The role of the gut MIcrobiota in the SyStemic Immune respONse during human endotoxemia

Published: 04-03-2014
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To investigate the role of the gut microbiota in the systemic priming of immune effector cells during human endotoxemia

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON38933

Source
ToetsingOnline

Brief title
MISSION-2

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
sepsis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Klinische fellowship beurs ZonMw

Intervention

Keyword: antibiotics, endotoxemia, gut microbiota, immune response

Outcome measures

Primary outcome

Laboratory parameters for inflammatory responses, functional assays (ex vivo

stimulation assay) and gut microbiota composition.

Secondary outcome

Not applicable

Study description

Background summary

Sepsis ranks among the top ten leading causes of death worldwide. Most nonsurvivors die in a state of immunosuppression. The gut microbiota exerts numerous beneficial functions in the host response against infections. Gut flora components express microorganism-associated molecular patterns (MAMPs) such as lipopolysaccharide (LPS), which are recognized by pattern recognition receptors (PRRs) expressed by neutrophils and macrophages. MAMPs from the intestinal microbiota constitutively translocate to the circulation and prime bone marrow derived neutrophils via PRRs. Antibiotic treatment, which is standard of care for all patients with sepsis, depletes the gut microbiota and leads to a diminished release of MAMPs and other bacteria derived products. This causes diminished priming of systemic immunity, which may attribute to sepsis associated immunosuppression and an increased susceptibility to invading bacteria.

Study objective

To investigate the role of the gut microbiota in the systemic priming of immune effector cells during human endotoxemia

Study design

Within-subject-controlled intervention study in human volunteers

Intervention

All subjects will receive lipopolysaccharide intravenously (endotoxin; 2 ng/kg body weight) to induce experimental endotoxemia. Eight subjects will be pretreated with broad spectrum antibiotics (ciprofloxacin, vancomycin, metronidazole) for seven days (washout period of 36 hours before endotoxemia), in order to deplete the gut microbiota. Blood and faeces will be sampled before, during and after endotoxemia.

Study burden and risks

The burden of this study includes a screening visit, a second visit and one day hospital admittance. Endotoxemia will induce complaints consisting mainly of myalgia, headache, fever and nausea that attenuate within 6 hours. Furthermore blood will be drawn and faeces has to be collected by subjects. Half of the volunteers will ingest antibiotics, which have potential side effects: mostly gastrointestinal symptoms and (rarely) allergic reactions. Future patients with sepsis may benefit from the outcome of this study, as its ultimate aim is to develop new therapeutic strategies to restore immunity, such as administration of selective components of the microbiota.

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

1. Healthy (medical history, no use of medication; normal physical examination, ECG and laboratory tests)
2. Male between 18 and 35 years of age
3. Normal defecation pattern

Exclusion criteria

1. Recent major illness or chronic medical illness
2. History of malignancy
3. Gastrointestinal and liver diseases
4. Known positive test for hepatitis B or C or HIV
5. Smoking; drug abuse; alcohol abuse
6. Clinically relevant ECG abnormality
7. Subject has received an investigational product within three months of day 1 of the current study
8. Use of prescription or non-prescription drugs
9. Recent (< 12 months) use of antibiotics
10. Allergy to antibiotics
11. Difficultly in donating blood or limitied accessibility of a vein in left or right arm.
12. Subject has donated more than 350 mL of blood in last 3 months
13. Difficulty swallowing pills
14. Body mass index >28 kg/m2

Study design

Design

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

Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-04-2014
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	04-03-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-12-2015
Application type:	Amendment
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

ID: 27487
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL45198.018.13
OMON	NL-OMON27487