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Therapeutic plasma exchange (removal of the non-cell portion of blood) in critically ill adult patients with serious SARS CoV-2 disease (COVID-19)

Submission date
15/05/2020

Recruitment status
No longer recruiting

Registration date
18/05/2020

Overall study status
Completed

Last Edited
10/06/2025

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed.
People with COVID-19 may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe. A minority of patients develop life-threatening disease involving severe pneumonia, septic shock (a severe fall in blood pressure caused by the body's response to infection) and multisystem organ failure as well as a storm of inflammation (cytokine release syndrome) requiring intensive care unit (ICU) admission and urgent treatment.
Therapeutic plasma exchange (TPE) is a technique that has been used in hospitals for over 20 years. The aim is to remove antibodies and/or other proteins as well as inflammatory mediators (substances that increase inflammation, such as cytokines). It involves passing a patient's blood through a machine that removes plasma (the liquid containing free proteins and other substances) and returns the blood cells to the patient. The patient's plasma is replaced with plasma from a healthy blood donor or a protein solution.
TPE has been studied in sepsis, a life-threatening condition where a person's immune system has been triggered by an infection and responds excessively, causing the release of substances that damage the person's organs. It is thought that deaths from COVID-19 might involve a similar over-reaction of the immune system (cytokine release syndrome). This study aims to investigate whether TPE can reduce deaths in patients in the intensive care unit (ICU) who are severely ill with COVID-19 and are at risk of organ damage or death due to an excessive immune response.

Who can participate?
Adults in the ICU who have COVID-19, are on a ventilator and are at risk or showing symptoms of an excessive immune response.

What does the study involve?
The participants will be randomly allocated to one of two groups. Both groups will continue to receive treatment and care as usual. One group will also receive TPE daily or on alternate days for 5-7 sessions.

What are the possible benefits and risks of participating?
TPE is an established technique that has few side effects. The most common include hives, itching and low blood pressure. The participants will be sedated because they are on a ventilator, so these side effects might not affect them as much as they might fully conscious patients. The potential benefit is that TPE reduces the excessive immune response and reduces damage to the participant's organs.

Where is the study run from?
King Saud Medical City Riyadh (Saudi Arabia)

When is the study starting and how long is it expected to run for?
April 2020 to December 2020

Who is funding the study?
King Saud Medical City Riyadh (Saudi Arabia)

Who is the main contact?
1. Professor Dimitrios Karakitsos, jkd97227@gmail.com
2. Dr Fahad Faqihi, dr.faqihi677@gmail.com

Contact information

Type(s)
Scientific

Contact name
Prof Dimitrios Karakitsos

ORCID ID
https://orcid.org/0000-0003-3370-7099

Contact details
King Saud Medical City
Riyadh
Saudi Arabia
12714-3232
+966 509816296
jkd97227@gmail.com

Type(s)
Scientific

Contact name
Dr Fahad Faqihi

Contact details
King Saud Medical City
Riyadh
Saudi Arabia
12714
+966 568005000
dr.faqihi677@gmail.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
KSMC-IRB-H1R1-29-Apr20-01

Study information

Scientific Title
A pilot randomized clinical trial of therapeutic plasma exchange (TPE) in serious SARS CoV-2 disease (COVID-19)

Study objectives
Therapeutic plasma exchange (TPE) reduces mortality when added to usual care in patients with serious or life-threatening COVID-19.

Serious COVID-19 is defined as acute respiratory failure: Dyspnea, respiratory rate ≥30/min, blood oxygen saturation ≤93%, partial arterial pressure of oxygen to fractional inspired concentration of oxygen (PaO2/FiO2) ratio <300 and/or development of bilateral pulmonary infiltrates within 24 to 48 h. Life-threatening COVID-19 is defined as: Acute respiratory distress syndrome (ARDS; according to the Berlin criteria), Acute Physiology and Chronic Health Evaluation II (APACHE II) score ≥20 upon ICU admission, presence of severe sepsis, septic shock and/or multi-system organ failure (MSOF), and risk of cytokine release syndrome (CRS).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/04/2020, King Saud Medical City Riyadh Institutional Review Board (King Saud Medical City, Riyadh, Saudi arabia; +966 435 5555 Ext 2345; irb@ksmc.med.sa), ref: H-01-R-053, IORG0010374, H1RI-29-Apr20-01

Study design
Pilot interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Serious and life-threatening COVID-19 requiring ICU admission

Interventions
The researchers aim to conduct a pilot prospective design of 6 to 12 months duration regarding the use of therapeutic plasma exchange (TPE) in serious COVID-19. The study will be multicenter. Adult ICU patients with serious/life-threatening COVID-19 receiving standard empiric therapies as per institutional and international protocols such as available antiviral treatments, hydroxychloroquine, mechanical (ARDS-net and prone position) ventilation, fluid resuscitation, vasoactive substances, antibiotics amongst other usual ICU supportive therapies will be randomised to control or TPE groups. Those in the control group will receive usual care. Those in the TPE group will receive usual care plus TPE therapy.

Randomization of the aforementioned groups will be done as follows. Eligible consented patients will be randomized after their stratification by ICU center and two PaO2/FIO2 ratio categories (>150 and <=150). Randomization will occur in variable block sizes of 4 to 8 patients. The researchers will utilize a web-based randomization service (randomize.net) to allocate patients to their respective strata prior to the intervention or control therapy. Given the nature of the TPE technology, the intervention will be unblinded (open label); hence, no enrollment concealment will be expedited. However, the lack of allocation concealment will be mitigated as much as possible by the following measures. First, the primary outcome of mortality will not be disputable. Second, the researchers have standardized co-interventions that impact on mortality as much as possible. These interventions include:
1. Concomitant drug therapies for COVID-19
2. Algorithms for mechanical ventilation including the early use of prone-ventilation, low tidal volume ventilation and neuromuscular blockade
3. The standard use of a broad spectrum antibiotic(s) for a minimum of 7 days to treat any potential superinfection, i.e. a bacterial pneumonia
4. Standard criteria to initiate intermittent hemodialysis or CRRT such as hyperkalemia, profound metabolic acidosis, oliguria unresponsive to furosemide challenges of 1-1.5 mg/kg
5. The presence or development of coagulopathy defined as INR >3.0 or fibrinogen <1.0 will be treated in a standard fashion in both the intervention and control group
The research team will define the date/time of appropriateness for ICU transfer irrespective of treatment allocation. They also recognise that some COVID-19 patients randomized to the intervention group may improve to the point of appropriateness to transfer to the medical ward but require ICU care only to deliver the remaining TPE doses as outlined in the protocol.

TPE will be initiated via venous vascular access using the Spectra Optia™ Apheresis System equipped with the Depuro D2000 Adsorption Cartridge (Terumo BCT Inc., USA). A dose of 1.5 plasma volumes is used for the first dose then one plasma volume on alternate days or daily for five to seven doses per clinical case. The Spectra Optia™ Apheresis System operates with acid-citrate dextrose anticoagulant (ACDA) as per Kidney Disease Improving Global Outcomes (KDIGO) 2019 guidelines. Plasma is replaced with albumin 5% or fresh frozen plasma in patients

with coagulopathy (prothrombin time >37 s; international normalized ratio >3; activated partial thromboplastin time >100 or fibrinogen level <100 mg/day). TPE sessions are performed daily over 4 h and laboratory markers are measured daily.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. 28-day mortality assessed using patient medical records
2. Safety assessed by measuring adverse events and serious adverse events collected as usual for TPE treatment using the Saudi FDA reporting standard during the TPE session and the following 48 h

Key secondary outcome(s))
1. Organ function assessed using Sequential Organ Function Assessment (SOFA) score before and after each TPE session
2. Inflammation markers (including lymphocyte counts, C-reactive protein [CRP], lactate dehydrogenase [LDH], ferritin, D-dimer, interleukin-6 [IL-6]) measured using usual hospital laboratory assays before and after each TPE session
3. Days on mechanical ventilation assessed using patient medical records
4. ICU length of stay assessed using patient medical records

Completion date
29/12/2020

Eligibility

Key inclusion criteria
1. Aged ≥18 years
2. Admitted to ICU and intubated
3. Serious COVID-19 as per World Health Organization and Saudi Centers for Disease Control and Prevention case definition. SARS-CoV-2 infection should be confirmed by real-time polymerase chain reaction (RT-PCR) assays
4. At risk of cytokine release syndrome (CRS)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
87

Key exclusion criteria
1. Previous allergic reaction to plasma exchange reagents (e.g. sodium citrate) or equipment
2. Two consecutive negative RT-PCR tests for SARS-CoV-2 taken at least 24 h apart
3. Mild COVID-19 cases not requiring ICU admission
4. Terminally ill patients receiving palliative care

Date of first enrolment
01/05/2020

Date of final enrolment
29/10/2020

Locations

Countries of recruitment
Oman

Saudi Arabia

United Arab Emirates

Study participating centre
King Saud Medical City
King Saud Medical City
Riyadh
Saudi Arabia
12714-3232

Study participating centre
Al Imam Abdulrahman Al Feisal Hospital
Al Imam Abdulrahman Al Feisal Hospital
Riyadh
Saudi Arabia
12714

Sponsor information

Organisation
King Saud Medical City

ROR
https://ror.org/03aj9rj02

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
King Saud Medical City

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from the principal investigator Dr Fahad Faqihi, dr.faqihi677@gmail.com.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/04/2021	14/06/2023	Yes	No
Protocol article	protocol	01/12/2020	10/06/2020	Yes	No
Other publications	Case report	07/10/2020	10/06/2025	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes