Apheresis based treatment of sepsis

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To determine the efficacy of a filter-based depletion of RBC-pathogen complexes by a single apheresis tretatment in patients with sepsis.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Red blood cell disorders
Study type	Observational invasive

Summary

ID

NL-OMON45881

Source
ToetsingOnline

Brief title
ASSIST

Condition

- Red blood cell disorders
- Bacterial infectious disorders

Synonym
blood poisoning

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Sanquin

Intervention

Keyword: Apheresis, ICU, Sepsis, Treatment

Outcome measures

Primary outcome

- Reduction of RBC-pathogen complexes after 1 session of apheresis with processing 1.5 times the patients total blood volume which is calculated based on Nadlers formula.

- Haematological parameters, such as RBC, platelet and leukocyte counts, before and after apheresis

Secondary outcome

- Vital parameters during apheresis (blood pressure, saturation, pulse, heart rhythm)

- total Ca, ionized Ca, lactate, Mg,

- SOFA score day of inclusion and day after inclusion

- Outcome (28 day mortality)

- Duration of ICU stay

- Duration of hospital stay

- Bloodgas analysis

Study description

Background summary

The presence of pathogens in the bloodstream can cause the onset of sepsis or septic shock. It is thought that release of endotoxins from circulating bacteria contributes to a hyperinflammatory response. One of the mechanisms to protect the host from blood-borne infections is immune adherence clearance (IAC), the process by which complement opsonized pathogens are bound by red blood cells (RBCs) and transported to the liver and spleen where they are engulfed by macrophages. Recently, we found that during sepsis a large number of RBC-pathogen complexes, as a consequence of IAC, can be detected in the

patients* blood. The percentage of RBC-pathogen complexes was found to be as high as 1-2% of the total number of circulating RBCs, which corresponds to a pathogen load of 10-20.106/ml blood. Studying the mechanisms of pathogen transfer from RBC to macrophages in vitro, we discovered that RBC that carry pathogens adopt a particular phenotype. This phenotype facilitates the binding of the RBC-pathogen complex to macrophages. Next, we were able to develop a method that specifically captures RBC-pathogen complexes in peripheral blood through an apheresis procedure, by capturing the RBC-pathogen complexes with a specific filter in an apheresis setup. With this method the depletion of RBC-pathogen complexes from the blood that is subjected to this procedure is typically *95%, independent of the pathogen that the RBCs are carrying. We expect to be able to use this method to deplete the number of circulating RBC-pathogen complexes in vivo to >70% by processing the blood volume of the patient 1,5 times by the apheresis machine. Thereby, we have potentially identified a new generic treatment for sepsis. In this clinical trial, which consists of two phases, we will investigate the efficacy of our apheresis setup to deplete RBC-pathogen complexes. In the first phase, we will test the safety of our setup on three healthy volunteers, to establish that there are no effects on the quality of plasma and blood cell types including RBCs, platelets and leukocytes and to ensure that our procedure is absolutely safe. If safe, during the second phase we will treat ten septic patients with a one time apheresis procedure, to determine whether the procedure is able to effectively reduce the number of circulating RBC-pathogen complexes.

Study objective

To determine the efficacy of a filter-based depletion of RBC-pathogen complexes by a single apheresis tretatment in patients with sepsis.

Study design

The study consists of two phases, the first phase is a small safety study on healthy volunteers, the second phase is a prospective, single center safety trial on 10 sepsis patients.

Study burden and risks

At the start of apheresis, the patient may have a (transient) limited decrease in blood pressure. Given that the extracorporeal blood volume is limited and that patients in severe shock are excluded, we expect that the risk of a transient lower blood pressure is negligible. Thereby, it is anticipated that there are no burden or risks associated with participation except for the known well described small risks associated with an apheresis procedure, especially hypocalcaemic symptoms due to citrate infusion with the re-infusion of all blood components. Patients with hepatic or renal insufficiency may be at increased risk of citrate toxicity due to impaired metabolism of citrate.

Therefore, as part of standard care, ionized calcium levels of all patients will be measured regularly and prophylactic calcium will be administered. Since this is a new apheresis-based procedure the procedure will first be performed on three healthy volunteers. The outcome of this first part of the trial will first be communicated with the METC before starting the second part, involving the septic patients. By following this schedule, we minimize any potential risks associated with this procedure.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Volunteers:
- >18 years old
- Healthy male volunteer

- Meet eligibility criteria for donating whole blood in the Netherlands
- Informed consent;Patients:
- ICU patient recovering from sepsis, who have detectable RBC-pathogen complexes in their blood.
- * 18 years old
- Existing vascular access preferably a double lumen dialysis catheter
- Informed consent

Exclusion criteria

Volunteers:
- Any abnormal test result during the screening prior to inclusion of the study (medical history, physical examination, and blood examination)
- History of drugs or alcohol abuse
- Any present medication use on prescription
- Participation in any other intervention study during the course of this study;Patients:
- Hemodynamic instability as defined by requiring >0.1 mcg/kg/minute of norepinephrine to reach a MAP of > 60 mmHg.
- Active bleeding as assessed by the treating physician
- Haematological disorders.
- Pregnant or lactating women

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Generic name:	Apheresis device
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	15-01-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL67018.018.18