counts
C. Oxygen level in the blood improved
D. C-reactive protein lowered.
E. Undetected viral load
F. Computerised tomographic features in the chest was improved.
G. Rapid wean from ventilators in two patients.

Amongst them 3 patients were discharged and rest 7 patients were much improved. This treatment was successful in those patients received treatment within 14 days of onset of symptoms. Where as in case same number control group of patients not receiving this convalescent plasma therapy, 3 patients died, 6 were stable and one was a bit improved.

In another study in Shenzhen Third People's hospital, China, five critically ill COVID-19 patients with acute respiratory syndrome from January to March 2020 were treated with convalescent sera between 10 to 22 days of admission and clinical of those patients prior and post administration of sera were measured. Their blood demonstrated COVID-19 specific IgG antibodies titer of more than 1 in 1000 by ELISA test and neutralisation titer of greater than 1 in 40 and recovered from this disease. Measures of clinical outcomes were the following[11]:

A. Temperature level
B. Sequential organ measurement score
C. PaO2/FiO2
D. Serum antibody titer
E. Viral load in the body
F. Routine blood biochemistry
G. Acute respiratory distress syndrome prior and post-administration
H. Ventilatory support prior and post-administration
I. Extra-corporeal membrane oxygenation prior and post-administration.

Process of donating plasma is the same that of blood, it takes one hour to transfuse. Houston Methodist, the first Academic medical Centre transfuse the plasma from COVID-19 patient to a critically ill COVID patient. Later on, three Indian-American critically ill patients were transfused with convalescent plasma, all of them were recovered.

In the process of donation, donor is hooked up to a small device, which only removes plasma returning the red blood cells into the donor body. So, there is no loss of plasma and the donor can donate plasma twice a week. But most of the sufferers are mainly aged and with large number of co-morbidities, so the effectiveness of convalescent plasma is questionable. Critically ill patient receives passive immunization but it will be present in the patient's blood stream for less than a week. So, it is opposite to the vaccine in terms of days of immunity as effective vaccine immunity persists for life long.

Plasma therapy is the infusion of convalescent patient's plasma containing IgG antibody against corona virus antigenic protein, mainly spike protein and nucleocapsid protein. But prior to administration plasma should be checked for neutralizing antibodies. Person can be accepted as donor 14 days after hie or her reported full recovery. According to different researchers these antibodies develop immunity in the sick patients. Immunity develops much early in asymptomatic patients or mildly symptomatic patients but in case of severely ill or critically ill COVID-19 patients it will develop later. In case of HIV patients, a school demonstrated that 3BNC117 based immunotherapy containing neutralizing antibody to HIV virus reduced viral load, accelerated clearance of virus and blocked new viral infection[12]. Since in first 14 days there is primary immune response followed by viral clearance, hence convalescent plasma should be effective in early stage of therapy[4]. Till date WHO is not able to declare any definitive therapy of COVI-19 other than emphasizing on the case detection, monitoring and prevention of it, so convalescent plasma-based therapy should be the choice in early phase of disease.

In India, Kerala first received the permission to start clinical trial as that State has already has enough task force. after getting approval from Indian Council of Medical Research SVP hospital, Ahmedabad run by Ahmedabad Municipal corporation will start on 19/04/2020 convalescent plasma therapy as a trial in patients of COVID-19. In the first trial in Gujrat, doctor first extracted plasma from a 24 years patient, discharged from the hospital on 6th April and negative post-treatment.

CONCLUSION:

Since million and millions of peoples are affected by COVID-19, so, obviously a large pool of plasma should be in fridge to save the life of critically ill patients worldwide.

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