Immunologic profile of tears and conjunctiva in Sjögren*s syndrome

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Primary Objective: Detect a difference in immunological profile between primary Sjögren*s syndrome patients in comparison with subjects from the other study groups.Secondary Objective(s): Other objectives will be the assessment tear osmolarity in...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Ocular sensory symptoms NEC
Study type	Observational non invasive

Summary

ID

NL-OMON38566

Source
ToetsingOnline

Brief title
SIMPLE

Condition

- Ocular sensory symptoms NEC

Synonym
Sjogren syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: SNOO (Stichting Nederlands Oogheelkundig Onderzoek)

Intervention

Keyword: conjunctiva, cytokines, Sjogren, tears

Outcome measures

Primary outcome

The main study endpoint is to assess biomarkers, including anti-Ro/SSA, anti-La/SSB, BAFF, APRIL and chemokine CXCL10, in the tears of patients with primary Sjögren*s syndrome compared to that of other subjects of non Sjögren*s syndrome dry eye patients and healthy subjects.

Secondary outcome

Secondary endpoints will be the assessment tear osmolarity in the tears of primary Sjögren*s syndrome patients in comparison to non Sjögren*s syndrome dry eye patients and healthy subjects. Furthermore, assessment of immunologic characteristics of conjunctival epithelial cells in patients with primary Sjögren*s syndrome in comparison to non Sjögren*s syndrome dry eye patients and healthy subjects.

Study description

Background summary

Sjögren*s syndrome (SS) is a chronic autoimmune disease affecting the exocrine glands, primarily the salivary and lacrimal glands. The disease can be primary or secondary to other auto-immune diseases as rheumatoid arthritis, systemic lupus erythematosus, or others. The precise mechanism responsible for the reduced tear production in SS is not known.
The diagnosis requires 3 areas of speciality practice: rheumatology, oral medicine and ophthalmology. Currently, diagnosis is made on American-European Consensus Sjögren*s Classification Criteria. These criteria include ocular and oral symptoms, objective ocular and oral signs, histopathology of the salivary glands and the presence of auto-antibodies, anti-SSA and anti-SSB in serum.

Ocular diagnosis is made on subjective findings and objective measurements. Ocular symptoms are labelled positive if one of the following questions is answered positive: Do you have dry eyes >3 months? Do you have foreign body sensation in the eyes? Do you use artificial tears >3x per day?
The objective measurements are the ocular staining score with Lissamine green (>= 3 either eye) and tear production with Schirmer*s test (<= 5mm/5 minutes).
Recently preliminary new criteria have been introduced by the American College of Rheumatology (ACR)1. In these new criteria, the ocular criteria for making diagnosis have been changed and have become one of the major criteria in classifying Sjögren*s syndrome. Ocular staining score according to the preliminary ACR criteria is composed of Lissamine green staining on the conjunctiva and fluorescein staining on the corneal surface. This new scoring system is called SICCA. Although these preliminary ACR criteria are an considered improvement in scoring eye involvement, Lissamine green staining can be difficult to perform if the investigator is not experienced.
Moreover, Schirmer testing is not always reliable; several studies showed low sensitivity and specificity, which was one of the major reasons of excluding this test in the preliminary ACR criteria.
It is known that patients with primary Sjögren*s syndrome have an immunological profile in their blood and saliva dissimilar of that from healthy subjects.
Although it is known that the tear fluid has a different immunologic profile in patients with keratoconjunctivitis sicca compared to healthy subjects, it hasn*t been investigated yet if there is a difference between keratoconjunctivitis sicca due to Sjögren*s syndrome and other dry eye diseases. This is an important issue, as differences in the immunological profile between Sjögren*s patients and non Sjögren*s patients with dry eyes may provide clues for earlier and better diagnosis and treatment decisions of this disorder in Sjögren*s patients.
It is known that the cytokines, including BAFF and APRIL play a major role in the pathology of Sjögren*s syndrome and that they can be detected in a significant higher level in serum of patients with Sjögren*s syndrome compared to healthy individuals. But is this also true for tears?
Therefore we would like to assess whether this different serological immunological profile is applicable for tear composition and is rather specific for Sjögren*s syndrome. Several biomarkers, including BAFF, APRIL and chemokine CXCL10 can be detected in tear fluid of dry eye patients. Until now, it has not been investigated if there is a difference between the different causes of dry eye disease and between these groups and healthy subjects. If this can be detected, it might be a new objective tool, non invasive and easy, in diagnosing Sjögren*s syndrome. Also, in the future it could help developing new treatments.
Another point of interest is the conjunctival epithelial cell. It is known that metaplasia of the conjunctival cell takes place in dry eye disease, also overexpression of inflammatory markers has been seen. We would like to asses if primary Sjögren*s patients have a different immunologic profile of their epithelial cells in comparison to non Sjögren*s patients with dry eye disease. These findings could also be a new tool in diagnosing or give clues on the

pathophysiology Sjögren*s syndrome.

Study objective

Primary Objective: Detect a difference in immunological profile between primary Sjögren*s syndrome patients in comparison with subjects from the other study groups.

Secondary Objective(s): Other objectives will be the assessment tear osmolarity in the tears of primary Sjögren*s syndrome patients in comparison to non Sjögren*s syndrome dry eye patients and healthy subjects as well as an assessment of immunological characteristics in conjunctival epithelial cells in these three patient/control groups.

Study design

We will assess the difference between immunological profile of tears and conjunctival epithelial cells between patients with dry eye disease due to Sjögren*s syndrome and non Sjögren*s syndrome dry eye disease and healthy subjects. To accomplish this we need three groups. These groups will be age and sex matched. The Sjögren*s syndrome group will be recruited from the rheumatology and clinical immunology outpatient department through random selection. The non Sjögren*s syndrome dry eye group will be recruited from our outpatient department for dry eye disease.
Healthy subjects will be recruited through social media, like Facebook and Twitter.
Primary Sjögren patients will be included if they are diagnosed by our department of rheumatology and clinical immunology with primary Sjögren*s syndrome according to the American-European classification criteria for Sjögren*s syndrome . The non Sjögren*s syndrome dry eye patients are included if they are diagnosed with dry eye disease without Sjögren*s syndrome criteria: tear production should be normal (Schirmer >=10mm) and staining with Lissamine green should be less than 3. Exclusion criteria are: use of topical steroid eye drops, use of anti-glaucomatous eye drops, ocular surgery in the year before participation, chronic contact lens wear, history of ocular herpes keratitis. Healthy subjects should have no ocular history or complaints and cannot use artificial tears.
The measurements needed to investigate this will be analysis of tear osmolarity and sampling of tears. Routine investigation would be Schirmer testing, measuring tear break up time, lissamine green testing and quantification of mucus in the conjunctival sac. Also, ocular impression cytology will be performed. Subjective symptoms will be measured with the Ocular Surface Disease Index and the Xerostomia Index.
These examinations will take place on one single occasion during the visit to our outpatient clinic.
Tear samples and impression cytology samples will be stored appropriately with

our lab rheumatology en clinical immunology and will be analyzed on a later occasion.

Study burden and risks

The aim of our study is to make diagnostics in Sjögren*s syndrome easier in the future. We also hope this study will give us some more insight in the disease and clues for better therapy.
Although patients don*t benefit directly from this study, it could be that the results could be used in future investigations on medication and their efficacy. Non Sjögren*s syndrome dry eye disease patients will benefit because the study will provide insight in their immunological tear profile and tear osmolarity which can also give insight in their disease and may benefit the choice of the most appropriate treatment for that specific subject.
Healthy subjects will benefit from the study because they will undergo an ophthalmic exam. If there is found something wrong with their eye, they will be helped sooner in contrast to when they don*t participate in this study.

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

Sjögren syndrome patients
- Primary Sjögren's syndrome diagnosed by our rheumatology departement,
- >18 years;Other dry eye patients:
- dry eye disease without Sjögren*s syndrome criteria (punctate keratitis or BUT<10sec)
- tear production should be normal over 10mm on Schirmer
- and staining with Lissamine green should be less than 5
- Age >18 years. ;Healthy subjects
- Age >18 years
- No dry eye complaints
- a tear production higher than 10mm on Schirmer
- Lissamine green staining score less than 5

Exclusion criteria

Use of topical steroid eye drops, use of anti-glaucomatous eye drops, ocular surgery in the year before participation, chronic contact lens wear, history of ocular herpes keratitis. Use of immunomodulating drugs (prednison, cyclosporin);Healthy controls extra exclusion criteria will be a history of ocular disease or ocular complaints and use of artificial tears < 3 months of study.

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:	Will not start
Enrollment:	87
Type:	Anticipated

Ethics review

Approved WMO Date:	15-05-2013
Application type:	First submission
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	NL42936.042.13