Role of Innate Lymphoid Cells in primary SJÖgren*s syndrome salivary gland damage

Published: 30-01-2019
Last updated: 11-04-2024

To assess the presence of absence of ILCs in preclinical (early) pSS biopsies as well as to assess their potential interaction with epithelial cells.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON45875

Source
ToetsingOnline

Brief title
ILCSJO

Condition

- Autoimmune disorders

Synonym
Can a special type of early immune cells trigger loss of saliva production in Sjögren's syndrome?

Research involving
Human

Sponsors and support

Primary sponsor: ReumaNederland,
Source(s) of monetary or material Support: Reuma Nederland (Long Term Research Grant)

Intervention

Keyword: Autoimmune disease, Hyposalivation, Innate lymphoid cells (ILCs), Sjogren's syndrome

Outcome measures

Primary outcome

: For the patient, the harvesting of a parotid gland biopsy represents the

endpoint of the activities involved in the ILCSJO study. No further

interventions or samples from the patient are required. The biopsy will be

harvested during a routine biopsy procedure as part of the diagnostic work-up.

Secondary outcome

N/A

Study description

Background summary

One of the most commonly recognized characteristics of pSS, yet most poorly understood, is that of hyposalivation. Long before presence of lymphocytic foci that are often used to characterize pSS, when SG morphology still looks histologically perfect, production of saliva production already drops. We have recently shown that in the long term, this persistent hyposalivation is most probably caused by senescence of tissue resident salivary gland stem cells (SGSCs), in combination with the ongoing inflammatory process. Our data suggest that proinflammatory cytokines induce this premature SGSC senescence. The cellular origin of these proinflammatory signals remains unresolved, however. Epithelial cells of the salivary gland may also be susceptible to signals from innate lymphoid cells (ILCs) present in the gland, in early pSS. ILCs are a recently described family of lymphoid effector cells who can best be viewed as innate homologues of effector T cells, without the need for antigen presentation via MHC complex for activation. Cytokines secreted by ILCs may provide the first signal triggering the development of hyposalivation in pSS.

Study objective

To assess the presence of absence of ILCs in preclinical (early) pSS biopsies

as well as to assess their potential interaction with epithelial cells.

Study design

Goal 1. Flow cytometric analysis of processed SG biopsies will generate a hit list of innate lymphoid cells subsets over or under represented in early pSS SGs, in comparison with pSS and non-SS sicca controls. Specific immune subsets that will be examined include intraepithelial CD4+ and CD8+ T cells (CD103+CD69+), innate lymphoid cells type 1, 2 and 3 and natural killer (NK) cells. Goal 2 Examine the potential of identified ILCs or other tissue resident innate immune cell populations for interaction with epithelial cells, in terms of their transcriptome, single cell RNAseq will be performed on FACS sorted cell subsets. Goal 3 Probe interaction of ILCs with epithelial cells by co-culture of FACS-sorted ILC population in transwell culture system with healthy control SGSCs.

Study burden and risks

This is a minimal risk study. As mentioned, the biopsy will be part of the subject*s routine clinical care for diagnostic purposes. The parotid gland tissue needed for the experiments will be collected simultaneously with the diagnostic biopsy via the same surgical approach. Taking this extra amount of tissue, similar to the amount of tissue needed for the diagnostic work-up, will not increase the morbidity of the diagnostic procedure and will prolong the routine biopsy procedure with, at most, 30 seconds. Our intervention studies (rituximab, abatacept treatment) have shown that taking repeated biopsies from the same parotid gland is not accompanied by increased morbidity of the surgical procedure. Although the patient has no direct benefit from this study, there a significant benefits for future pSS patients.

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 in the Sjogren*s syndrome work-up traject must meet all of the following criteria:;• Presents with subjective dry mouth symptoms.
• Willing to have exam of oral cavity and a parotid biopsy.
• Scheduled for parotid biopsy for routine diagnosis and care.
Further classification into non-Sjogren*s syndrome sicca (for example induced through medication), early pSS or pSS, performed based on the decision tree and associated clinical parameters in Figure 1.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• History of radiation therapy to the head or neck.
• Another auto-immune disease, lymphoma, sarcoidosis, hepatitis C, IgG4 disease, HIV (all exclusion criteria for classifying a subject as pSS).

Study design

Design

Study type:	Observational invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-04-2019
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	30-01-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Not approved Date:	12-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-07-2023
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	NL67707.042.18