Sjögren-Larsson Syndrome: Clinical and Biochemical Studies

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1. To further unravel biochemical abnormalities in SLS patients2. To study neuro-retinal changes over time to learn more about involved neurons and pathomechanism of ophthalmologic abnormalities in SLS patients 3. To study quality of life and daily...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON45720

Source
ToetsingOnline

Brief title
Sjögren-Larsson Syndrome

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Retina, choroid and vitreous haemorrhages and vascular disorders
- Lipid metabolism disorders

Synonym
Sjögren-Larsson Syndrome

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Metabolomics, Ophthalmology, Paediatric neurology

Outcome measures

Primary outcome

1. Biochemical study

- First we aim to do targeted metabolomics on plasma samples. We aim to measure chlorinated lipid species and other targeted lipid analyses. For this targeted metabolomics gas chromatography mass spectrometry will be used. This laboratory research will take place at the Translational Metabolic Laboratory (TML) at the Radboudumc Nijmegen, in collaboration with the laboratory of professor Ford in the United States of America, the PI of the research group who first described this metabolic route.
- Next to this targeted metabolomics, we also aim to further examine the abnormal metabolic routes in SLS patients by untargeted metabolomics. Liquid chromatography in combination with Qtof mass spectrometry will be applied to the body fluids of SLS patients. Depending on the results of this screening, we might also use (already stored and cultured) skin fibroblasts for further research.

2. Ophthalmological tests

With ophthalmologic tests we want to combine normal control appointments with some extra research to learn more about the structure of the retina and the abnormalities in the retina. With OCT-A we want to learn more about the vascularisation of the retina. OCT-A is one of the newest techniques to

visualize the retinal vasculature. This is not been studied in SLS patients before as far as we know. We will examine all patients and then compare results with normal population. Goal of this ophthalmologic study is to get better insight in the ophthalmologic abnormalities, their course over time and the pathomechanism.

3. Questionnaire

A questionnaire will be sent by email, with questions about daily functioning and quality of life.

Secondary outcome

Not applicable

Study description

Background summary

Sjögren-Larsson Syndrome (SLS) is an autosomal recessive inherited disorder, with a clinical triad of intellectual disability, spastic di- or tetraplegia and ichthyosis. This syndrome is caused by a deficient microsomal fatty aldehyde dehydrogenase (FALDH). FALDH is part of the fatty alchohol nicotinamide adenine dinucleotide (NAD) oxidoreductase complex (FAO) and catalyzes oxidation of many different medium- and long-chain fatty aldehydes into fatty acids. Deficiency results in the accumulation of fatty aldehydes and fatty alcohols in body fluids and tissues, which is considered the principal causative mechanism leading to the overall clinical phenotype of SLS. The FALDH gene, named ALDH3A2, is located on gene 17p11.2, and mutations in this gene have been identified in SLS patients.

Our research group already did several studies in this patient group. With new techniques we would like to find out more about the biochemical abnormalities. Further elucidation of the underlying (biochemical) mechanisms of disease, especially the identification of affected pathways and involved lipid species, potentially leads to the development of novel therapeutic strategies. With new ophthalmologic diagnostic techniques, we aim to get a completer image of

ophthalmologic abnormalities in this group.

Parents were curious about the quality of life and life habits of all patients. That is why a questionnaire was added to the study. This way we hope to improve the care for these patients.

Study objective

1. To further unravel biochemical abnormalities in SLS patients
2. To study neuro-retinal changes over time to learn more about involved neurons and pathomechanism of ophthalmologic abnormalities in SLS patients
3. To study quality of life and daily habits of SLS patients

Study design

Monocenter, interdisciplinary, cross-sectional, observational cohort study

Study burden and risks

Patients have to come to the hospital for one visit. In this visit, several eye examinations will be done (part of routine care). The ophthalmologist will do a regular check up as well. After this, a venous blood sample and a urinary sample will be taken. There are negligible risks in these ophthalmologic examinations and collecting the blood and urinary samples. There could be some physical and psychological discomfort, especially with the blood drawing. We will locally anesthetize the skin with EMLA. Since we combine the examinations in one session, with only one venous puncture, we hope to minimalize the burden.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- genetically confirmed SLS patient
- subject and/or his parents is/are able and willing to sign the Informed consent before screening evaluations

Exclusion criteria

- Not genetically confirmed SLS patient
- Subject and/or his parents is/are not able or willing to sign the Informed Consent before screening evaluations.

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):	28-04-2017
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	08-02-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-05-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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: 22068
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL58544.091.16
OMON	NL-OMON22068