SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 5.
Issue: 5.
Page N. 147-150
Year: 2021

Review Article www.wjahr.com

CONVALESCENT PLASMA THERAPY CAN PROVE EFFECTIVE AGAINST COVID 19 AFTER TESTING ITS SAFETY AND EFFICACY

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Received date: 24 July 2021 **Revised date:** 14 August 2021 **Accepted date:** 04 September 2021

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ABSTRACT

The COVID 19 infection is currently going to be the big threat for the worldwide health. It is turning out to the worldwide pandemic as declared by WHO. In current situation there is no antiviral therapy is available. The antivirals like remdisivir, Favipiravir is being used treat infection. The hydroxychloroquine can be used for prophylaxis for limited population only. By taking some background information of previous pandemic of SARS, Ebola virous, Machupo virus, Juninvirus, influenza H1N1, the convalescent plasma therapy is currently recommended for treatment of COVID 19 infection. There were pilot study shows the positive results with convalescent plasma treatment for COVID 19 infection. The convalescent plasma therapy can be proved effective against COVID 19 but should be used for treatment by testing safety and efficacy of convalescent plasma therapy. Therefore, most of the countries like China, USA, India going to perform safety and efficacy of Convalescent plasma therapy along with randomized trials before using for treatment.

KEYWORDS: COVID 19, Convalescent plasma therapy, US FDA, ICMR.

1. Convalescent plasma therapy

The convalescent plasma from is collected from the infected patient of covid-19 who had recovered from the infection and transfused to the new patient as a postexposure prophylaxis.[1] This convalescent plasma contains antibodies to severe acute respiratory syndrome-CoV-2 (SARS-CoV-2) that is COVID 19. This is one of the hopeful treatments on COVID 19 outbreaks.[2]

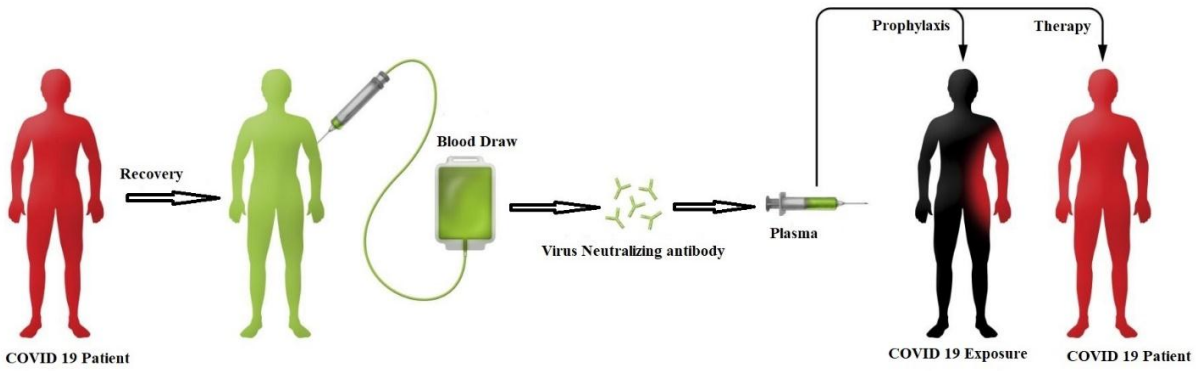

Fig. 1: Block diagram of convalescent plasma therapy.

2. Background

In the year of 2003 dated in between 20 March and 26 May, the study was carried out to evaluate the safety and efficacy of the convalescent plasma therapy at Prince of Wales Hospital, Hong Kong. This study was carried out on 80 SARS (Severe acute respiratory syndrome) patients. The gives the best results in the area of discharge from hospitalization and decreases the rate of

death. In this study the discharge of patient at day 22 with onset of SARS symptoms. The death rate and hospitalization were declined beyond 22 days. The discharge rate of 58.3% was observed at 22 day who were given the convalescent plasma before day 14 of infection which was 15.06 % previously. The discharge rate was 66.7% in the patient who were tested positive after testing with PCR and seronegative for SARS at time plasma infusion which was at 20% previously. Convalescent plasma therapy was used previously for the treatment of the Bolivian hemorrhagic fever that is Machupo virus, Argentinian hemorrhagic fever that is Juninvirus, Lassa fever and Ebola Virus. The mice infected from West Nile encephalitis were recovered after giving convalescent plasma of patients who were recovered from same disease.[1] The convalescent plasma therapy was proved last option for improvement of survival rate of SARS patients having sever infection even if taking methylprednisolone. There were several studies showed that there was a shorter hospital stay and lower mortality rate in convalescent plasma treated patients. At the time of Ebola virus outbreak in 2014, the WHO recommends the convalescent plasma treatment. In 2015, the protocol for treatment by convalescent plasma therapy for the treatment of Middle East respiratory syndrome. At time of 2009 influenza A H1N1 pandemic, there were significant results by convalescent plasma therapy. There was reduction in viral load after convalescent plasma therapy of the patients who were at intensive care. There were no as such adverse effect of convalescent plasma therapy. The results show that the convalescent plasma therapy is satisfying the safety and efficacy of SARS-CoV-2 infected patients.[3]

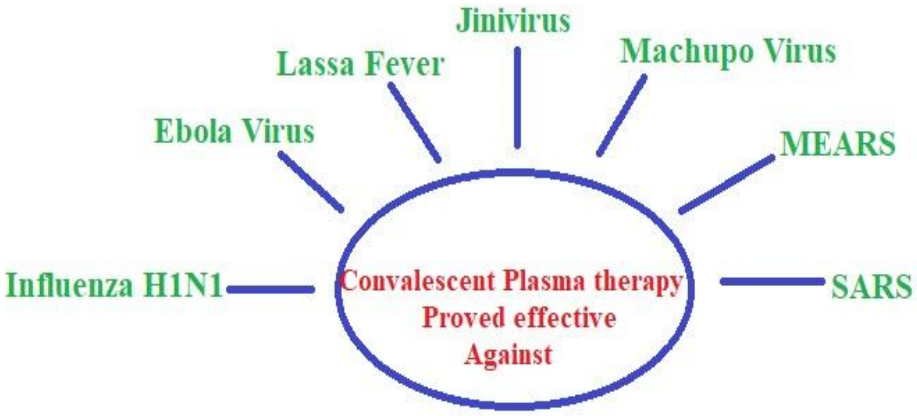

Fig. 2: Background behind convalescent plasma therapy.

3. Case study COVID 19 in China

The virological and clinical characteristics of the SARS, Middle east respiratory syndrome (MERS) and COVID 19 are similar that is important background for convalescent plasma therapy for the treatment of COVID 19 patients. On this ground there was pilot study was performed in three participating hospitals to carry out safety and efficacy of convalescent plasma treatments on ten severe COVID 19 patients. In this pilot study the 200 ml dose of convalescent plasma was given to 10 patients which was previously taken from COVID 19 recovered patients. That dose was well tolerated by the patients. There was significantly rise in neutralizing antibodies at high level which leads to disappearance of viremia. The clinical symptoms and paraclinical criteria improved within three days. The radiological examination showed varying degrees of absorption of lung lesions within the seven days. These results show that the convalescent plasma therapy proves the important option for severe COVID 19 which should be justified by randomized trials. The effect of convalescent plasma therapy shows improvement of clinical symptoms, reduction of pulmonary lesions on chest CT examinations, amelioration of routine laboratory criteria and pulmonary function, increase of neutralizing antibody titers and disappearance of SARS-CoV-2 RNA. In this study there were no as such serious adverse effects observed except evanescent facial res spot in two patients.[4]

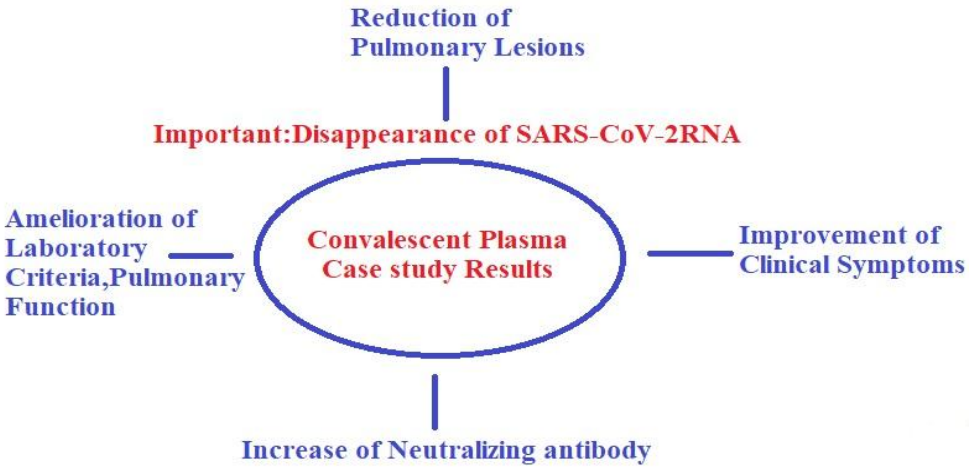

Fig. 3: Results of case study of COVID 19 in China.

4. US FDA recommendations for IND COVID 19 Convalescent Plasma

The US FDA has not approved the convalescent plasma therapy but it was regulated as the investigational product. It is under investigational new drug application (IND) under the regulatory guidelines available previously for IND. It can be treated as s single-patient emergency investigational new drug application.

4.1. Single patient emergency IND

The convalescent plasma therapy is currently not available for all patients. There is public health emergency due to COVID 19 pandemic, clinical trials are going on and national expanded access protocol is available, the convalescent plasma therapy can be used for the patients with serious or life threatening COVID 19 infections. For this purpose, the physician has to request for eIND for individual patients under the 21 CFR 312.310.

4.2. Patient eligibility

The patient eligibility should be decided according to the National Expanded Access Treatment Protocol. This protocol has following points to decide patient eligibility for eIND of COVID 19.

- The patient should be laboratory confirmed COVID 19 positive
- The patient condition must be critical or life threatening
  - Shortness of breath≥ 30/min. respiratory frequency
  - Blood oxygen saturation ≤93 %
  - The partial pressure of arterial oxygen to fraction of inspired oxygen ratio<300
  - Lung infiltrates >50% in 24 to 48 hrs.
- The patient with life threatening disease who shows respiratory failure, septic shock and multiple organ failure.
- The patient must be provided with informed consent or by any healthcare proxy.

4.3. Donor eligibility

The convalescent plasma should be collected from the patients fulfilling following criteria: -

- There should be documented evidence of COVID 19 tested by a diagnostic test
- The patient should be confirmed with positive serological test for SARS-CoV-2 antibodies after recovery
- There should not be any symptoms for at least 14 days prior the donation not necessary to negative COVID 19 diagnostic test.
- The male of female should be tested negative for Human leukocyte antigen antibodies (HLA)
- Female donors should not pregnant or having negative HLA antibodies.
- In case SARS-CoV-2 neutralizing antibody titers are available, the titer 1:160 are recommended. In case 1:80 can also be acceptable if previous is not available. The storage of samples for single patient eIND is not recommended

The convalescent plasma should be collected by the registered and licensed blood banks and they must follow their standard operating procedures and regulations. [(2)]

5. Current trend of convalescent plasma therapy in India

In India ICMR going to perform Phase II open Label randomized controlled study to assess the safety and efficacy of convalescent plasma therapy. In current situation ICMR does not recommends the convalescent plasma therapy as a treatment for COVID 19 beyond the clinical trial. The ICMR invites the letter from health institutions showing infrastructure and equipment facility available to carry out clinical trial for the study of safety and efficacy of convalescent plasma therapy in COVID 19 patients. The ICMR website shares a news from the THE HINDU dated 1 May 2020 “Plasma therapy is no silver bullet, to recommend it without undertaking a robust scientific study may cause more harm than good” as an opinion of Dr. Balram Bhargava, Director General, Indian council of Medical research. [(5)]

CONCLUSION

The COVID 19 infection is currently declared worldwide outbreak by WHO. The studies of previous outbreaks especially viral infection show positive results of convalescent plasma therapy. China, during current outbreak of COVID 19, was carried some pilot study of convalescent plasma therapy which shows effective results. Accordingly, US FDA gives guidelines for industry for investigational new drug application (IND) or eIND for convalescent plasma therapy and recommend criteria related to patient and donors. Although the safety and efficacy should be tested by randomized trials is the aim behind IND or eIND application. Indian Council for Medical research suggests the safety and efficacy study of convalescent plasma therapy and currently not been recommended for treatment of COVID 19 infection but randomized trials are recommended. The various studies do not show any serious and remarkable adverse effect of convalescent plasma therapy. In conclusion it can be said that convalescent plasma therapy is the effective for the treatment of COVID 19 infection but its safety and efficacy should be obtained prior the use.

Conflict of Interest

There is no conflict of interest with this article.

ACKNOWLEDGEMENT

The author is thankful to Dr. M. J. Chavan, Principal and Management of Amrutvahini College of Pharmacy, Sangamner, M.S., India

List of Abbreviations

COVID 19-Coronavirus disease 2019
SARS-Severe acute respiratory syndrome
MERS-Middle east respiratory syndrome
US FDA-United state Food and Drug Administration
IND-investigational New drug application
eIND-emergency investigational new drug application
WHO-World health Organization

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