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Use of COVID-19 Convalescent Plasma in the Patients Infected With COVID-19 (SARS-CoV-2) - Efficacy and Safety

Sponsor:
Institute for Transfusion Medicine of RNM

Collaborator:
University Clinic for Infectious Diseases, North Macedonia

Investigators:

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Study Protocol

There are currently no proven effective therapeutic options for coronavirus disease (COVID-19), the infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Human convalescent plasma is an option for treatment of COVID-19. Experience from prior outbreaks with other coronaviruses, such as SARS-CoV-1, MERS and H1N1 shows that convalescent plasma can be effective and its safety was shown as well.

Objective

To explore potential efficacy and safety of COVID-19 convalescent plasma in hospitalized patients infected with COVID-19 (SARS-CoV-2).

Study intervention description

Convalescent plasma will be obtained by plasmapheresis or regular whole blood donation in subjects who recovered from COVID-19 and who are otherwise eligible for donation according to the Institutional protocol in the Institute for Transfusion Medicine of RNM. Recipients will be confirmed COVID-19 patients requiring hospitalization. A blood-type matched transfusion of convalescent plasma will be infused using standard transfusion guidelines and recipients will be followed up. Study was approved by the Ethical Committee and all relevant bodies in RNM. All relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.

Research population
Hospitalized patients with SARS CoV-2 infection will receive anti SARS-CoV-2 convalescent plasma

Intervention
Administration of anti-SARS-CoV-2 convalescent plasma obtained from donors with prior documented SARS-CoV-2 infection

Eligibility criteria

Inclusion Criteria

Blood donors:

1. Age: >18 and <60 years, if first time donors, between 18 and 65 if regular donors
2. Body weight : >55 kg
3. Confirmed previous SARS CoV-2 infection
4. Minimum 28 days after the last symptom or finishing of the isolation, or
5. 21 day without symptoms from the date of the negative SARS CoV-2 test
6. Written informed consent to participate in this clinical trial, to donate plasma and to store the specimen for future testing.
7. Concentration of COVID-19 IgG antibodies more than 5 AU/ml
8. Male donors, or female donors who have not been pregnant, or female donors who have been pregnant tested negative for HLA antibodies

9. Individuals who meet all regular voluntary donor eligibility requirements

Patients/recipients:

1. Age: >18 years
2. Laboratory confirmed diagnosis of infection with SARS-CoV-2
3. Admitted to an acute care facility for the treatment of COVID-19 complications
4. Patients with severe or immediately life-threatening COVID-19, or
5. Patients who are judged by a healthcare provider to be at high risk of progression to severe or life-threatening disease.
6. Informed consent provided by the patient or healthcare proxy

Exclusion Criteria

Blood donors:

1. Age : <18 and >60 years, if first time donors, and > 65 if regular donors
2. Female subjects who are pregnant
3. HIV1,2 hepatitis B, hepatitis C or syphilis infection
4. Donors ineligible for regular voluntary blood donation

Patients/recipients:

1. Age : <18 years
2. Contraindication to transfusion (severe volume overload, history of anaphylaxis to blood products)
3. Patients who received in the past 30 days immunoglobulin therapy
4. Females who are pregnant or breastfeeding

Outcome Measures

Primary Outcome Measures:

1. Duration of oxygenation and ventilation support [Time Frame: 28 days after transfusion or until hospital discharge (whichever comes first)]

The total number of days patients required respiratory support.

2. Hospital length of stay (LOS) [Time Frame: 28 days after transfusion or until hospital discharge (whichever comes first)]

Total number of days patients were admitted to the hospital.

3. ICU admission [Time Frame: 28 days after transfusion or until hospital discharge (whichever comes first)]

Total number of subjects to be admitted to the ICU after the convalescent plasma transfusion.

4. Ventilator free days [Time Frame: 28 days after transfusion or until hospital discharge (whichever comes first)]

Days without oxygenation support after receiving convalescent plasma

5. Incidence of serious adverse events [Time Frame: 28 days after transfusion or until hospital discharge (whichever comes first)]

Cumulation incidence of serious adverse events during the study protocol

Secondary Outcome Measures:

1. Type of respiratory support [Time Frame: 28 days after transfusion or until hospital discharge (whichever comes first)]

Type of supplemental oxygen support (e.g. nasal canula, high flow nasal canula, noninvasive ventilation, intubation and invasive mechanical ventilation, rescue ventilation)

2. Number of participants with different clinical outcomes including death, critical illness and recovery [Time Frame: 28 days after transfusion or until hospital discharge (whichever comes first)]

Number of participants with different clinical outcomes including death, critical illness and recovery

Statistical Analysis

The following statistical programs will be used: STATISTICA 12.0; SPSS 20.0.

Descriptive statistics will be presented as frequencies and percentages. Measures of central tendency and measures of dispersion of data will be determined (mean, median, standard deviation and interquartile range). Analytic data will be presented as point estimates and 95% confidence intervals (± 95% CI). P-values less than 0.05 will be considered statistically significant. Percentage of structure will be used and differences will be tested with Difference test.
Significance of the differences in more variables will be tested with Analysis of Variance test, and afterwards with Post hoc Turkey HSD test. Significance of the differences in two variables will be tested with Student t-test (t). The Pearson coefficient of correlation will be used. The survival curve by Kaplan-Meier will be done. Log-Rank test will be used for association of two variables and for more variables $–X^2$ test will be used (Pearson Chi-square). Cox regression will be used for analysis of possible predictive variables on survival.