Establishing an etiological role of the gut microbiome in the antiphospholipid syndrome phenotype

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Primary Objective: - to establish if a gut microbiome perturbation affects APS disease phenotype.Secondary Objective(s): - to identify biomarkers that are responsive gut microbiome perturbation.- to establish if gut microbiome perturbation affects...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Observational invasive

Summary

ID

NL-OMON55745

Source
ToetsingOnline

Brief title
ROMAS study

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Autoimmune disorders
- Abortions and stillbirth

Synonym
antiphospholipid syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: antiphospholipid syndrome, gut microbiome

Outcome measures

Primary outcome

The main study outcome is the composite of a broad panel of APS

pathophysiology-related blood biomarkers. These biomarkers are regarded to

collectively reflect the APS phenotype.

Secondary outcome

The secondary outcome is gut permeability as measured by lactulose/mannitol

test.

Study description

Background summary

Antiphospholipid syndrome (APS) is a common autoimmune disease. Thrombosis, recurrent miscarriage, pre-eclampsia, placental insufficiency, fetal death and the often fatal catastrophic antiphospholipid syndrome, are all manifestations of APS. The origin of the autoantibodies that characterize the syndrome is unknown. The gut microbiome, the ecosystem of microbes residing in the intestinal tract, is contributes to autoimmunity, and recent animal studies suggest an etiological role of the microbiome in APS. We aim to establish proof-of-concept for an etiological role of the gut microbiome in human APS.

Study objective

Primary Objective:
- to establish if a gut microbiome perturbation affects APS disease phenotype.
Secondary Objective(s):
- to identify biomarkers that are responsive gut microbiome perturbation.
- to establish if gut microbiome perturbation affects intestinal permeability in APS patients.

Study design

The study will have a pretest posttest design in which all subjects undergo a short course of antibiotic treatment between measurement time points. During the study all patients will undergo a 7 day treatment course of oral vancomycin, 500mg 4 times daily, a standard antibiotic.

Study burden and risks

There are four site visits. The first visit will last 1 hour, the other visits will last 4 hours each. No serious side effects are suspected of vancomycin as it is administered orally and is very poorly absorbed from the gut. Side effects of oral administration include temporary abdominal discomfort, bloating, flatulence and nausea. Subject will drink a single dose of mannitol and lactulose at each visit which might cause mild temporary bloating and flatulence. Subjects will have to be sober for approximately 10 hours overnight for these tests. 60 ml of blood will be drawn on three occasions.

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

In order to be eligible to participate in this study, a subject must meet the revised Sapporo classification criteria for antiphospholipid syndrome:

At least one of the clinical and at least one of the laboratory criteria below

Clinical criteria

1. Thrombosis
One or more clinical episodes of arterial, venous, or small vessel thrombosis, in any tissue or organ. Thrombosis must be confirmed by objective validated criteria (i.e., unequivocal findings of appropriate imaging studies or histopathology).

2. Pregnancy morbidity
(a) One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation, with normal fetal morphology documented by ultrasound or by direct examination of the fetus, or
(b) One or more premature births of a morphologically normal neonate before the 34th week of gestation because of: (i) eclampsia or severe pre-eclampsia de*ned according to standard de*nitions, or (ii) recognized features of placental insu*ciency*,or
(c) Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded.

Laboratory criteria

a Lupus anticoagulant (LA) present in plasma, on two or more occasions at least 12 weeks apart, detected according to the guidelines of the International Society on Thrombosis and Haemostasis (Scienti*c Subcommittee on LAs/phospholipid-dependent antibodies).

b. Anticardiolipin (aCL) antibody of IgG and/or IgM isotype in serum or plasma, present in medium or high titer (i.e. >40 GPL or MPL, or >the 99th percentile), on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA.

c. Anti-b2glycoprotein-I antibody of IgG and/or IgM isotype in serum or plasma (in titer >the 99th percentile), present on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA, according to recommended procedures.

Exclusion criteria

- Age below 18 years
- Current use of antibiotics
- History of gastro-enteritis in the past month
- History of inflammatory bowel disease
- Current use of a vitamine K antagonist
- Planned change in the following medication during the study period (either start, stop or dose change): platelet aggregation inhibitors, oral anticoagulants, heparins, hormonal therapy.
- Current pregnancy or pregnancy in the past 6 weeks
- Arterial or venous thrombosis in the past month
- Allergy to vancomycin

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-11-2019
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	22-03-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2021
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

No registrations found.

In other registers

Register	ID
CCMO	NL67782.018.18