The role of the microbiota in the systemic immune response

Published: 05-11-2012
Last updated: 15-05-2024

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

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

Summary

ID

NL-OMON36859

Source
ToetsingOnline

Brief title
MISSION- 1

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: ZonMw Klinische Fellowship beurs

Intervention

Keyword: antibiotics, gut microbiota, immune response

Outcome measures

Primary outcome

Side effects, laboratory parameters for inflammatory responses, functional

assays (ex vivo inflammatory responses) 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 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. This may attribute to sepsis associated immunosuppression. Our ultimate aim is to develop new therapeutic strategies to restore immunity, such as faeces transplantation or administration of selective components of the microbiota.

Study objective

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

Study design

Within-subject-controlled intervention study in human volunteers, n=12

Intervention

Subjects self-administer antibiotics for seven days:
- ciprofloxacin 500mg 2dd1 (Gram negatives and positives)

- vancomycin 250mg 3dd2 (Gram positives)
- metronidazol 500mg 3dd1 (anaerobes)
Blood and feces will be collected before taking antibiotics and 24 hours and 6 weeks after taking antibiotics.

Study burden and risks

Volunteers may experience side effects when using antibiotics, mostly gastrointestinal complaints like diarrhoea. Subjects known with any allergic reaction to any previously administered antibiotic will be excluded from participation, but novel allergic reactions are possible. The burden also includes 3 visits - after the initial screening for eligibility visit * to draw blood and collect faeces (subject himself at home). Subjects are not allowed to smoke, drink (until 48 hours after the last dose of antibiotics) or travel to tropical countries.

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

18-35 years of age
male
healthy (medical history, physical exam, no medications, laboratory screening)
non- smoking
normal defecation pattern (<3x/ day, >3x/week)

Exclusion criteria

allergic to antibiotics (any kind)
recent use of antibiotics (<12 maanden)
difficulty swallowing pills

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-03-2012
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	05-11-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2013
Application type:	Amendment
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: 27808
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL42072.018.12
OMON	NL-OMON27808