Effectiveness of ACB-IP 1.0 Universal Pathogen Free Concentrated Cocktail Convalescent Plasma in COVID-19 Infection

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Abstract

BACKGROUND

The efficacy of SARS-CoV2 single donor convalescent plasma (CP) varied according to the application time and the amount of antibody that is administered. Single donor CP has some drawbacks; such as the insufficient levels of neutralizing antibody activities, the requirements of blood group compatibility, and the risk of infection transmission. In this study, the safety and efficacy of pathogen inactivated, isohemagglutinin-depleted (concentrated) and pooled CP product was investigated.

METHODS

A total of sixteen patients were treated with either single donor CP (n=9) or pathogen-free, concentrated, pooled CP (ACB-IP 1.0) (n=7).

RESULTS

Five out of six single donor plasma SARS-CoV2 antibody titers remained below 12 s/co, but the antibody titers of all ACB-IP 1.0 plasma were above 12 s/co. SARS-CoV2 total antibody titers of ACB-IP 1.0 plasma were statistically higher than the antibody titers of single donor CP. Mean total plasma neutralizing antibody activity of ACB-IP 1.0 plasma (1.5421) was found statistically higher than single donor CP (0.9642) in 1:256 dilution (p<0.01)

The mortality rates of the patients treated with ACB-IP 1.0 plasma were statistically lower (p< 0.05) than the patients treated with single donor CP. The administration of either single donor CP or ACB-IP 1.0 plasma to the patients within eight days significantly shortened the length of hospitalization (p< 0.05).

CONCLUSION

The present study established ACB-IP 1.0 plasma product as a safe and potentially effective treatment for COVID-19, allowing rapid access to patients in need.

TRIAL REGISTRATION

Trial Registration Number: NCT04769245

Trial Registration Date: 17.03.2021

Introduction

On 31 December 2019, a new case of pneumonia of anonymous etiology emerged in Wuhan City, Hubei Province China and humanity was confronted with a new pandemia. The World Health Organization (WHO) officially announced the causative organism as 2019-nCoV/SARS-CoV2.[1] Viral genome sequence of this new human pathogen was released and found to be closely related to viral species called Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) which caused outbreaks in 2002 and 2003 in China.[2] The SARS-CoV2 virus has spread from Wuhan to whole of China and 231 countries worldwide, affecting more than 680 million individuals and resulting over 6,800,000 million deaths.[3]

WHO recommends the use of Ivermectin, thromboprophylaxis, IL-6 blocker, Lopinavir/ritonavir, Colchicine, Vitamin D, and corticosteroid in treatment of COVID-19.[4] Nevertheless, the exact clinical benefits of this COVID-19 therapeutics are not yet determined. Hence, clinicians seek for alternative treatment options such as monoclonal antibodies and CP. Fundamental mechanism behind monoclonal antibodies and CP are similar with both therapies generating passive immunization for viral neutralization.[5] However, CP may be preferable over monoclonal antibodies in terms of being
effective against new strains, being accessible and cost-effective. Furthermore, CP is the safest treatment alternative for emergency use. CP containing antibody from SARS-CoV2 individuals who have recovered from the disease, has been suggested as an investigational treatment option by FDA.[6]

Our knowledge regarding convalescent human plasma comes from the treatment of viral infections, such as SARS-CoV, avian influenza A (H5N1) virus, influenza A (H1N1), MERS, and Ebola virus.[7-13] Even though there is still no consensus about its effectiveness, efficacy of CP varied according to virus type, time of application, amount of the antibody and most importantly to the neutralizing capacity of the antibodies administered.[14] There are similar concerns regarding studies conducted in SARS-CoV2. FDA report and Mayo Clinic study involving 20,000 hospitalized patients indicated that early and adequate plasma use would reduce mortality[15, 16], while PLACID and RECOVERY trial reported single donor CP did not improve survival or other clinical outcomes.[17, 18] In the most recent article published investigates short and long effects of both high titer convalescent and standard plasma on respiration impairment (PLACO COVID trial), showed no significant difference.[19]

Conflicting outcomes of these studies may be due to the different times of administration, donor antibody titers (since SARS-CoV2 antibody titer was perceived to be the same as neutralizing antibody titer and the latter was therefore not demonstrated in most studies) and whether CP is strain-specific. Variations in these parameters have made the results debatable.

Single donor plasma has some drawbacks such as requirements of blood group compatibility [17, 20, 21] and risk of viral infection, for instance HIV, HBV, HCV transmission by donors who do not meet the standard donor criteria in pandemic conditions. In addition, excess of procoagulant factors in standard donor plasma increases the risk of thrombosis. [22, 23] These factors necessitated the search for a new CP product. Hence, ACB-IP 1.0 cocktail plasma, where SARS-CoV2 antibody titers and neutralizing antibody activity were standardized by pooling, was designed. Furthermore, Immunoglobulin M (IgM) which is responsible for most of the isohemagglutinins[24-26], was depleted by using both cryodepletion[25] and pooling method until Anti-A and Anti-B isohemagglutinin titers were below 1/8. Procoagulant factors were depleted by cryodepletion in order to eliminate the risk of thrombotic events. Furthermore, it was concentrated and safety of the plasma was improved by subjecting it to pathogen inactivation.

This proof of concept study was designed with the hypothesis that ACB-IP 1.0 universal pathogen free concentrated cocktail CP is superior compared to the single donor CP in terms of both product quality and clinical efficacy.

**Methods**

According to the criteria specified in the COVID-19 Immune Plasma Procurement and Clinical Use Guidelines of FDA[8], donor candidates who were eligible according to apheresis donor criteria were invited to Therapeutic Apheresis Center of Acibadem Altunizade Hospital. Blood products were taken from the donor plasma candidates.

This study was conducted with participation of 16 patients. The CP samples obtained from 9 Turkish Red Crescent donors and 7 ACB-IP 1.0 products, where each one of the 7 plasma samples were prepared from 8 different donors, were compared according to the product quality and clinical effectiveness.

**Plasma Collection:**

ACB IP 1.0 plasma was obtained from donor using Trima Accel (Trima Accel, Terumo BCT, Inc. Colorado, USA) device. 400 ml - 600 ml plasma was collected according to the patient’s height, weight, and blood count results. During this process, an ISBT code was obtained from the Turkish Red Crescent.
Pathogen Inactivation:

Plasma collected by plasmapheresis was connected to Cerus Intercept Blood System plasma treatment bags (Intercept Blood System Pathogen Reduction System, Cerus, CA, USA) using bag joining device (Terumo TSCD-II TSCD Welders, Terumo BCT, Inc. Colorado, USA). Prior to pathogen inactivation process, 2 ml of 2 tubes of witness samples were taken from the collected plasma. Witness samples were stored at -40 °C. According to the manufacturer instruction, plasma was initially treated with amotosalen followed by photochemical irradiation with UVA at 320-400 nm wavelengths in Intercept INT100 illuminator (INTERCEPT INT100 Illuminator, Cerus, CA, USA). Following inactivation process, plasma was passed through the adsorption filter to remove unreactive amotosalen and free photoproducts, and then it was divided into 2 or 3 equal volumes, depending on the volume of the collected plasma. Following this process, 2 ml of 2 witness sample tubes were taken and stored at -40 °C. Pathogen inactivated plasma was stored at -40 °C for labeling until the pooling process prior to clinical usage.

Isohemagglutinin Assay:

Ready to use (commercial) A and B kits (ID-Diacell ABO, Bio-Rad Laboratories, Inc., Cressier, Switzerland) were provided by Bio-Rad and gel centrifugation method was performed according to the manufacturer's protocol (NaCl, Enzyme Test and Cold Agglutinins, Bio-Rad Laboratories, Inc., Cressier, Switzerland).[27]

IgM Detection:

IgM titers were obtained by using Siemens Advia 1800 Chemistry System. The photometric method was performed according to the manufacturer's protocol.

Isohemagglutinin Depletion and Concentration of Plasma:

Following plasma donation, Anti-A and Anti-B hemagglutinin titers were determined. To reduce the isohemagglutinin titer two separate steps were performed. Firstly, isohemagglutinins, most of which were of IgM nature, were reduced by cryodepletion, while simultaneously concentrating the product. Secondly, isohemagglutinin titer was reduced by pooling of Anti- A and Anti-B free plasma and the plasma containing them.

- Cryodepletion Method[24, 25]

Plasma samples from the apheresis product of 200 ml were transferred to plasma storage bags (Teruflex, Terumo BCT, Inc. Colorado, USA) frozen in a deep freezer at -40 °C. One bag consisted of eight donors' apheresis plasma and volume in each bag was approximately 1600 ml. Frozen samples were kept at + 4 °C for defrosting for approximately 8-12 hours. Liquid plasma was separated from cryoprecipitate by centrifugation. Witness samples were taken and stored at -40 °C. The bag where cryodepleted pool would be produced was connected to the plasma bag (Terumo BCT, Inc. Colorado, USA) using a bag joining device (Terumo TSCD-II TSCD Welders, Terumo BCT, Inc. Colorado, USA).

- Plasma Pooling:

Plasma bag was placed in the extractor and cryopoor plasma was transferred to the pooling bag. Finally, pooling was achieved by mixing the low SARS-CoV2 antibody titer with high antibody titer plasma prior to cryodepletion and the total product was packaged in 200 ml bags and stored at -40 °C until clinical use.

SARS- CoV2 Specific Immunoglobulin Analysis:
SARS-CoV2 RBD specific total antibody analyzes were performed using CLIA method (ADVIA Centaure XP, Siemens Healthineers, Erlangen, Germany).

**Neutralizing Antibody Assay:**[28]

Modified micro neutralization test was performed. 100 TCID50 / 50 microliter SARS-CoV2 virus was placed in 96 Well U Bottom plate and 50 µl diluted human sera (1:64, 1:128, 1:256 sera concentration) were added.

Following one hour of incubation at room temperature, 10000 Vero cell/well was placed in a 96 well flat bottom plate with 100 µl of complete DMEM (4% FBS + 1% PSA). Supernatants were removed after 72 hours of incubation, 50 µl of MTT solution and 50 µl serum-free media were added to the remaining cells. Following incubation at 37 °C for 4 hours, 100 µl of Isopropanol dispersion was added to each well and placed on a shaker for 10 min. Results were obtained by ELISA Reader at an absorbent value of 570 nm. Neutralizing antibody activity was performed in 1:64, 1:128 and 1:256 dilution based by cell viability index.

**Endotoxin Analysis:**

Gel-clot technique was used for detecting or quantifying endotoxins (Gel-Clot Endotoxin Test, Division of Charles River Laboratories Inc, CA).

**Microbiological Quality Control:**

Pooled CP was placed on to Bactec Fx device for microbiological quality control analysis (Bactec FX, Becton Dickinson, New Jersey, USA).

**Sars-CoV2 Quantitative Real-Time Polymerase Chain Reaction (PCR) Test:**[29]

Nasopharyngeal swap sample was obtained by an experienced healthcare provider from a COVID-19 positive patient for the qualitative detection of nucleic acid from SARS-CoV2 in upper respiratory specimens. Analysis was performed by using Quantitative Real-Time PCR Coronavirus Detection test kit according to the manufacturer’s instructions (QuantiVirus™ SARS-CoV-2 Test kit, Diacarta, CA, USA).

**Trial Design (Trial is recorded under; NCT04769245):**

A total of 16 hospitalized adults were screened for enrollment and included in the study if they had positive reverse-transcriptase–polymerase-chain-reaction (RT-PCR) for SARS-CoV2 and radiologically confirmed pneumonia. Treatment of all patients was performed according to Covid-19 treatment algorithms (Table-1).

A total of 16 patients were treated with two different CP products. Nine patients were treated with single donor CP and seven were treated with pathogen-free, concentrated, pooled CP.

Written informed consent was obtained from all patients or their first degree relatives, and trial was conducted under the principles stated in the Declaration of Helsinki and Good Clinical Practice guidelines and approval of Acibadem University ethics committee (Approval No: 2020-06/02).

Clinical information of the patients was obtained from the hospital’s electronic medical records. Demographic data, presenting symptoms as well as a radiological presentation at the onset of disease including fever, cough, fatigue, dyspnea, diarrhea, oxygen requirement, treatments received, duration of hospitalization stay, duration of intensive care unit (ICU) stay, cycles and volume of CP received, symptom and radiological improvements and current status of the patients were collected. Patients were compared according to product safety and efficacy, followed up for transfusion-related
reactions and findings were recorded. Shortened hospital stay and/or decreased mortality rates and side effects were the main endpoints for the assessment of the therapeutic effects and safety of both plasma products.

**Statistical Analysis:**

SARS-CoV2 Antibody titers, neutralizing antibody activities, and duration of hospitalization were analyzed by employing Mann Whitney test. Mean age of the groups was compared by the Kolmogorov-Smirnov test. Survival differences between the two plasma groups were analyzed by Chi-Square test. Fisher exact test was used to compare the categorical variables such as radiological presentation, co-existing disease and supplemental oxygen requirement among the groups. Results were analyzed with a %95 confidence interval and a significance level of p=0.05 was used for all statistical analysis.

**Results**

- **Laboratory Results:**

Results of the Isohemagglutinin Titers:

Pre-pooling cryodepletion process caused a statistically significant reduction in Anti-A titers (53.85%), Anti-B titers (44.44%), and in IgM levels (11.62%) (Table-2, Figure 1). Following pooling process, maximum Anti-A titers in ACB-IP 1.0 was reduced to 1/4 and Anti-B titers to 1/8, while maximum Anti-A titers were 1/64 and Anti-B titers were 1/128 in single donor plasma. Results show that cryodepletion and pooling process effectively reduce isohemagglutinin levels, giving ACB-IP 1.0 a universal character (blood-group free CP).

Results of the SARS-CoV2 Antibody Titers in Plasma:

Five out of six single donor plasma SARS-CoV2 antibody titers remained below 12 s/co, however antibody titers of all ACB-IP 1.0 plasma were above 12 s/co. Mean antibody titer of single donor plasma was 9.2083 s/co and mean antibody titer of ACB-IP 1.0 plasma was 32.700 s/co. SARS-CoV2 total antibody titers of ACB-IP 1.0 plasma were statistically higher in comparison with the antibody titers of single donor plasma (Figure 2).

Results of SARS-CoV2 Neutralizing Antibody Activity:

Neutralizing capacity of single donor plasma was higher than their antibody titers. Only 50% neutralizing antibody activity of the single donor plasma was below %100 cell viability threshold in 1:256 dilution (Figure 3), whereas neutralizing activity of all ACB-IP 1.0 plasma was above %100 cell viability threshold in 1:256 dilutions (Figure 3).

Mean plasma neutralizing antibody activity of ACB-IP 1.0 plasma (1.5421) was found to be statistically higher than single donor plasma (0.9642) in 1:256 dilution (p=**0.0087) (Figure 3).

No correlation was found between SARS-CoV2 antibody titers and neutralizing antibody activity in both groups (single donor plasma antibody and neutralizing antibody activity correlation coefficient: 0.54, regression coefficient (R²): 0.44. ACB-IP 1.0 plasma antibody and neutralizing antibody activity correlation coefficient: -0.36, regression coefficient (R²): 0.79).

- **Clinical Results:**

Clinical characteristics of single donor plasma patients were presented in Table-3. Six out of nine single donor CP patients were male. Median age of the patients was 65 years and none of them had a history of smoking. Three male patients age 40, 54 and 63 had no coexisting disease.
Treatment of all patients was performed according to Covid-19 treatment algorithms. Five patients received dornase-alpha and three patients received IL-6 blocker.

One of the patients had two cycles of single donor CP total of 400 ml volume. Volume loading due to transfusion was detected in one patient. No other side effects were observed.

Mean duration of hospital stay was 41 days (11-101 days) and mean duration of ICU stay was 35 days (7-90 days). Following the treatments and CP administration, four out of nine patients had clinical improvement, three patients had radiological improvement, two patients were not evaluated. Five out of nine patients died in total.

Clinical characteristics of SARS-CoV2 infected patients who received pathogen-free, concentrated, pooled, CP is presented in Table-4. All of the patients treated with pathogen-free, concentrated, pooled CP were males. Median age of the patients was 51 years and none of the patients had history of smoking. Two patients age 50 and 59 had no coexisting disease.

Treatments of all seven patients were performed according to Covid-19 treatment algorithms. One patient received dornase-alpha and one patient received IL-6 blocker.

One of the patients had two cycles of pooled CP total of 286 ml volume. No transfusion-related reactions had been observed. The mean duration of the hospital stay was 44 days (5-172 days) and the mean duration of ICU stay was 30 days (0-139 days).

Following treatments and CP administration, all seven patients had clinical improvement and five patients had radiological improvement. All patients were discharged from the hospital.

There was no statistical difference between groups of patients that received single donor plasma and ACB-IP 1.0 plasma with respect to age ($\rho=0.160$), radiological presentation ($\rho= 0.999$), co-existing disease ($\rho= 0.999$), supplemental oxygen requirement ($\rho= 0.596$) and plasma administration time ($\rho= 0.176$)

Mortality rate of the patients treated with ACB-IP 1.0 plasma were statistically lower ($p= 0.033$) than the patients treated with single donor plasma. (Figure 4)

Median length of hospital stay was 24 days for single donor plasma patients, and 19 days for ACB-IP 1.0 plasma patients and it is statistically insignificant. Administration of either single donor or ACB-IP 1.0 plasma to the patients within eight days of disease onset significantly shortened the length of hospitalization in comparison with administration of either plasma later than eight days ($p= 0.014$) (Figure 5).

**Discussion**

There are conflicting results regarding the beneficial effect of administering CP in SARS-CoV2 pneumonia. An initial report of five critically ill patients with COVID-19 and Acute Respiratory Distress Syndrome (ARDS), where single dose of CP was administered, indicated clinical improvement.[25] In another study CP of 200ml was administered to ten patients with COVID-19 infection. Results showed that patients had clinical benefit, and common laboratory parameters of infection such as decreased lymphocyte count and increased CRP is normalized.[20] A prospective and propensity score-matched study, comparing survival rates of CP transfused 136 patients with non-transfused 251 patients, recommended administration of CP within 72 hours of hospital admission showed significant reduction in mortality rate.[30] In a matched study, 20 severely and critically ill hospitalized COVID-19 patients and 20 controls were examined according to their laboratory, respiratory parameters and mortality rate. Although the study had some limitations, such as short follow-up time and small sample size, results indicated that CP could improve survival if given at the early onset of disease.[17] Liu et al. reported 39 hospitalized patients with severe life-threatening COVID-19, who received CP, compared with a non-transfused control group. Results showed that patients receiving CP therapy had improved survival and reduced oxygen requirement 14 days post-transfusion. In the mentioned study, authors also recommended transfusion of CP immediately
following hospitalization.[31] Mayo Clinic study involving 20,000 hospitalized patients and a randomized controlled study conducted by Libster et al. in elderly patients also suggested that early administration of CP reduced clinical symptoms and progression of Covid-19 to severe illness.[16, 32]. A recent double-blind randomized clinical trial conducted including 39 participants concluded that CP is safe and decreased mortality despite the small number of participants.[33] One year follow up of CAPSID trial demonstrated that patients receiving CP containing higher amounts of neutralizing antibody showed significant better outcome (long term survival, time to discharge from ICU and hospital) compared to the control group.[34]

On the other hand, a number of studies failed to show beneficial effect of CP in SARS-CoV2 pneumonia patients. [17, 18, 35] One of these studies was PLACID trial, even though it had a number of limitations, such that there was no neutralizing antibody titer measurement of the donor plasma and also CP was administered to the patients later than 3 days, contrary to what was recommended by the FDA. V.A. Simonovich et al. also showed no relationship between SARS-CoV2 antibody titers, early plasma administration, and clinical efficacy.[35] However, hypoxia was one of the patient selection criteria and treatment was not commenced within 72 hours of the disease onset and neutralizing antibody titers could only be assessed in 56% of the donors in this study. Latest PLACO trial investigate the short and long term effect of convalescent or standard plasma versus standard care in respiratory impairment caused by COVID-19 showed both plasmas did not improve the outcomes of the patients with acute respiratory failure regardless of antibody level. Although small sample size and the inclusion of pneumonia patients who received CP after respiratory impairment are among the limitations of this clinical trial.[19]

Largest trial conducted so far, RECOVERY Group trial, also indicated that even if CP is used in early onset of disease, it does not reduce respiratory support requirement, hospital stay, and mortality.[18] However; CP was again administered later than 72 hours following the onset of disease in aforementioned study. Also the CP was not strain-specific because a new SARS-CoV-2, B.1.1.7 dominated most regions of UK at the time of the study. Hence, it is likely that modified antigenicity further reduced neutralizing capacity of the plasma. Furthermore, all CP were chosen based on high anti-spike concentration. This was on the assumption that IgG concentration shows correlation with the neutralizing antibody titer. [18] Although, Salazar et al. showed that there is a correlation between antibody titers and neutralizing capacity, they reported this correlation in only 80% of single donor plasma. The fact that the correlation between IgG concentration and the neutralizing antibody titer was not shown in %20 of single donor plasma is a high ratio that can make the results questionable.[36]

Results of the current study for single donor plasma showed heterogeneity of SARS-CoV2 antibody titers and neutralizing antibody activity. However, ACB-IP 1.0 plasma which is a pooled concentrated plasma product showed higher SARS-CoV2 antibody titers and neutralizing antibody activity. There was no correlation between SARS-CoV2 antibody titers and neutralizing antibody activities in single donor plasma and ACB-IP 1.0 plasma. This may have been due to use of only SARS-CoV-2 S1 spike protein antigen for antibody detection in this study. More reliable results could possibly have been obtained using nucleocapsid and matrix protein antigen in addition to the spike protein antigen for antibody detection.

Presence of re-infected cases despite high antibody titers confirms that this is not a reliable parameter for protection against COVID-19. ACB-IP 1.0 plasma had less variance of SARS-CoV2 antibody and neutralizing antibody titer, and hence more standardized CP could be obtained.

Findings of this study showed significantly decreased in mortality in ACB-IP 1.0 plasma in comparison with single donor CP. There was also a reduction of length of hospital stay in both groups if the plasma was administrated within 8 days onset of disease (p=0.014). When the side effects of the two plasma products were examined, no difference was observed and both plasma products were found safe in clinical practice. However, these results while preliminary and subject to important study limitations such as small sample size and unstandardized plasma administration time should stimulate a randomized controlled study with a larger patient group.
Another, significant clinical result was difficulty in accessibility of single donor plasma, which requires blood group compatibility, especially in the early stages of the pandemic due to the lack of sufficient available donors. However, as a result of cryodepletion and pooling processes, ACB-IP 1.0 plasma does not require blood group compatibility, and hence can be employed immediately. Furthermore, by containing pooling of plasma from various convalescent individuals, ACB-IP 1.0 plasma may be more advantageous in the treatment of variant mutations.

Single donor plasma also has the disadvantage of increased risk of transfusion-transmitted infections due to individuals who may not meet the standard donor criteria. With the help of pathogen inactivation process, transfusion-transmitted infections are minimized. However, due to its small scale, no data could be obtained to determine the advantage of pathogen inactivation in this study and a randomized, controlled study with a larger patient group is required.

**Conclusion**

ACB-IP 1.0 pooled pathogen inactive universal CP leads to a better clinical response in comparison with single donor CP with a neutralizing antibody activity against SARS-CoV2. The product is safe and does not require blood group compatibility allowing fast access for patients in need.

**Abbreviations**

- ARDS: Acute Respiratory Distress Syndrome
- CP: Convalescent plasma
- CRP: C-Reactive Protein
- FDA: Food and Drug Administration
- HBV: Hepatitis B Virus
- HCV: Hepatitis C virus
- HIV: Human Immunodeficiency Virus
- H1N1: Influenza A virus subtype
- H5N1: Influenza A virus subtype
- IGG: Immunoglobulin G
- IGM: Immunoglobulin M
- IL-6: Interleukin-6
- MERS: Middle East respiratory syndrome
- RT-PCR: Reverse transcriptase polymerase chain reaction
- SARS-CoV2: Severe acute respiratory syndrome coronavirus 2
- s/co: Signal-to-cutoff
- UVA: long wave ultraviolet A
WHO: World Health Organization

Declarations

Ethics approval and consent to participate: Acibadem University Ethics Committee (Approval No: 2020-06/02).

Consent for publication: Not Applicable

Availability of data and materials: All data generated or analyzed during this study are included in this published article

Competing interests: The authors declare that they have no competing interests

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References


Tables

### Table 1: Treatment Schema of COVID-19
(Recommendation of Turkish Ministry of Health)

<table>
<thead>
<tr>
<th>Progressive Disease</th>
<th>Loading Dose</th>
<th>Maintenance Dose</th>
<th>Duration</th>
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<td>Favipiravir 200 mg</td>
<td>2 x 1600 mg</td>
<td>2 x 600 mg</td>
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<td>or</td>
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<tr>
<td>Lopinavir 200 mg/ritonavir 50 mg</td>
<td>2 x 2 tb, oral</td>
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<td>10-14 days</td>
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Table 2: Effects of Cryodepletion on Isohemagglutinin and IgM levels of single donor plasma
<table>
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<th></th>
<th>N=8</th>
<th>Mean Anti-A titers</th>
<th>Mean Anti-B titers</th>
<th>Mean IgM titers</th>
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<td>% Change</td>
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* significant level by t test for p<0.05.

Clinical Characteristics of SARS-CoV-2-Infected Patients Who Received Single Donor Convalescent Plasma

Table 3.
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Clinical Characteristics of SARS-CoV-2-Infected Patients Who Received Pathogen-Free, Concentrated, Pooled, Convalescent Plasma Table-4.
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</table>
Figure 1: Effects of cryodepletion on Isohemaglutinin and IgM levels

![Figure 1](image)

**Figure 1**

Effects of cryodepletion on Isohemaglutinin and IgM levels

**Figure 2**

Single Donor Plasma and ACB-IP 1.0 Plasma SARS-CoV2 Antibody Titers
Figure 3: SARS-CoV2 Total Neutralizing Antibody Activity of Single Donor Plasma and ACB-IP 1.0 Plasma (in 1:256 dilution).

A. Single donor plasma neutralizing antibody activity of each donor.  
B. ACB-IP 1.0 plasma neutralizing antibody activity of each pooled product.  
C. Comparison of mean neutralizing antibody activity (**; p=0.0087)

Figure 3

SARS-CoV2 Total Neutralizing Antibody Activity of Single Donor Plasma and ACB-IP 1.0 Plasma (in 1:256 dilution).
Figure 4: Comparison of the mortality rate between the two different plasma groups (*p=0.033)

Figure 4
Comparison of the mortality rate between the two different plasma groups (*p=0.033)
Figure 5: Effect of early plasma administration (8 days) on the length of hospitalization (**p=0.014)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementData1.docx