Diagnosing small fiber neuropathy in sarcoidosis patients using corneal confocal microscopy

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Primairy objective: Validating of nerve fiber length, nerve fiber density, nerve fiber branches and tortuosity of a healthy control group, sarcoidosis patients with small fiber neuroapthy and sarcoidosis patients without small fiber neuropathy....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON49119

Source
ToetsingOnline

Brief title
SFN in patients with sarcoidosis

Condition

- Respiratory disorders NEC

Synonym
painfull neuropathy - autonomic neuropathy

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: ZonMw,St. Antonius Innovatiefonds

Intervention

Keyword: Corneal confocal microscopy, Sarcoidosis, Small fibre neuropathy

Outcome measures

Primary outcome

Corneal CNFD, CNFD, CNFB and CNFT

Secondary outcome

skin wrinkling grades: grade 0-4

Electrochemical skin conductance

Blood pressure (mmHg)

SFNSL-score: <11 no SFN, >48 SFN confirmed

Phenotypes: SFSCD, SFMNP, SFMWP and SFMAD

Study description

Background summary

Recently, it is recognized that small fibre neuropathy (SFN) occurs in many patients suffering from sarcoidosis and may be the underlying cause of the poor HRQL. The precise prevalence of SFN in patients with chronic sarcoidosis remains unknown, but some studies suggests it might be as high as approximately 75%. SFN only affects the small myelinated A* and unmyelinated C-fibres, also known as small somatic and autonomic fibres respectively. With common nerve conduction tests, only large myelinated nerves are investigated. As consequence, SFN is complicated to diagnose following the regular procedures.
Currently, the diagnosis of SFN is highly underestimated due to lack of a gold standard and awareness among clinical physicians. The most commonly available diagnostic tools for SFN are nerve conduction studies and electromyography, in order to exclude polyneuropathy, skin wrinkling test, skin biopsy and quantitative sudomotor axon reflex testing (QSART). Skin biopsies show a decreased intra-epidermal nerve fibre density (IENFD) in patients with SFN. Corneal confocal microscopy (CCM) is a

relative new technique. As well as skin biopsies, it measures the amount of small nerve fibres. Although CCM and IENFD show comparable sensitivity and specificity, CCM has some major advantages. It is a quick, non-invasive technique, it shows higher reproducibility and allows multiple replicates in both cross-sectional and longitudinal studies. Moreover, it can be evaluated manually, semi-automatically, and automatically. Additionally, it is even suggested that corneal nerve fibre density is inversely related to symptoms in patients with painful sarcoidosis related neuropathy. The translation of CCM from research domain to clinical diagnosis has been limited by lack of normative reference values, the requirement of specific training and limited clinical question. In order to support the diagnostic value of CCM, additional research is required. Introduction of phenotyping SFN, might explain the great variety between different outcome measures, from different diagnostic methods. Additionally, sudoscan and blood pressure measurements will be performed. Those can measure 2 types of autonomic small fiber functions. This way, all phenotypes can be measured with corresponding diagnostic methods. Consequently, it can be confirmed whether or not phenotypes can be distuighuised.

Study objective

Primairy objective:
Validating of nerve fiber length, nerve fiber density, nerve fiber branches and tortuosity of a healthy control group, sarcoidosis patients with small fiber neuroapthy and sarcoidosis patients without small fiber neuropathy.

Secondary objectives:
- Validating skin wrinkling grade: grade 0-4
- Validating Electrochemical skin conductance
- Validating BP to postural change
- SFNSL-score: <11 no SFN, >48 SFN confirmed
- Phenotypes: SFSCD, SFMNP, SFMWP and SFMAD

Study design

This is a prospective observational study with all sarcoidosis patients admitted in one year to the ILD-department of the St. Antonius hospital.

Study burden and risks

The participants have to answer the SFN-scoring list (SFNSL) with 21 multiple choice questions, give a VAS-score, CFQ-score and FAS-score and perform the skin wrinkling test. Nerve conduction studies (NCS) and electromyography (EMG) measurement are performed to exclude polyneuropathy. Blood pressure to postural change measures the autonomic function of small never fibers. Except for the

questionnaires, those tests are all part of standard care. With the temperature threshold test, a thermode is used to apply different temperatures at the thenar eminence of digit 1 and at the foot. The thermode does not apply harmfull temperatures. The sudoscan measures skin conductance between two electrodes. Blood pressure measurements are routine measures, which can be performed within 10 min and do not show any detrimental effects. Skin biopsy is a safe and easy procedure and part of standard care for dermatologists. Serious or major adverse events are not expected and the risk of an increase in morbidity or mortality is considered negligible. Detrimental effects may be: bleedings, bruises, allergic reaction on anesthaetics and scars. For the CCM measurements, ophthalmic anaesthetics are applied on the eyes of interest. The CCM measurements takes 2 minutes. Serious or major adverse events are not expected and the risk of an increase in morbidity or mortality is considered negligible. Possible negative effects of the CCM are infection and abrasion. The lens will be carefully disinfected to minimize the risk. Patients with epithelial defects, ulcers and corneal epithelial or basement dystrophies, may be at higher risk of corneal abrasion. The obtained information has a great value for the diagnosis to SFN in patients suffering from sarcoidosis. It is expected that CCM is a reliable, non-invasive and quick method to diagnose SFN.

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

* Age 18-75 years
* Patients with sarcoidosis and SFN symptoms
* Patients with sarcoidosis and without SFN symptoms

Exclusion criteria

* Ocular disease
* Ocular surgery
* Allergy to the anaesthetic or contents of eye gel
* Diseases with possible polyneuropathy
o Diabetes (type I & type II)
o Vitamin B12 deficiency
o Metabolic syndrome
o Impaired glucose intolerance
* Clinical relevant abnormal history of physical and/or mental health
* Pregnancy
* High alcohol intake

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-01-2022
Enrollment:	100
Type:	Actual

Medical products/devices used

Generic name:	Corneal confocal microscopy
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	29-10-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-11-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-05-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL71552.100.19