Use of Convalescent Plasma in the treatment of COVID-19 patients

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Introduction to Convalescent Plasma

Use of convalescent plasma, which is described as convalescent plasma therapy (CPT) is a form immunization, acquired passively. It is primarily used to treat or prevent disease through transfusion of an antibody-containing plasma. It involves collection of plasma from a convalescent person and infuse to a person as therapeutic or prophylactic measure. CPT was used first used more than 100 years ago. It was used on a small scale to treat various diseases such as poliomyelitis, measles and mumps (Transfus Apher Sci 59, 2020) . However, during Spanish flu pandemic CPT was used on a larger scale and it proved to be an effective strategy in reducing mortality risks in infected persons.

When CPT was first initiated, the plasma was usually collected from animals including rabbits and horses. Currently, donors who fit a specific donor selection criteria are allowed to donate convalescent blood products (CBP). As seen in cases of Ebola, Spanish flu, and recently in the prevention of COVID-19, it is used when treatment or vaccine is not available for an infectious disease. When collecting CBP, the donor must have recovered from the targeted disease and has humoral immunity. The plasma must contain high titer human immunoglobulins. The administration is through the intravenous or intramuscular route. Different forms of CBP can be used, including convalescent whole blood, convalescent plasma, and convalescent serum. Apheresis plasma is preferable as it can be collected in larger volumes, it is frequently donated, and it does not affect hemoglobin.CBP usage in areas other than those where it was collected has proven, in some cases, to be ineffective due to the possibility of strain variation.

Convid-19 and Convalescent Plasma

On August 23, 2020 FDA issued conditional approval for CPTan emergency use authorization (EUA) for COVID-19 cases.,2020. It has been used in severe and hospitalized patients suffering from the virus. However, randomized clinical trials are still continued as the data remains insufficient as initial therapy was unrandomized. The action of CP remains unclear due to the fact that the patient received additional therapy such as antivirals, antibiotics, or antifungals.

A research was done on 10 patients with severe cases of COVID. The patients were given a dose of 200ml, in which the CP contained neutralized antibody titers of 1:640. It was reported that the patients' neutralized antibodies increased or were maintained at high levels. Provided that an increase in lymphocyte count and a decrease in C-reactive protein have been observed. Varying degrees of absorption of lung lesion have been shown on radiological examinations. Overall, the study reported no major side effects and that it can improve outcome as well as neutralize viremia in severe cases.

Symptom improvement, especially fever, cough, shortness of breath, and chest pain improved greatly after the transfusion. After CP treatment, two patients weaned from mechanical ventilation to high-flow nasal cannula, one patient discontinued high-flow nasal cannula, and one patient was shifted from conventional nasal cannula oxygenation to intermittent oxygenation.

According to the FDA, no specific test for measuring neutralizing antibodies is currently available and the antibody titer in recovered patients is highly variable. In addition, this form of therapy may not be as effective in patients with pre-existing levels of neutralizing antibody titers comparable to the levels in donors. Analyses suggest that high-titer antibodies are more effective particularly when taken within 72 hours of diagnosis. CP as a potential therapeutic option should be given as early as possible before the disease progresses in order to attain optimum results.

PLACID, a large trial in India, has reported that CP has no effect on moderate cases even when recipients had low or no antibodies. A randomized, double-blinded, placebo-controlled multicenter trial in Argentina enrolled hospitalized patients a median of 8 days from onset of symptoms using high titer antibodies with no clinical or mortality benefits. Eligible donors were men or nulliparous women who were aged between 18 and 65 years, weighed more than 50 kg, had received a diagnosis of covid-19 confirmed by a RT-PCR test result, and had experienced symptoms of covid-19 with at least fever and cough. Another study, also in Argentina, observed a favorable outcome in elderly patients administering CP within three days of symptom onset.

According to available data, serious adverse effects are infrequent after the administration of CP and those reported were not directly related to it. The risks observed were associated with plasma infusions including transfusion-transmitted diseases (HIV, HBV, HCV), allergic reactions anaphylactic reactions, febrile nonhemolytic reactions, transfusion-associated acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), hypothermia, metabolic disorders, post-transfusion purpura, and hemolytic reactions. Additional theoretical risks include of antibody-dependent enhancement and suppressed long-term immunity. Effectiveness of convalescent plasma in pregnancy and children is yet to be evaluated. Several clinical trials are ongoing to evaluate its efficiency.

To conclude, studies on convalescent plasma are still ongoing and it has not been approved nor amended so far. CP has proven to be safe, reduce mortality in severe cases, increase neutralizing antibody titer and disappearance of SARS-CoV-2 RNA, and improvement of symptoms. The challenge is to find both suitable patients and suitable plasma donors. Additionally, this challenge could limit the use of convalescent plasma to a small subset of patients.

References

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