The oral and gut microbiome in patients with primary Sjögren's syndrome - a pilot study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON41780

Source
ToetsingOnline

Brief title
Sjögren microbiome study

Condition

- Other condition
- Autoimmune disorders

Synonym
Primary Sjögren's syndrome, Sjögren

Health condition

rheumatische aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Boeringstichting - Oral and Maxillofacial Research Fund Groningen

Intervention

Keyword: Microbiome, next-generation sequencing, Sjögren's syndrome (SS)

Outcome measures

Primary outcome

Mouth wash, buccal swab and stool samples

Microbiome data:

• Relative abundance; quantitative measure of the number of micro-organisms, operational taxonomic units (OTUs), or sequences detected in a sample, in relation to all other micro-organisms in the same sample.

• Richness; the number of unique organisms detected in one sample.

• Diversity; (measured with the species richness and abundance) within (alpha-diversity) and between (beta-diversity) samples.

• Distance; a measure of the differences between samples (conducting principal component analysis) based on beta-diversity.

• UniFrac phylogenetic distance; the phylogenetic distance between sets of taxa in a phylogenetic tree as the fraction of the branch length of the tree that leads to descendants from either one environment or the other, but not both.

Laboratory parameters:

• Levels of IgA and IgM in mouth wash and stool samples

Secondary outcome

- Dutch Periodontal Screening Index score (DPSI score)

- Food consumption

- Data on perinatal period (birth weight and length, type of delivery,

breastfeeding y/n) (6 questions)

- Xerostomia Inventory (11 questions)

- WHO Oral Health questionnaire for adults (16 questions)

Study description

Background summary

Sjögren*s syndrome (SS) is one of the three most common auto-immune disorders. SS is characterized by infiltration of lymphocytes in the salivary and lacrimal glands leading to a reduced secretion of saliva and tears which in turn leads to sicca symptoms of the mouth and eyes. Primary SS (pSS) is a multifactorial disease because genes, environment, ductal gland epithelial cells and an altered immune system play important roles in the pathogenesis. Bacteria in the human gut affect the local and systemic immune system of the host. A dysbiosis or specific bacteria can induce a chronic inflammatory reaction and may cause autoimmunity in the host. Associations between specific gut microbiota and rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) have been found in clinical studies. We will investigate whether pSS is associated with changes in the microbial composition in the gut and the oral cavity.

Study objective

Primary objective: To identify specific bacteria or a characteristic bacterial composition in the oral and gut microbiome of pSS patients compared to non-Sjögren*s syndrome sicca (non-SS sicca) patients, SLE patients and healthy controls.

Secondary objective: To associate characteristics of the oral and gut microbiome of pSS patients with clinical, functional, laboratory and histological parameters of pSS.

Study design

The Sjögren microbiome study has an observational case-control design.

Four study groups are included:
1) Patients with pSS: 30
2) Non-SS sicca patients: 30
3) SLE patients: 30
4) Healthy controls: 100

Study burden and risks

Patients with pSS and non-SS sicca patients who visit the outpatient clinic of the department of Rheumatology and Clinical Immunology and the department of OMF-Surgery as part of the *UMCG zorgtraject Sjögren* will be asked to participate in the Sjögren microbiome study. The UMCG zorgtraject Sjögren is a standardized diagnostic work-up protocol in which patients who are suspected to have SS routinely visit the Rheumatology and Immunology department, the department of OMF-Surgery and the department of Ophthalmology. Patients with SLE will be informed about this study two weeks prior to their outpatient clinic visit. No extra visits to the hospital are required for any of the participants of this study. Extra interventions of the Sjögren microbiome study are: one mouth wash sample, one buccal swab and one stool sample (collected by the patient at home), 4 questionnaires and a short periodontal condition examination. Overall, the burden for the participants is low, because no extra visits are necessary, samples are collected only once and at home and the sampling methods are non-invasive. The risk of participation is negligible as no invasive procedures specifically for this research project will be performed. Patients do not have a direct benefit of participating in the study. However, with the results obtained in this study we will create a foundation for future research on the role of the oral and gut microbiome in pSS and SLE patients. This may lead to new insights in pathogenesis and new ways of treating pSS and SLE.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

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, all subjects must meet all of the following criteria:
• Age >= 18 years
• Live in Groningen, Friesland or Drenthe
• Signed informed consent;Subjects must meet the following criteria to be included in one of the four study groups:
• Group 1: Confirmed diagnosis of pSS according to the AECG criteria [4] after complete diagnostic workup.;• Group 2: non-SS sicca. After complete diagnostic workup defined as:
o Presence of symptoms of dry eyes and/or symptoms of a dry mouth according to the questions in the AECG criteria (supplement 15.1)
o Negative minor salivary gland biopsy according to the Chisholm and Mason scoring system(30)
o Absence of anti-Ro/La (SSA/SSB) auto-antibodies
o Low clinical suspicion of pSS;• Group 3: Newly diagnosed SLE patients. After excluding alternative diagnoses, SLE is diagnosed in patients who fulfill the 1997 American College of Rheumatology (ACR) criteria or the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria.
o Disease duration of a maximum of 1 year;• Group 4: Healthy controls from the LifeLines Deep cohort. Healthy is defined as:
o No chronic illness of any kind (cardiovascular, cancer, renal / liver failure, etc. etc.)
o No use of immunosuppressive medication

Exclusion criteria

A potential subject for the Sjögren Microbiome study who meets any of the following criteria will be excluded from participation:
* Presence of other systemic auto-immune connective tissue disease than SS or SLE (i.e., RA

or systemic sclerosis)
* Presence of IgG4-related disease, Hepatitis C, HIV, sarcoidosis, amyloidosis, active TBC, graft versus host disease
* Past head and neck radiation treatment
* Subjects who are impaired, incapacitated, or incapable of completing cohort-related assessments such as a questionnaire
* Serious comorbidity or laboratory abnormalities that, in the opinion of the investigator, unacceptably increases the burden of participation in the study
* Severe psychiatric or physical illness
* Following an extreme diet (e.g. parenteral nutrition or macrobiotic diet)
* Use of antibiotics within the previous two months
* Use of immunosuppressive medication
* Gastro-enteritis when taking the stool sample

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-04-2016
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	21-01-2016
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-08-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL51722.042.15