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RECUPERATING PLASMA THERAPY AGAINST VIRAL INFECTION

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ABSTRACT

A passive immunization technique and recuperating plasma therapy, may be a better choice for viral infection treatment. Previously, it has been used to treat outbreaks of Ebola, influenza, MERS-CoV, and severe acute corona virus syndrome Respiratory viruses (SAR). The use of recuperating plasma during Spanish pulmonary influenza A (H1N1) (pandemic of 1918-1920) outbreak was widely accepted as its first application. Recuperating Plasma Therapy (CPT) appears to be an improvised supporting therapy for severely infected patients with COVID-19 until long-term treatment options are available. After the introduction of several pathogen reduction technologies, the plasma therapy has become more secure. The current pandemic has resulted in recuperating plasma therapy for controlling the viral infection. Generating protective antibodies and restoring endothelium glycocalyxx are two suggested mechanisms for the action of plasma recuperating therapy.

Keywords: recuperating plasma therapy, passive immunization technique, COVID-19, antibody

INTRODUCTION:

Immunity response develops against any disease either due to viral infection and administration vaccine for specific disease that triggers immune response. The active immune response takes time to generate antibodies and time differs depending upon the recipient's immune system **[1]**.

Vaccination is certainly a feasible goal, it is a preventative approach that has no use in the therapeutic setting. Contrarily, for the therapeutic environment, the use of antivirals is crucial **[2]**.

Financial costs are big issue with the limited number of antiviral agents currently available, unless they are provided free of charge to developing countries. In addition, production is difficult to scale up in a short span of time. Passive antibody administration is the only technology that can provide immediate immunity to susceptible people over a short period of time. Potential antibody sources for viral infections are human recuperating plasma from those people who have recovered from viral infection and preparation is made in certain animal hosts such as genetically engineered cow producing human antibodies **[3]**.

Plasma therapy:

Plasma therapy is also known recuperate plasma therapy. This is a medical procedure in which blood of previously infected but completely recovered patient, is infused to create antibodies in infected patient.

Standard operating procedure for recuperating plasma collection

In the course of plasma donation, plasma and blood cells are removed and segregated from the body using a machine known as plasmaphoresis. Plasma is stored and blood cells are transferred to the donor. Plasma products are stored as frozen plasma before they are used. With respect to plasma therapy in view of the present pandemic situation it is important to note the following practical points:

Plasma can only be obtained from selected recovered individual diagnosed with COVID-19 for minimum three weeks.

- At least two weeks must have elapsed since the full recovery to lessen the potential risk of SARS-CoV-2 in the blood.
- Anti-SARS-CoV-2 IgG titers must be calculated and the methods for inactivating the virus must be strictly followed.
- Suggested viral neutralization titer cut-off for COVID-19 recuperating plasma required to be at least ≥1: 160.
- Optimal dose of recuperating plasma to be prescribe to a COVID-19 patient ranges from 200 ml to 500 ml.

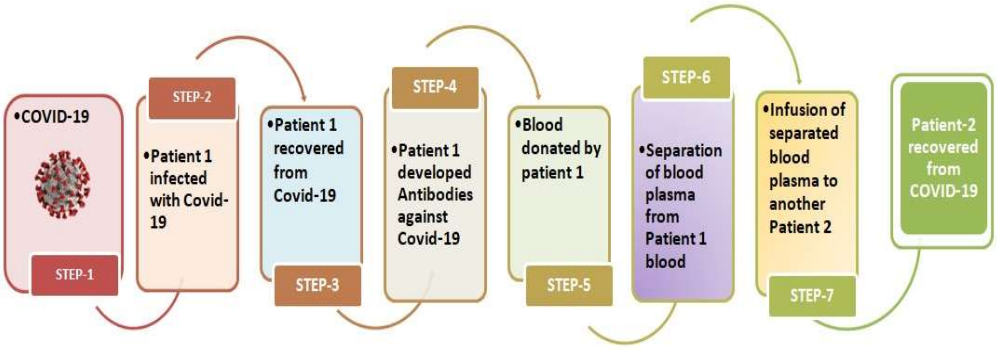


Figure 1: Steps involved during recuperating plasma therapy

Pathogen reduction technologies:

Numerous national authorities suggest that donor screening and conventional viral nucleic acid testing i.e. HIV, hepatitis C virus and hepatitis B virus nucleic acid testing would not be sufficiently adequate for making sure recuperating plasma safety in emergency situations **[4]**.

Under this situation additional virological tests and pathogen reduction technologies almost double the overall price of therapeutic dose. So many pathogen reduction technologies have been authorized and are available in the market.

Solvent/detergent filtered plasma causes small scale reduction in virus load, even though technology has been developed and is commonly used for large plasma pools. The technology is based on a set of steps: addition of 1% tri (n-butyl) phosphate-1% triton X-45, removal by oil extraction of solvent and detergent and at last sterile filtration **[5]**.

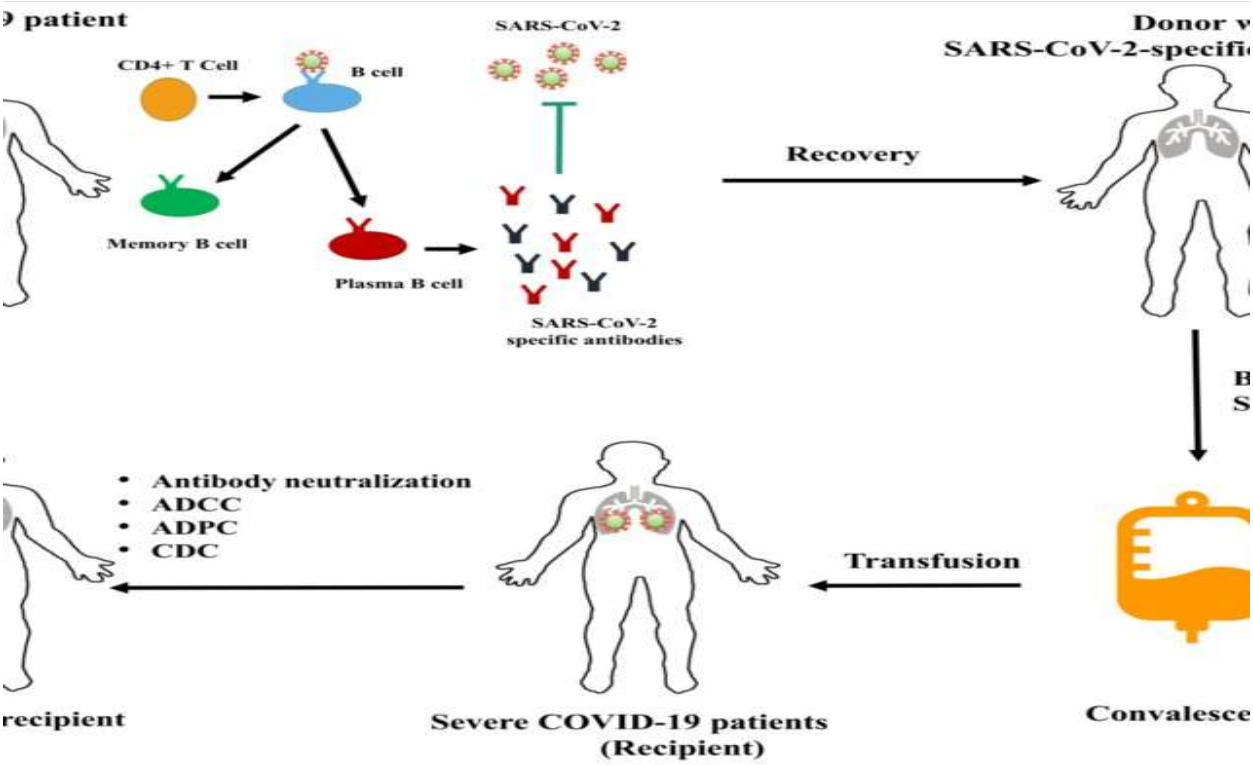
Large viruses like beta corona viruses could be eliminated by filtration through hollow fibres of 35 to 75 nm pore size while retaining IgG **[6]**.

Photo inactivation has become the standard for single unit inactivation in the presence of a photosensitizer in recent years; approved technologies usually involve combination of methylene blue and visible light **[7]** amotoselen and UV A **[8]** and riboflavin and UV B **[9]**.

Fatty acids may also be used for reduction of pathogens. Caprylic acid **[10]** and octanoic acid **[11]** have been reported to be effective for inactivating enveloped viruses. Plasma heat treatment has been used in the earlier days **[12]**; however there is a risk of aggregation of immunoglobulin **[13]**.

Action mechanism of recuperating plasma therapy

There is no full statement of the precise mechanism of action of recuperating plasma therapy. There are some presumptions: First and probably most important presumption is that recuperating plasma contains protective antibodies by neutralizing the pathogen, resulting to its elimination from circulation in the blood. Faster viral clearance would inhibit further replication and stimulation of the cytokine cascade **[14]**. Another presumption is that other healing factors, like preventing excess vascular leakage, procoagulant or antifibrinolytic factors, can be transmitted by recuperating plasma, restoring the endothelium glycocalyx **[15, 16]**.



Schematic mechanism of convalescent plasma therapy for COVID-19. ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; CDC, complement-dependent cytotoxicity [29]

History of recuperating plasma therapy

Recuperating plasma therapy has been used for the prevention and treatment of epidemic infections for more than hundred years **[17]**. It has been designed and implemented during the latest COVID-19 pandemic **[18]**.

Several researches performed during the pandemic concluded that recuperating plasma could be effective in reducing the risk

of mortality, as was later revealed by a meta-analysis conducted in 2006 by Luke *et al*. **[19]**, covering a total of 1703 patients out of 8 appropriate reports.

Reported use of recuperating plasma is several outbreaks are mentioned in following **Table 1**.

Table 1

S.N.	Name of pandemics	Year	References
1	Spanish flu	1917-1919	20
2	Measels	1930s	21
3	Arenaviruses	1950s to 1980s	22
4	Bunyaviruses	Mid 1980s	23
5	HIV/AIDS	1990s	24
6	Coronaviruses (SARS)	2002-2003	25
7	Influenza viruses	2009	26
8	Chikungunya virus	2005-2006 and onwards	27
9	Ebola virus	2014	28

CONCLUSION

This technology can provide immediate immunity to susceptible individuals over a short period of time is passive antibody administration. The most important presumption about the mechanism of plasma therapy is that, by neutralising the pathogen, it contains protective antibodies, resulting in its elimination from blood circulation. During the latest COVID-19 pandemic, the use of recuperant plasma that has been used for the prevention and treatment of epidemic infections for more than a hundred years was designed and implemented.

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