Het effect van antibiotica en de darmflora op afweerreacties

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27487

Source
Nationaal Trial Register

Brief title
MISSION-2

Health condition

Endotoxemia

Sponsors and support

Primary sponsor: Academic Medical Centre, Amsterdam
Source(s) of monetary or material Support: ZonMW

Intervention

Outcome measures

Primary outcome

Cytokine production in blood

Secondary outcome

Activation of coagulation

Composition of gut microbiota

Study description

Background summary

Rationale: 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.

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

Study design: Randomized, between- and within-subject-controlled intervention study in human
volunteers

Study population: Sixteen healthy male subjects, 18-35 years of age

Intervention: All subjects will receive lipopolysaccharide (endotoxin; 2 ng/kg bodyweight) intravenously 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.

Main study parameters/endpoints: Laboratory parameters for inflammatory responses, functional
assays and gut microbiota composition.

Study objective

Broad-spectrum antibiotics, which many patients with infectious diseases receive, deplete the gut microbiota. Several studies suggest that the gut microbiota may have a "priming" effect on the innate immune system. Broad- spectrum antibiotics would thus lead to a decreased innate immune response in disease states such as sepsis or endotoxemia.

Study design

Day 0

Day 9: t = 0 and at 0.5, 1, 1.5, 2, 3, 4, 6 and 8 hours after LPS injection

Intervention

The control group receives no antibiotics
The antibiotics group receives ciprofloxacin 500mg 2dd1, vancomycin 250mg 3dd2 and metronidazole 500mg 3dd1; all during 7 days

Both groups receive (on day 9) LPS (endotoxin) 2 ng/kg intravenously

Contacts

Public
CEMM, Department of Internal Medicine
Academic Medical Center
University of Amsterdam
Meibergdreef 9
J.M. Lankelma
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5665247
Scientific
CEMM, Department of Internal Medicine
Academic Medical Center
University of Amsterdam
Meibergdreef 9
J.M. Lankelma

Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5665247

Eligibility criteria

Inclusion criteria

1. Healthy, as determined by a responsible physician, based on a medical evaluation including medical history, physical examination and laboratory tests

2. Male between 18 and 35 years of age

3. Capable of giving written informed consent

4. Chemistry panel, including renal and liver function tests, without any clinically relevant abnormality as judged by the investigator

5. Normal defecation pattern

Exclusion criteria

1. Subject has had a major illness in the past 3 months or any significant chronic medical illness

2. Subjects with a history of any type of malignancy

3. Subject has a past or current gastrointestinal disease

4. The subject has a known positive test for hepatitis C antibody, hepatitis B surface antigen or human immunodeficiency virus (HIV) antibody 1 or 2

5. Current or chronic history of liver disease

6. Subject uses tobacco products

7. Subject has a history, within 3 years, of drug abuse

8. History of alcoholism

9. Any clinically relevant abnormality noted on the 12-lead ECG as judged by the investigator or an average QTc > 450 msec

10. The subject has received an investigational product within three months

11. Use of prescription or non-prescription drugs and herbal and dietary supplements

12. Recent (< 12 months) use of antibiotics

13. Known allergy to antibiotics (any kind)

14. Subject has difficultly in donating blood or accessibility of a vein in left or right arm.

15. Subject has donated more than 350 mL of blood in last 3 months

16. Difficulty swallowing pills

17. 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:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2014
Enrollment:	16
Type:	Anticipated

Ethics review

Positive opinion

Date:	30-04-2014

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 38933
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL4425
NTR-old	NTR4549
CCMO	NL45198.018.13
OMON	NL-OMON38933

Study results