Original Article

Effectiveness of Plasma Therapy in Patients with COVID-19 Infection – A Retrospective Record-based Descriptive Study

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Abstract

Introduction: The COVID-19 pandemic presented an unprecedented challenge to the medical community, leading to numerous therapeutic interventions being explored. Convalescent plasma therapy (CPT), derived from recovered COVID-19 patients, was one such treatment used in the absence of proven therapies. However, its efficacy remained a topic of debate. **Materials and Methods:** This retrospective study aimed to assess the effectiveness of CPT in patients admitted to the intensive care unit (ICU) with moderate-to-severe COVID-19 infection. Data included comorbidities, treatment regimens, partial pressure of oxygen/fraction of inspired oxygen (PaO2/FiO2) ratios, oxygen therapy duration, and outcomes. Patients were divided into groups based on CPT receipt. Statistical analysis was performed to compare the two groups. **Results:** Out of 72 patients, 36 received CPT, and 36 did not. Patients who received CPT had longer ICU and hospital stays. The mortality rate was higher in the CPT group (50%) compared to the non-CPT group (22.2%). Patients with comorbidities experienced higher mortality rates. Notably, the CPT group exhibited improved PaO2/FiO2 ratios on day 2. Complications related to CPT were minimal. **Conclusion:** The use of CPT in COVID-19 treatment did not impact overall survival or hospital stay duration.

Keywords: Convalescent plasma therapy, COVID-19, oxygen therapy, partial pressure of oxygen/fraction of inspired oxygen ratio, SARS COV 2

Introduction

The medical field faced a huge challenge due to the surge of novel coronavirus COVID-19 in recent years. The pandemic has created significant mortality and morbidity in India as well as across the globe.[1] Since this was a new virus and there was no specific proven treatment, many therapies were tried initially including antiviral agents, immunomodulators, monoclonal antibodies, steroids, and convalescent plasma therapy (CPT).[2] A few treatments proved effective while a few did not and subsequently, they were excluded from the treatment guidelines as the scientific evidence emerged.[3] Although most parts of the world vaccine is available and a significant population is fully vaccinated, a few of the vaccines provide suboptimal protection.[4] Moreover, new variants of the virus are emerging which may make current vaccines less effective. This calls for a further look into the data of the previous treatments used for COVID-19.[5]

One of the treatments used during the pandemic was CPT. It was derived from the individuals who recovered from COVID-19 infection. CPT has been used effectively in many other human respiratory virus diseases in the past.[6] Since there was no effective proven treatment against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), this treatment was tried in many hospitals. The effectiveness of plasma therapy was debated initially, since very limited data were available, some studies proved it as effective and some as ineffective.[7]

In our institution, convalescent plasma derived from people who recently recovered from COVID-19 infection with a neutralizing antibody titer above 1:640 was transfused in patients admitted to the intensive care unit (ICU) with moderate-to-severe COVID-19 infection. This study was

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conducted to assess the effectiveness of CPT by reviewing the case records of the patients who had been admitted to the ICU with COVID-19 infection.

Materials and Methods

Study design and study settings

A retrospective record-based study was designed. The study was conducted on patients who tested positive for the reverse transcription polymerase chain reaction (RT-PCR) test for COVID-19 and were admitted to the ICU of Justice K S Hegde Charitable Hospital from June 2020 to November 2020.

Ethical permission and patient consent

The study was initiated after obtaining the Institutional Ethics Committee clearance (Reg. No: EC/NEW/INST/2020/834). Patient consent was not required as the study was retrospective and record-based.

Sample size

Records of 72 patients who tested positive for the RT-PCR test for COVID-19, admitted to the intensive care were analyzed. The records that did not have proper documentation of arterial blood gas analysis and patients who died within 48 h of admission were excluded from the study.

Method of collection of data

The primary objective of the study was to assess the duration of the ICU stay in patients who underwent CPT for SARS-CoV-2. The secondary objective was to assess the partial pressure of oxygen/fraction of inspired oxygen ($PaO_2/FiO_{2)}$ ratio at 48 h of post-plasma therapy, the requirement of oxygen therapy, and the mortality rate. The following information was gathered: the number of days since the onset of symptoms, the number of days until RT-PCR confirmed the presence of COVID-19, the number of days from the onset of symptoms to the beginning of treatment, the number of days from the onset of symptoms to the beginning of plasma therapy, the comorbidities involved, the treatment administered for COVID 19, the PaO2/FiO2 ratio, the ventilator settings and mode of oxygen therapy before beginning treatment and plasma therapy, the number of days of oxygen therapy requirement, inflammatory markers, the hospital and intensive care unit discharge, the treatment outcome, and complications.

Once data were collected, patients were divided into two groups according to their reception of plasma therapy status, Group P was those who received plasma therapy and Group N was those who did not receive plasma therapy and managed only with oxygen and antiviral drugs.

Statistical analysis

The collected data was entered in the MS Excel master sheet. Both groups were compared for PaO_2/FiO_2 ratio, oxygen therapy requirement, outcome, and complications by statistical methods. Data were tabulated and analyzed using MS Excel and SPSS version 22. Categorical data were presented as percentages (%). Qualitative variables were analyzed using Pearson's Chi-square test and Fisher exact test. Quantitative variables were presented using mean and standard deviation and analyzed using the Student's-*t*-test. Logistic regression analysis was used to calculate the adjusted odds ratio with a 95% confidence interval.

Results

A total of 72 patients were included in the study, 36 patients were in Group P (who received plasma therapy) and 36 patients were in Group N (who did not receive plasma therapy). Demographic data were comparable in both groups. Both the groups were comparable in having comorbidities such as diabetes mellitus, hypertension, and ischemic heart disease [Table 1].

In both groups, 75% of the patients had one or more associated comorbidities. Out of 36 patients who received plasma therapy, 33 received 1 pint of plasma whereas 3 patients received 2 pints of plasma. In Group P, 50% (18) of patients died whereas in Group N, only 22.2% (8) of patients died ($P = 0.014$) [Figure 1].

It was noted that the death rate was higher in patients with comorbidity (42.6%) than in those who did not have any comorbidity (16.7%) which was significant ($P < 0.05$).

Most of the patients had received remdesivir, dexamethasone, enoxaparin, Vitamin C, and zinc as a treatment for SARS-CoV-19 [Figure 2].

The onset of symptoms to admission to the hospital in Group P was 5.25 days and Group N was 5.13 days. The onset of symptoms to plasma therapy was 8.4 days. After plasma therapy, ICU stay was 7.25 days, received oxygen therapy 7.52 days, and hospital stay was 10.72 days. The number of days from admission to death was 13.22 days in Group P and 7.3 days in Group N. The total number of days of ICU stay in Group P was 10.5 ± 6.63 days and Group N was 5.97 ± 3.36 days, hospital stay in Group P was 14.17 ± 8.01 days and Group N was 10.69 ± 4.28 days. The oxygen therapy was given in Group P for 10.53 ± 6.48 days and Group N for 5.56 ± 3.47 days which were clinically significant ($P < 0.05$). The number of days from admission

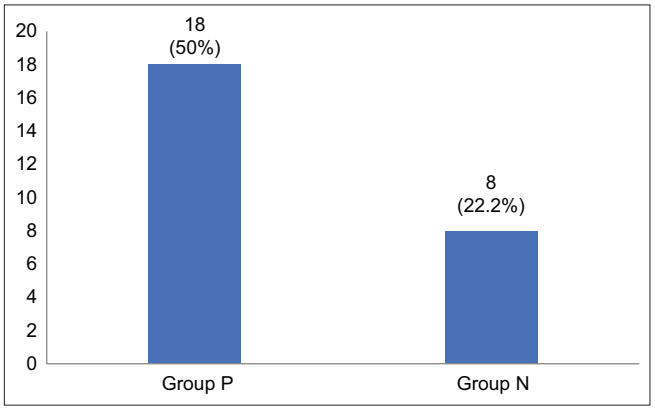

Figure 1: The number of deaths in Group P and Group N

to death in Group P was 13.22 ± 7.77 and in Group N was 8.25 ± 4.62 days. Baseline SPO2 in Group P was 93.28 ± 5.12 and in Group N was 94.28 ± 4.46 and day 2 SPO2 in Group P was 94.42 ± 4.94 and Group N was 96.06 ± 3.88. The PaO2/FiO2 ratio in Group P was 213.8 ± 127.32 and in Group N was 307.29 ± 142.46. On day 2, the PaO2/Fio2 ratio in Group P was 233.24 ± 198.50 and Group N was 247.3 ± 153.76 which was clinically insignificant [Table 2]. Complications such as allergic reactions and anaphylaxis were not reported in patients who received plasma therapy.

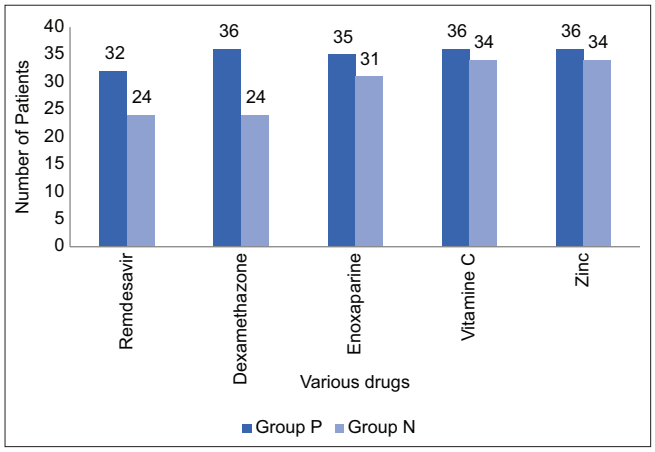

Figure 2: Various drugs used in COVID-19 received by patients, x-axis -Number of Patients

Table 1: The demographic data and percentage of comorbidities in the Group P and Group N patients

Parameter	Group P, *n* (%)	Group N, *n* (%)	*P*
Male	26 (72.2)	26 (72.2)	1
Female	10 (27.8)	10 (27.8)	
Age (mean±SD)	61.4±14.33	59.94±14.71	0.728
Number of associated comorbidities			
No comorbidities	9 (25)	9 (25)	0.846
One comorbidities	8 (22.2)	10 (27.8)	
Two or more comorbidities	19 (52.8)	17 (47.2)	

SD: Standard deviation

Discussion

The present study noted that the patients who received CPT had a longer duration of ICU stay and hospital stay. Convalescent plasma was used only in patients with severe disease and who were already on oxygen therapy, hence there could be chances of selection bias. A systemic review by Klassen *et al*. showed that early use of CPT with a higher titer had better outcomes when compared with late use of CPT.[8] If the patients had gotten CPT early, the outcome would probably have been better. Using CPT as a last resort would have caused poor outcomes for the CPT.

There was also improvement in PaO_2/FiO_2 on day 2 in patients who received plasma therapy compared to those who had not received it. This is an indication that CPT had some benefits which reduced the severity of the disease. However, the end result showed that there was not much of a survival benefit, in fact, the death rate was higher in patients who received plasma therapy. Our study findings are similar to a study conducted by ICMR, where there was an initial improvement in symptoms and oxygenation parameters, CPT did not improve the outcome of the mortality.[9] Focosi *et al*., in their study, have advised against indiscriminate use of CPT for COVID-19 and also advised to use it at the early stage of COVID-19 (3–7 days from the onset of the symptoms, but not later than 10 days).[10] The studies conducted by Li *et al*., in China and Gharbharan *et al*., in the Netherlands also showed no significant benefit of CPT.[11,12]

The CPT was used with the rationale of neutralizing the virus with antibodies present in the convalescent phase. However, those patients with COVID-19 who were afebrile, were beyond the viremia phase and the symptoms were probably due to the antibodies against the host tissues such as the lungs. Another possible explanation is increased oxygen demand secondary to microembolism in the lungs caused by a widespread inflammatory response to the viral infection.[13] In both instances, convalescent plasma may not have any significant role in the pathophysiology. However, blood and blood product transfusion are known to be immunosuppressant. Dexamethasone (proven to be effective if used early) acts

Table 2: Comparison of various parameters between Group P and Group N

Parameters	Group P	Group N	*P*
Number of days from onset of symptoms to admission	5.25	5.13	0.893
Number of days from onset of symptoms to plasma therapy	8.4	0	NA
Number of days in the ICU	10.5±6.63	5.97±3.36	0.001
Number of days in the hospital	14.17±8.01	10.69±4.28	0.026
Number of days from admission to death	13.22±7.77	8.25±4.62	0.108
Number of days of oxygen therapy	10.53±6.48	5.56±3.47	0.001
Baseline SpO_2	93.28±5.12	94.28±4.46	0.380
Day 2 SpO_2	94.42±4.94	96.06±3.88	0.122
Baseline PaO_2/FiO_2 ratio	213.8±127.32	307.29±147.46	0.004
Day 2 PaO_2/FiO_2 ratio	233.24±198.5	247.3±153.76	0.738

NA: Not applicable as only one group underwent plasma therapy, ICU: Intensive care unit, PaO_2/FiO_2 ratio: Partial pressure of oxygen/fraction of inspired oxygen ratio

by decreasing the immune and inflammatory response and hasten recovery in such patients. Therefore, CPT might have produced some beneficial effects among patients who did not receive systemic steroids early on during the pandemic. In the current study, most of the patients received systemic steroids once there was an increase in the need for oxygen.[14]

In desperate situations, the healthcare team and patient attendants get solace in performing some treatment or act of sympathy purportedly to help the patient. Since there was no other known or accessible therapeutic option in the early stages of the pandemic, CPT may have offered some degree of satisfaction to both of these communities. Later, despite numerous alternative interventions being offered, none of them were successful, leaving all onlookers in shock, helplessness, and desperation. Higher mortality in the CPT group can be readily explained if a treatment technique fails during such times, which is understandable.

The clinical parameters of the severity of the disease also point to the same and explain the worse outcome in the CPT group.[15] Although in our study, there were no immediate side effects noted, transfusion-related reactions cannot be ruled out in CPT. Since the other drugs used such as steroids and antivirals also have a significant impact on the outcome, it is difficult to comment on the effectiveness of the CPT alone.[16]

Multiple comorbidities greatly impacted the outcome of the disease as death rates and severity were higher than those with no comorbidities or single comorbidities. Sanyaolu *et al*. conducted a meta-analysis and noted that patients with comorbidities were susceptible to getting COVID-19 infection as well as severe disease.[17]

Limitations of the study

The limitations of the study are the smaller sample size since many patients had to be excluded from the study due to improper documentation and it is a retrospective record-based study. CPT was given to those patients who had severe disease in Group P because of the lack of availability of CPT.

Conclusion

Patients who received CPT had longer ICU and hospital stays. The mortality rate was higher in the CPT group compared to the non-CPT group. Patients with comorbidities experienced higher mortality rates. The CPT group exhibited improved PaO2/FiO2 ratios on day 2. Complications related to CPT were minimal. The use of CPT in COVID-19 treatment did not impact overall survival or hospital stay duration.

Ethical approval and patient consent

a. This study has been approved by the institute ethical committee with approval letter number – (Reg. No: EC/NEW/INST/2020/834)
b. This study has been conducted following the ethical principles mentioned in the Declaration of Helsinki (2013)
c. Patient consent was not required for the retrospective study.

Authors contribution

All the authors are equally involved in designing the entire work and contributed in making necessary corrections and revisions of the manuscript.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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