An open-label randomized controlled experimental endotoxemia study on the effects of the cytokine-adsorbing hemofilter CytoSorb on the development of immunoparalysis in humans

Published: 22-07-2020
Last updated: 12-04-2024

To determine the effects of the CytoSorb hemoperfusion column on the development of immunoparalysis in a repeated human endotoxemia model, which is reflected by attenuated plasma cytokine levels during the second LPS challenge.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON55310

Source
ToetsingOnline

Brief title
The EndoSorb study

Condition

- Immune disorders NEC
- Bacterial infectious disorders

Synonym
Blood stream infection, immunoparalysis

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: CytoSorbents Europe GmbH

Intervention

Keyword: Blood purification, Endotoxemia, Immunoparalysis, Sepsis

Outcome measures

Primary outcome

Plasma IL-6 levels during the second LPS challenge. Comparison of CytoSorb group with control group. IL-6 is an archetypal pro-inflammatory cytokine with high relevance to sepsis.

Secondary outcome

- Plasma levels of other inflammatory cytokines (including, but not limited to IL-6, IL-8, IL-10, MCP-1, CXCL-10, MIP-1*, MIP-1*, and G-CSF) during the second LPS chal-lenge.

- mHLA-DR expression.

- Plasma levels of inflammatory cytokines (including, but not limited to IL-6, IL-8, IL-10, MCP-1, CXCL-10, MIP-1*, MIP-1*, and G-CSF) during the first LPS challenge

- Norepinephrine sensitivity during the first LPS challenge.

- Cytokine concentrations in afferent and efferent tubing of the CytoSorb filter. Togeth-er with the blood flow, cytokine clearance by the filter can be calculated.

- Endotoxemia-induced changes in leukocyte numbers and differential count

- Endotoxemia-induced increase in body temperature

- Endotoxemia-induced symptoms

- Endotoxemia-induced hemodynamic alterations

- Endotoxemia-induced increase in markers of endothelial injury (VCAM/ICAM)

Study description

Background summary

Sepsis is a major health care burden with high mortality rates and increasing incidence. Over the last couple of decades, it has become increasingly clear that not hyperinflammation, but a protracted immunosuppressive state known as immunoparalysis is the overriding immune disorder in sepsis. Patients suffering from immunoparalysis are highly susceptible towards infectious diseases, and secondary infections attribute to the high mortality in these patients to a great extent. Immunoparalysis is mainly caused by high concentrations of inflammatory cytokines in the early stages of sepsis. These cytokines are produced primarily in the tissues. Treatment options aimed at capturing these cytokines might aid in the prevention of immunoparalysis and might thereby improve outcome for sepsis patients. The cytokine-adsorbing hemofilter CytoSorb might represent such an option. In the present study, we aim to investigate whether CytoSorb hemoperfusion prevents immunoparalysis effectively in a group of healthy volunteers who will undergo an endotoxin challenge twice.

Study objective

To determine the effects of the CytoSorb hemoperfusion column on the development of immunoparalysis in a repeated human endotoxemia model, which is reflected by attenuated plasma cytokine levels during the second LPS challenge.

Study design

Open-label randomized controlled trial. Twenty-four healthy subjects will be divided into two groups (12 vs 12): the CytoSorb group and a control group. Both groups will undergo an endotoxin challenge twice. The CytoSorb group will be treated with CytoSorb hemoperfusion for six hours during the first endotoxin challenge, whereas the control group will receive no intervention. Blood samples will be obtained at predefined timepoints throughout the experiment to construct time-concentration curves of various inflammatory cytokines. One week later, the experiment will be repeated, this time without hemoperfusion treatment. After 12 subjects (6 vs 6) have completed the study, an interim analysis on safety data will be performed.

Intervention

CytoSorb hemoperfusion for six hours

Study burden and risks

Participants will visit the hospital four times: for the screening visit, twice for the endotoxin challenges and once for follow-up. Total time-investment will be approximately 21 hours in 8 days. We have extensive experience with performing endotoxin experiments, which are classified as being of negligible risk. CytoSorb hemoperfusion has been applied in > 60.000 patients without any safety concerns. Taking all of this into account, we feel that the remaining risks do not outweigh the medical and scientific relevance of the study and that the study is proportional.

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

- Written informed consent
- Male
- Age * 18 and * 35 years
- Healthy (as determined by medical history, physical examination, vital signs, 12-lead electrocardiogram (ECG) and routine clinical laboratory parameters)

Exclusion criteria

- Use of any medication
- Smoking
- Hypersensitivity to any of the (non)investigational products or their excipients
- History of:
- Any immune-related disorder
- Aneurysmal or hemorrhagic disease
- Renal or hepatic impairment
- Recent infection (<2 weeks)
- Previous LPS administration

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-09-2020

Enrollment:	24
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	22-07-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-11-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-03-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL71293.091.19