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Original Article

Pathology Section

Single Donor Plasmapheresis for COVID-19: An Experience from a Tertiary Care Hospital Based Blood Centre

ARCHANA L KHADE[1], SANDHYA V POFLEE[2], SANJAY N PARATE[3], SWATI B GADHAVE[4], VEDITA S GOLHAR[5], DINKAR T KUMBHALKAR[6]

ABSTRACT

Introduction: Corona Virus Disease-2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) became a global health problem since December 2019. No single treatment was found to be effective against COVID-19. Transfusion of COVID Convalescent Plasma (CCP) was found to be a useful and logistically feasible therapeutic strategy in COVID-19.

Aim: To study the feasibility of single donor plasmapheresis for COVID-19, to analyse statistical significance of clinico-demographical data and biochemical parameters of convalescent plasmapheresis donors and to further study the adverse reactions and technical problems that occurred during the procedure of single donor plasmapheresis.

Materials and Methods: A prospective observational study was carried out over a period of 10 months from June 2020 to March 2021. The study included 235 screened donors and 50 procedures for single donor plasmapheresis (SDPs). Donors were selected as per the standard criteria given by Indian Council of Medical Research (ICMR). All plasmapheresis procedures were performed on an automated blood cell separator. The results were tabulated and statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software.

Results: Out of 235 prospective CCP donors, 164 (69.78%) were found eligible. The causes of non eligibility donors were unwillingness to donate, absence of SARS-CoV-2 antibody, Transfusion Transmitted Disease (TTD) positivity, and improper haematological parameters. Actual plasma donations were carried out in 50 (21.27%) eligible donors. Therapeutically needed amount of CCP (400 mL) could be collected from most of the donors. Adverse reactions were seen in 4 (8%) donors.

Conclusion: Adequate amount of CCP could be collected by single donor plasmapheresis with satisfactory technical support. The procedure was well accepted by the prescreened donors with minimum adverse reactions.

Keywords: Adverse reaction, Apheresis procedure, Convalescent plasma, Donors parameters

INTRODUCTION

The COVID-19 is caused by novel severe acute respiratory SARS-CoV-2. The viral disease had spread all over world, became a global health emergency within short period of time and was declared as pandemic by World Health Organisation (WHO) on 11 March 2020 [1].

Since its outbreak, various treatment modalities were tried especially in moderate to severe cases [2,3]. Treatment plan consisted of mainly supportive care with supplemental oxygen, mechanical ventilation along with medicines and infusion of CCP in selected cases [4].

World Health Organisation recommended CCP administration for its potential benefit of providing antibodies that may neutralise infectivity of SARS-COV-2 [5]. Reports of encouraging results with passive immunisation in the form of Convalescent Plasma (CP) were published in the form of case series and controlled clinical trials [6-8]. Blood center based in tertiary care hospital received guidelines from ICMR and Government directives to carry out : SDPs for collection, storage and issue of CCP in blood centre premises [9,10]. The SDPs using newly installed automated blood cell separator (apheresis machine) was carried out for the first time in blood centre.

Study Objectives

- To study feasibility of single donor plasmapheresis for COVID 19, in blood center
- To analyse statistical significance of clinico-demographical data and biochemical parameters of CCP donors,
- To study the adverse reactions and outcome of the procedure.

MATERIALS AND METHODS

A prospective observational study was undertaken at Blood Centre of Government Medical College and Hospital, Nagpur, Maharashtra, India, from June 2020 to March 2021. Ethical approval for this study was obtained from the Institutional Ethical Committee (No.3571/EC/Pharmac/GMC/NGP dated 27/12/2021). List of potential donors for CCP collection was obtained from the hospital record of the Institute.

Inclusion and exclusion criteria: Symptomatic patients in COVID wards, who were admitted, treated and cured of COVID-19 disease, were considered for CCP donation. Selection of donors for single donor plasmapheresis was performed by using guidelines issued by National Authority of India for the clinical trial of CCP in COVID-19 patients [9]. The eligibility criteria for CP donation were same as that of whole blood donation with following added specific criteria [9,11].

- Males or nulliparous donors of weight >50 kg.
- Prior diagnosis of COVID-19 documented by a laboratory test (real time-polymerase chain reaction) with symptomatic disease with at least fever, cough or chest x-ray infiltrates and complete resolution of symptoms at least 28 days prior to donation.

Donors who had transfusion of blood products in last 8 weeks and COVID diagnosis more than 4 months prior were not considered for CCP donation.

Study Procedure

All safety protocols and guidelines regarding COVID-19 disease given by National Blood Transfusion Council of India (NBTC) were strictly followed by all staff members and donors throughout the study period [12]. All the prospective donors were counselled properly and then screened for demographic details like age, sex, weight, and

height, address and contact number. The essential haematological, biochemical and serological parameters of donors, who fulfilled the basic criteria for donation, were evaluated as follows- For pre-donation screening tests, 10 mL of venous blood was collected in two Ethylene Diamine Tetraacetic Acid (EDTA) anticoagulated vacutainer tubes and two plain vacutainer tubes from each donor. Complete blood count including haemoglobin (Hb), haematocrit (Hct), total and differential white blood cell count and platelet count were performed on calibrated, automated cell counter.

Total serum proteins estimation was done using automated biochemistry analyser. Anti SARS-CoV-2 antibody screening was done by immunoassay method and antibody kits recommended by ICMR. Blood grouping and testing for Transfusion Transmitted Diseases (TTD) that included Human Immunodeficiency Viruses (HIV1 and 2), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), syphilis and malaria were done by standard procedure.

The eligible and willing donor was given an appointment next day for CCP donation. Donor demographical data such as age, gender, and weight, height and laboratory details such as blood group, Hb, Hct, and platelet count were entered into the machine. The machine then displayed details of actual plasmapheresis procedure such as total time required for procedure, total blood volume that will be processed, and amount of anticoagulant Acid-Citrate-Dextrose (ACD) that will be used and the same were recorded in donor proforma. All the donors were disease free at the time of donation.

The donor was explained the procedure of plasmapheresis in details in the language he/she could understand and written informed consent was obtained from the donor before starting the procedure.

All apheresis procedures for collection of CCP were performed by trained apheresis team on the latest-generation Trima Accel cell separator (version 6.0, Terumo) and recommended plasmapheresis kits. Standard Operating Procedure (SOP) and manufacturer's instructions were strictly adhered to. A single, smooth prick with 18 g sterile needle was given by an expert phlebotomist to connect the donor to the machine and given comfortable arm position. Prophylactic oral chewable calcium tablets were given to every donor to prevent citrate related adverse reactions. During whole procedure, the machine display screen was closely monitored for specific instructions.

As per the guidelines issued [9] total 400 mL of plasma was collected in two bags i.e. two bags each of 200 mL. The collected plasma bags were stored at -40°C. Additional 50 mL of CCP was collected in separate aliquots for SARS-COV2 neutralising antibody titre estimation and stored at -80°C. On completion of procedure, the needle was taken out gently. After giving compression for 10 minutes, adhesive bandage strip was applied at the prick site. Post procedure, donors were given oral fluids, beverages and asked to take rest, observed for 2 hours in blood centre and then allowed to leave.

STATISTICAL ANALYSIS

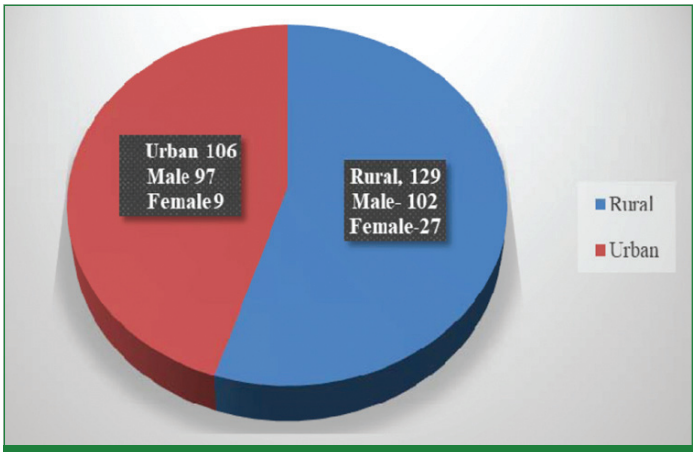
The results were tabulated and statistical analysis was performed using Statistical Package for Social Sciences (SPSS) software. The collected data was expressed in the form of mean±Standard Deviation (SD), frequency and percentage.

RESULTS

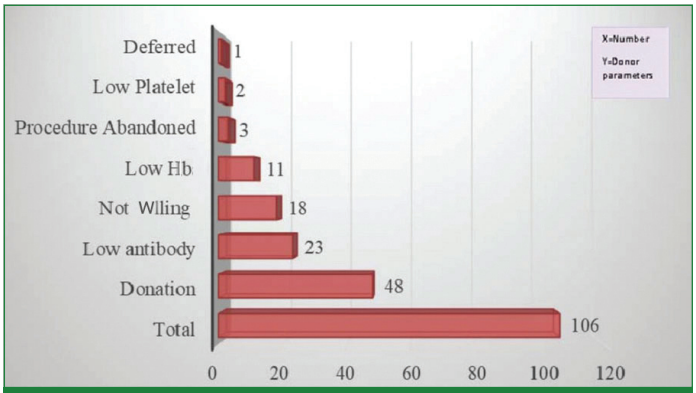
In the present study, total 235 numbers of donors were enrolled for single donor plasmapheresis.

Out of these, 106 donors were from urban area and 129 were from rural area [Table/Fig-1].

Out of 106 urban donors, 69 were eligible for donation and 37 were not eligible due to various reasons as shown in bar diagram [Table/Fig-2]. Out of 69 eligible urban donors, SDPs were carried out in 48 donors. 18 urban donors never turn up for donation to our blood centre even after repeated telephonic reminders. In three urban eligible urban donors, procedure had to be abandoned due to errors displayed on machine monitor.



[Table/Fig-1]: Pie diagram showing distribution of total enrolled donors for CCP donation (n=235).



[Table/Fig-2]: Bar diagram showing profile of prospective urban donors (N=106).

Out of 129 rural donors, 95 donors were eligible; actual donation was done by only two donors.

Thus total SDPs were carried in 50 donors (48 urban and 2 rural). All procedures were performed on latest generation Trima Accel cell separator (version 6.0, Terumo) which works on centrifugal separation.

Total 49 donors were males and one was female. The age ranged from 25 years to 58 years, with the mean age of 37 years. The mean weight and height was 73.06 kilogram (kg) and 1.73 meter^2 (m^2) respectively. The mean body mass index was 24.36 kg/m^2.

The mean haemoglobin value was 14.27 gm/dL, hemotocrit of 43.15%, serum protein 7.1 gm/dL and anti SARS-CoV-2 antibody was 8.97. Most common blood group was B positive in 18 donors followed by blood group A positive 15. The mean total volume of blood and mean volume of blood processed was 4803.26 mL and 1882 mL respectively, while mean ACD used was 206 mL. Average time required to collect adequate amount of plasma was 38.9 minutes. [Table/Fig-3] showed the details of demographic profile, haematological and serological parameters of 50 donors.

Direct relationship was seen between 1) body mass index (BMI) with volume of blood processed and ACD used, and 2) haematocrit with volume processed and time required for procedure on calculation of p-value. The statistical analysis of these parameters is shown in [Table/Fig-4]. All the parameters correlated with statistically significant p-value.

Out of 50 procedures, 400 mL of plasma was collected from 47 donors.

In three donors only 200 mL of plasma was collected. In two donors the procedure had to be discontinued mid-way due to development of hypotension in the donors. Machine itself calculated less plasma volume to be collected for the single female donor, depending upon her haematological parameters. A single eligible donor had donated 400 mL of CCP each, on two separate occasion within one month period.

Donor parameters	Statistical values, mean±SD (range)
Demography	
Age in years, median (range)	37 (25-58)
Gender (Female: Male)	1:49
Weight (kilogram)	73.06±9.36 (54-105)
Height (meter)	1.73± 0.062 (1.53-1.88)
Body mass index (Kg/m^2)	24.36±3.54 (18.04-34.78)
Total blood volume (mL)	
Male	4803.26±936.88 (4055-7500)
Female	3344
Haematology and biochemistry, mean±SD (range)	
Haemoglobin (gm/dL)	14.27±1.08 (12.6-17.3)
Haematocrit (%)	43.15±3.54 (34.5-49.6)
Total leukocyte count (×10^3/uL)	7.3±1.72 (4.6-11.8)
Platelet count (×10^3/uL)	230.98±45.29 (159-349)
Serum protein (gm/dL)	7.1±0.34 (6.2-8.1)
Serology, mean±SD (range)	
Anti-SARS-CoV-2 IgG (S/Co)	8.97±5.13 (3.19-13.4)
ABO group, n (%)	
A	15 (30%)
B	18 (36%)
AB	4 (8%)
O	13 (26%)

[Table/Fig-3]: Demographic details and biochemical parameters of actual CCP donors (n=50).

BMI in kg/m^2 (Mean±SD)	Volume of blood processed in mL (Mean±SD)	Two tailed probability p-value	Remarks
24.36±3.54	1882.16±390.09	0.00	p<0.05, Highly significant
BMI in kg/m^2 (Mean±SD)	**ACD Used in mL (Mean±SD)**	**Two tailed probability p-value**	**Remarks**
24.36±3.54	206.82±41.63	0.00	p<0.05, Highly significant
Hct in % (Mean±SD)	**Volume of blood Processed in mL (Mean±SD)**	**Two tailed probability p-value**	**Remarks**
43.15± 3.54	1882.16±390.09	0.00	p<0.05, Highly significant
Hct in % (Mean±SD)	**Processing time in minute (Mean±SD)**	**Two tailed probability p-value**	**Remarks**
43.15±3.54	38.9±7.09	0.00	p<0.05, Highly significant

[Table/Fig-4]: Statistical significance of BMI with BVP, HCT with BVP and processing time (n-50).
BMI: Body mass index; Hct: Haematocrit; ACD: Acid citrate dextrose, SD: Standard deviation; ml: milliliter; %: Percentage

Besides 50 SDPs, three procedures in recruited donors had to be abandoned due to the beep and indications of low return pressure displayed by the machine monitor. Adverse reactions were seen in two other donors in the form of mild hypotension, which could be managed conservatively and the procedure was completed successfully.

None of our donors suffered from citrate toxicity. None of the CCP donor informed about late reactions or discomfort in next 48 hours of plasmapheresis.

DISCUSSION

The unprecedented situation created due to COVID-19 pandemic brought to notice, inadequacy of diagnostic and therapeutic health care facilities and infrastructure at many centres in India. Many treatment modalities were tried for treatment of COVID-19 diseases, without much success [2,3]. Various case studies were carried out describing the use and benefits of CCP in treatment of moderate to severe COVID-19 disease [13,14].

Immunotherapy is a well established method of passive immunisation for preventing and/or treating an infectious disease by infusing plasma known as convalescent plasma, containing preformed antibodies into the susceptible host. It has been used since the late 19th century [15].

Convalescent plasma therapy involves collecting plasma containing antibodies from an individual who has recently recovered from infection and infusing it into a susceptible host. It was used in the past to treat several bacterial diseases like diphtheria, tetanus, pneumococcal pneumonia, meningococcemia and viral infections like rabies, poliomyelitis and measles [16].

Use of convalescent plasma for treatment of various diseases like H1N1 influenza, Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and Ebola are also available in literature [17-19].

Blood centre needed to set up unit for CCP collection by SDP on a short notice. Separate aphaeresis room within blood centre premises, was utilised for the purpose after acquiring permission from Food and Drug Administration of India (FDA). The guidelines for the collections and storage of CCP by SDP for COVID19 disease were received from the national authority [9,10].

Outcome of SDPs performed in blood centre depended upon the machine itself, the newly trained operators and on the anxious CCP donors.

Recruitments of donors for CCP collection was a major challenge before the authors, as donors were afraid of the procedure and reinfection of COVID-19. And hence prolonged counselling of the donors was needed.

As SDP was carried out for first time in our centre, this inexperience was the main cause of apprehension for the operators and the donors before actually performing plasmapheresis.

Similar problems are highlighted by an Indian study carried out at All Institute of Medical Sciences (AIIMS) New Delhi [20].

Single donor plasmaphreresis using automated blood cell separator is preferred method for collection of CCP, over plasma collected manually from whole blood, due to following advantages.

- Larger volume of plasma can be collected in a single setting.
- Repeat plasma collection is possible after 15 days.
- Minimal to nil contamination of by blood cells.
- No effect on the donor's blood cell, as all the cellular components return back to donor.

Many Studies showed that, the apheresis is a safer procedure with minimal adverse donor reactions as compared to whole blood donations [21].

Total 50 CCP procedures were successfully carried out, on the newly installed automated blood cell separator following guidelines by authority and technical instruction according to manufacturer's SOP. This latest version of the cell separator needed to give only single prick to the donor and was a completely closed unit, thus reducing chances of contamination. Continuous display of the procedure and beeps given if the procedure needed to be withheld for few minutes prompted operators to immediately rectify the errors with the help of technical advisors of the company.

All important donor parameters when entered into the machine, specific amount of plasma to be collected from the particular donor, total time that will be required for completion of the procedure were displayed on the monitor. Relationship between various donors' parameters and procedure of CCP collection revealed significant p-value indicating sensitivity of the machine used [Table/Fig-4].

Majority of CCP donors were introduced for first time to apheresis based collection of plasma.

Even after predonation counselling, actual CCP donations carried out were less in number due to anxiety about the apheresis procedure. Three procedures were abandoned, as machine detected high return pressure due to the thin vein of the donors. Single donor included in this study had donated CCP twice within a period of one month.

Most of the screened donors were males. Willing female donors could not be included due to multiparity and low haemoglobin. Preponderence of male donors in CCP donation is mentioned in other studies as well [22,23].

During the apheresis procedure adverse reactions can occur in the form of citrate toxicity, haematoma and vasovagal reactions [21]. Percentage of adverse reaction in our series is comparable to those quoted by other studies [22,23].

Although we could not compare performance of different apheresis machines, overall our experience of collecting CCP on the newly installed apheresis machine by method of SDP was satisfactory. Evaluation of therapeutic effectiveness of collected CCP was beyond scope of this study.

Limitation(s)

Small numbers of SDPs included in this study was the limitation of the study. However, further studies with larger sample size can be conducted for wider implementation of apheresis based plasma donations for providing better patient care in pandemic due to viral infections.

CONCLUSION(S)

Single donor plasmapheresis using automated blood cell separator can yield adequate amount of good quality CCP. Proper predonation screening, prompt technical action and management during the procedure minimise the donor adverse reaction.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Pathology, Government Medical College and Hospital, Nagpur, Maharashtra, India.
2. Associate Professor, Department of Pathology, Government Medical College and Hospital, Nagpur, Maharashtra, India.
3. Professor, Department of Pathology, Superspeciality Hospital, Nagpur and Medical Director, Model Blood Bank, Government Medical College, Nagpur, Maharashtra, India.
4. Junior Resident, Department of Pathology, Government Medical College and Hospital, Nagpur, Maharashtra, India.
5. Assistant Professor, Department of Pathology, Government Medical College and Hospital, Nagpur, Maharashtra, India.
6. Professor and Head, Department of Pathology, Government Medical College and Hospital, Nagpur, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Swati B Gadhave,
Department of Pathology, Government Medical College and Hospital, Hanuman Nagar, Ajni Road, Nagpur, Maharashtra, India.
E-mail: swatigadhave19@gmail.com

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