

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

<b>Submission date</b> 15/05/2020	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 18/05/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/06/2025	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> 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

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## **Additional identifiers**

**EudraCT/CTIS number**

Nil known

**IRAS number****ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

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  $\geq 30$ /min, blood oxygen saturation  $\leq 93\%$ , partial arterial pressure of oxygen to fractional inspired concentration of oxygen ( $\text{PaO}_2/\text{FiO}_2$ ) 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  $\geq 20$  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

## **Secondary study design**

Randomised controlled trial

## **Study setting(s)**

Hospital

## **Study type(s)**

Treatment

## **Participant information sheet**

Not available in web format, please use contact details to request a participant information sheet.

## **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 PaO<sub>2</sub>/FIO<sub>2</sub> 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 measure**

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

### **Secondary outcome measures**

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

### **Overall study start date**

01/04/2020

### **Completion date**

29/12/2020

## **Eligibility**

### **Key inclusion criteria**

1. Aged  $\geq 18$  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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

This will be a pilot randomized trial aiming on recruiting a convenience sample of cases over a 6 to 12 months duration. The targeted number is 20 cases and 20 controls per participating center.

**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  
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## **Sponsor information**

### **Organisation**

King Saud Medical City

### **Sponsor details**

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### **Sponsor type**

Hospital/treatment centre

### **Website**

<https://medicalcity.ksu.edu.sa/>

### **ROR**

<https://ror.org/03aj9rj02>

## **Funder(s)**

### **Funder type**

Hospital/treatment centre

### **Funder Name**

King Saud Medical City

## **Results and Publications**

### **Publication and dissemination plan**

We are aiming to publish our preliminary results as soon as possible as the study is currently running. We are expecting our first publication to be ready soon hence we wish to register the trial as soon as possible.

## Intention to publish date

30/07/2020

## 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?
<a href="#">Protocol article</a>	protocol	01/12/2020	10/06/2020	Yes	No
<a href="#">Results article</a>		07/04/2021	14/06/2023	Yes	No
<a href="#">Other publications</a>		07/10/2020	10/06/2025	Yes	No
	Case report				