

Review Article

Convalescent Plasma Therapy for COVID-19 still has the potential to save lives - The ICMR PLACID study dissected

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ABSTRACT

Convalescent plasma therapy has been extensively used across the world and is believed to save the lives of COVID-19-positive patients. The early preprint release of ICMRs PLACID study results has set the cat among the pigeons. This study consisted of 464 patients across 25 cities in India, involving both government and private hospitals. Methodology and results have valid points on both sides of the argument. Its publication in a peer-reviewed journal is awaited so that the details can be ascertained accurately. In the meantime, CTP should not be denied to COVID-19 patients. We share our current practical recommendations for its use. AmberHealth.in is providing an excellent platform to connect patients to potential nearby donors in real-time. This is a simple, intuitive, and free website connected to various social media that has been developed as a service to society by Dr. Tanvi Sood and Mr. Nikhil Joy.

Keywords: Pandemic, SARS-CoV-2, Immunotherapy, Donor, Antibody titer, Social initiative

INTRODUCTION

With the current COVID-19 pandemic continuing unabated, all potentially beneficial strategies are being aggressively pursued.^[1] Convalescent plasma therapy (CPT) is one such option being used globally. Hence, the recent newspaper reports of the unfavorable outcome of ICMRs PLACID study are unfortunate.^[2] Does this study results prove that CPT is not beneficial and should no longer be offered to patients? The answer is a clear no.^[3,4] Let us examine the finer aspects of the critical issues and take a closer look.

PLACID STUDY PROS

The commendable aspects of PLACID study were as follows:^[2]

1. Prospective study involving 464 patients
2. Involved 39 hospitals from 25 cities belonging to 14 states or union territories across India (29 teaching public hospitals plus ten private hospitals)
3. Patients included group of hospitalized COVID-19 patients with moderate illness (PaO₂/FiO₂: 200–300 or respiratory rate >24/min and SpO₂ ≤93% on room air)
4. They were randomized to control (best standard of care [BSC]; 229 patients) or intervention (CPT + BSC; 235 cases) arm

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- In the intervention arm, all patients received two doses of 200 mL CPT given at interval of 24 h.

If this is the case, we should believe the results that the primary measure of outcome, that is, progression to severe disease ($\text{PaO}_2/\text{FiO}_2 < 100$) or day 28 mortality did not reduce after CPT.

PLACID STUDY CONS

Reasons, why ICMRs PLACID study results should be interpreted with more than a pinch of salt, are as follows:

- Conclusions regarding benefit (or otherwise) of CPT cannot be based on a single study.^[5] PubMed online search done on September 13, 2020, revealed 322 articles on CPT, of which 36 were randomized studies.^[6] By April 20, ICMR had received 99 applications to use the CDSCO generic protocol to conduct prospective studies using CPT.^[7] Their results are still awaited
- The PLACID study authors have been quoted to state that intervention arm patients did benefit by reduction in shortness of breath and fatigue.^[8] They also had a higher rate of conversion to negative COVID-19 viral RNA levels^[9]
- The fundamental basis of the PLACID study (or any study investigating CPT) is that the infused plasma has sufficient neutralizing antibodies against COVID-19. This requires measurement of the antibody level before using the convalescent plasma to ensure that levels are above $>1:640$.^[3] Antibody titers were not reported in the PLACID study.^[2] Hence, we do not know how many patients in the intervention arm actually received “placebo” in the form of CPT without protective antibodies. According to some reports, this could be as high as two-thirds of the patients^[10]
- Publication is neither full text nor peer-reviewed – report is available only on medRxiv, a website that offers access to preprint articles before they are peer-reviewed (which is a rigorous process of scientific scrutiny of data before it is deemed robust enough to be accepted for publication in a medical journal).

CURRENT PRACTICAL RECOMMENDATIONS FOR CPT

Considering these facts, we believe that hospitalized patients with COVID-19 should continue to be offered the potential benefit of CPT – which has been proven to save lives in other trials.^[11-15]

- CPT for COVID-19 has been shown in clinical trials to reduce mortality of up to 30–50% in seriously ill COVID-19 patients
- The decision about which COVID-19 patient requires CPT is based on multiple factors – severity of illness,

vital parameters such as oxygen saturation, speed of deterioration, other comorbidities, and response to therapy. If CPT is used early in the course, it has a better chance of working. We have seen patients with Spo_2 of 60% respond dramatically to a single dose of CPT

- The plasma donor needs to be selected carefully using the following criteria
 - Donor should have been conclusively proven to have suffered from COVID-19 – documented by positive RT-PCR (swab test) COVID test report at the time of diagnosis
 - At least 28 days post-recovery from COVID-19 symptoms
 - At least 14 days post-negative COVID-19 RT-PCR report
 - Fulfill other criteria used for usual blood donors:
 - Age between 18 and 60 years
 - Women should not have been pregnant earlier
 - Weight should be more than 50 kg
 - No kidney, liver, lung, and heart diseases
 - No uncontrolled diabetes or high blood pressure.
- Donors should not have the fear that their immunity will go down by donating plasma making them more vulnerable to COVID-19 re-infection. Less than 10% of the antibodies are removed during the donation. And even, this is replenished automatically in the body within 48 h
- The plasma antibody levels are not the only line of defense in donors’ body. They also have cellular immunity through memory B cells and T Cells. This is why even after re-infection, patients usually have no or only mild symptoms
- A donor can safely give plasma every 15 days. One health worker in West Bengal has already donated 50 times.^[16]
- Plasma donation procedure is done in a licensed blood bank. It involves apheresis, in which the blood from the donor is continuously centrifuged at 4800 RPM, plasma taken into donor bag, and the rest of the blood continuously returned to the donor. The procedure usually takes about 30 min and is as safe as a normal blood donation.

CONCLUSION

While the demand for CPT remains unabated, there is a significant mismatch between demand and supply. Hence, there is an urgent need to facilitate the interaction between patients in need and donors in the vicinity who are eligible as well as willing to donate. Having faced six COVID-19-positive members in the family (including themselves) and one parent in ICU, Dr. Tanvi Sood and her husband Mr. Nikhil Joy had to scramble to find a suitable CTP donor.^[17] Their network of friends and relative made it a reality. Their

parent received CPT and quickly recovered. Being a doctor and an IT specialist, this newly-wed couple decided to make it their mission to give back to society. They worked hard and came up with the ideal solution, www.AmberHealth.in.^[18] This website and its connected social media platforms help the cause in a very intuitive and simple manner. To ensure only eligible and truly motivated donors get on board, they have a crisp FAQ and an online enrollment process. AmberHealth.in got a boost when Manipal Hospital officially decided to link it in their plasma donor initiative. Already thousands of patients have benefited from their selfless service. Anyone who requires their help can contact them at hello@amberhealth.in or +91-9910005181.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest. The author Purvish M Parikh is the editor of this journal. He does not have any competing interests.

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