Study into the effect of CytoSorb (cytokine adsorber) in relation to the MICrocirculation of patients with Septic Shock and Acute Kidney Injury at the ICU; MICSS-AKI

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Could cytokines removal therapy by CytoSorb adsorber cause any improvement in the microcirculation?

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53033

Source
ToetsingOnline

Brief title
Microcirculatory response to cytokine removal therapy

Condition

- Other condition
- Bacterial infectious disorders
- Nephropathies

Synonym
sepsis and acute kidney injury

Health condition

Microcirculatie en weefseldoorbloeding

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus Universiteit Rotterdam
Source(s) of monetary or material Support: Gedeeltelijk door CytoSorbents Europe GmbH

Intervention

Keyword: AKI, CytoSorb, microcirculation, Septic shock

Outcome measures

Primary outcome

Is cytokine removal with a CytoSorb adsorber during septic shock with AKI able

to alter the pathophysiologic changes of the microcirculation?

Secondary outcome

• To determine the systemic attenuation of cytokine concentrations in patients

with septic shock and AKI initiated on CVVHD in combination with the CytoSorb

membrane

• To investigate possible adsorption of Neutrophil Gelatinase-associated

Lipocalin by the CytoSorb membrane

• Determining the effect on ICU outcome, length of stay and SOFA score.

Study description

Background summary

Pathogenesis of septic shock and septic AKI are highly related to high-level of

cytokines release causing dysregulation of both pro-and anti-inflammatory responses during sepsis. Supra-high concentrations of a variety of cytokines upregulate the immunity and play an important role in the causality of the sepsis syndrome itself.
Based on this, extra corporeal blood purification therapies (ECBPTs) are intended to remove non-specifically a variety of low and middle molecular substances including cytokines to diminish the high peaks. One of the hemoadsorption techniques is The CytoSorb* technology (CytoSorbents Corporation, Monmouth Junction, NJ, USA).
This technique is routinely used in many countries in cases where cytokine levels are elevated especially in patients with septic shock. Animal studies and many case reports have shown that CytoSorb significantly reduces cytokine levels and improves global hemodynamics while improving the outcome.
Microcirculation is deteriorated in septic conditions due to several mechanisms. To measure this we will use a new technologically advanced version of hand held microscopes (CytoCam, Braedius Medical, Huizen, the Netherlands) based on Incident Dark Field (IDF) by quantifying images to provide the needed microcirculatory parameters directly at the bedside.
We will investigate the effect of cytokines removing therapy with the CytoSorb adsorbing membrane on the improvement of the microcirculation in patients with septic shock and AKI.

Study objective

Could cytokines removal therapy by CytoSorb adsorber cause any improvement in the microcirculation?

Study design

Multi-center, comparison study as prove of concept.

Intervention

Data obtained in septic shock patients with AKI treated with CVVHD+ CytoSorb (group 1) will be compared with microcirculatory measurements and biomarkers obtained in septic shock patients with AKI without CytoSorb treatment (group 2).

Study burden and risks

The patients will be randomized into two groups. The first group will have a CytoSorb filter added to the routine CRRT which has to be prepared by nurses who are exclusively trained for this by CytoSorb company. The second group is well known by the medical and nursing staff. They have large experience with the use of CRRT in patients with septic shock and AKI. All the patients in the two groups will be monitored continuously at the ICU. The CytoSorb filter will

be used in our Fresenius CRRT machines. In rare cases, hypersensitivity reactions may occur during CytoSorb treatment. A history of allergies will be carefully monitored at inclusion and during the study. Microcirculation assessment is a non-invasive procedure, and there are negligible risks. Blood and urine tests will be used for measuring cytokine, biomarkers, and drug levels. The risks associated with participation can be considered negligible.

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

Each patient, weight above 60 kg with septic shock needing vasopressors or lower dosis norepinephrine supplemented with dobutamine, vasopressin (argipressin) /terlipressin/epinephrine must meet all of the following criteria to be enrolled in this study:

1. Has written informed consent from patient or legal representative.
2. Is aged 18 to 85 years, inclusive a weight above 60 kg.
3. Is admitted to the ICU
4. Has diagnosis of septic shock according to the criteria defined by Singer et al in the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) published in JAMA, 2016.
• Organ dysfunction acute change in total SOFA score >=2 points consequent to the infection or Quick SOFA (qSOFA,): alteration in mental status, systolic blood pressure <=100 mm Hg, or respiratory rate >=22/min.
• Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP >=65 mm Hg and having a serum lactate level >2 mmol/L despite adequate volume resuscitation.
5. Has diagnosis of AKI, defined as the following:
AKI Stage 2 according to the following KDIGO guidelines criteria, based on changes in Serum Creatinine (SCr), urine output or both:
a. Increase in SCr 2.0-2.9 times baseline and or a Urine Output (UO) < 0.5 ml-kg-h for >= 12 hours compared with a SCr value within the previous 48 hours.
b. The reference SCr value is a SCr value in the following order of preference:
1. Lowest value within 3 months of hospital admission if not available:
2. At hospital admission. If not available:
3. At ICU admission. If not available:
4. Lowest value between 3 and 12 months prior to hospital admission
6. Has a deteriorated sublingual microcirculation measured by Cytocam-IDF imaging and quantified by determining the MFI as < 2,6.

Exclusion criteria

Patients meeting any of the following criteria will be excluded from the study:
1. Moribund
2. Woman of childbearing potential with a positive pregnancy test
3. Has a diagnosis of septic shock longer than 24 hours before inclusion
4. Has a normal sublingual microcirculation
5. Neutropenia; absolute neutrophil count less than 1000/um
6. Thrombocytopenia (less than 20.000/um)
7. Any body weight lower than 60 kg.
8. Treatment with intravenous aminoglycosids or antifungal therapy

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2020
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	CytoSorb adsorber
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	01-08-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-08-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

(Rotterdam)

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	NL61004.078.17