SARS-CoV-2 Antibodies Based IVIG Therapy for COVID-19 Patients

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STUDY PROTOCOL

Study Protocol

Objective:

To investigate clinical efficacy of anti COVID-19 Intravenous Immunoglobulin (IVIG) therapy for passive immunization of COVID-19 patients.

Methodology

Plasma collection from donors (recovered COVID-19 individuals):

1. Selection of donor according to World Health Organization (WHO) and Federal Drug Agency (FDA) guidelines

Inclusion Criteria for Donor	Exclusion criteria for Donor
1. Submitted signed consent	a. Pre-existing condition Contra indicative for donating blood (HIV, viral hepatitis, tuberculosis, syphilis, oncological conditions, malaria)
2. Eligible to donate blood	b. Bleeding tendency
3. Negative for HIV, HBV, HCV, syphilis and malarial parasite	c. Anemia
4. Prior diagnosis of COVID-19 documented by a laboratory test	d. Fever of unknown origin
5. Complete resolution of symptoms at least 14 days prior to donation	
6. Female donors negative for HLA antibodies or male donors	
7. Negative results for COVID-19 either from one or more nasopharyngeal swab specimens or by a molecular diagnostic test from blood.	
8. Defined SARS-CoV-2 neutralizing antibody titers, if testing can be conducted (e.g., optimally greater than 1:320)	

2. Plasma Collection and separation:

300-1000 ml plasma will be collected from consenting COVID-19 recovered patients (two weeks after recovery and having evidence of negative PCR for SARS CoV-2) using plasmapheresis technique. Plasmapheresis is a technique where using a machine the blood components are separated, keeping the required component, in this case plasma, and returning other components like RBCs. Plasma will be stored according to WHO guidelines. Aliquot of plasma will be subjected to ABO blood typing and screened for syphilis, malarial parasite HIV, HBV, HCV, and COVID–19 by Nucleic Acid Test (NAT). The screened stored plasma qualifying safety criteria will be pooled and fractionated to obtain Anti-COVID hyperimmune immunoglobulin.

Administration of extracted IgG in respective doses by medical Experts and researchers in selected recipient

Eligibility Criteria for Recipient:

Revised Inclusion criteria for study participant (Covid-19 patients)	**Exclusion criteria for Recipient**
1. Above 18 years of age	a. Pregnancy
2. Have positive COVID PCR on nasopharyngeal and/or oropharyngeal swabs	b. Previous allergic reaction to immunoglobulin treatment
3. Admitted in isolation ward and ICU of institutes affiliated with DUHS	c. Ig A deficiency
4. Have severe or life threatening COVID as judged by the treating physician	d. Patient requiring 2 inotropic agents to maintain blood pressures
5. Consent given by the patient or first degree relative	e. Known case of any autoimmune disorder
Severe COVID-19 is defined by one or more of the following:	f. Acute kidney injury or chronic renal failure
Dyspnea	g. Known case of thromboembolic disorder
Respiratory frequency ≥ 30/min	h. Aseptic meningitis
Blood oxygen saturation ≤ 90%	

Partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300	
Lung infiltrates > 50% within 24 to 48 hours	
Life-threatening COVID-19 is defined as one or more of the following:	
Respiratory failure	
Septic shock	
Multiple organ dysfunction or failure	

Study Design

This is a phase I/II single centered, randomized controlled, single-blinded trial, through parallel-group design with sequential assignment. Participants will be randomized either to receive both C-IVIG and standard care or only standard care (4:1). The study consists of intervention comprising of four arms with each study arm containing 10 participants. All participants receive standard hospital care which includes airway support, anti-viral medication, antibiotics, fluid resuscitation, hemodynamic support, steroids, painkillers, and anti-pyretic.

Randomized test patients will receive single dose of C-IVIG in following four dosage groups:

Group 1: 0.15g/Kg with standard hospital care

Group 2: 0.2g/Kg with standard hospital care

Group 3: 0.25g/Kg with standard hospital care

Group 4: 0.3g/Kg with standard hospital care

Group 5 (comparator) will receive standard hospital care only.