Multiple Sclerosis (MS) and autonomic dysfunction: Evaluating Peripheral Nervous System involvement using intra-epidermal nerve fibre density (IENFD).

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Ethical review	Approved WMO
Status	Completed
Health condition type	Demyelinating disorders
Study type	Observational invasive

Summary

ID

NL-OMON33791

Source
ToetsingOnline

Brief title
SFN in MS

Condition

- Demyelinating disorders

Synonym
multiple sclerosis, small fibre neuropathy

Research involving

Human

Sponsors and support

Primary sponsor: Orbis Medisch Centrum
Source(s) of monetary or material Support: Fonds prof dr Hupperts via CTCM MUMC

Intervention

Keyword: autonomic dysfunction, intraepidermal nerve fibre density, multiple sclerosis, small fibre neuropathy

Outcome measures

Primary outcome

The primary analysis will consider the difference in IENFD between MS patients

with symptoms and without symptoms of ANS dysfunction, as well as compared to

healthy participants.

Secondary outcome

In secondary analysis the results of the IENFD will be related to the other

outcome measures and clinical data.

Study description

Background summary

Multiple sclerosis (MS) is a chronic inflammatory disseminated illness of the central nervous system (CNS). White matter lesions are considered the hallmark of MS. Autonomic nervous system (ANS) failure in MS may also occur and has been reported in 10% to 90% of patients and may lead to various organ involvement, as well as a decrease in quality of life expectations. It remains unclear whether the expression of the peripheral autonomic involvement is present in MS. Peripheral ANS dysfunction, as an expression of small fibre neuropathic dysfunction (SFN) preferentially affects small-calibre myelinated (A*) and unmyelinated (C) fibres, leaving the larger myelinated fibres relatively unaffected. The diagnosis SFN is made on the basis of the clinical features, normal nerve conduction studies, and abnormal specialized tests of small nerve fibres. No gold standard test exists for assessing ANS dysfunction in MS. It is

also not known whether ANS dysfunction in MS is related to PNS involvement. A clearly defined standardization is necessary to describe the prevalence of the various aspects of autonomic dysfunction in patients with MS, including the challenges within the various forms and stages of the disease, e.g., at onset, according to different courses, or accompanying relapses.

Study objective

The key objectives of this study are:

1. To determine by means of IENFD whether the PNS is involved in patients with autonomic complaints in MS.
The obtained IENFD values will be compared with the age and
gender matched healthy normative data, available
in our lab.
2. To determine the correlation between IENFD and other outcome measures (SFN symptom inventory questionnaire
(SIQ), mdCompass scale, EDSS, MRI, FSS, pain scales and HRQoL)

Secondary objectives are:
3. To examine the validity (correlation studies) and reliability (test-retest)
of the compass and SIQ in patients
with MS and autonomic dysfunction.
4. To examine the impact of health-related quality of life (HRQoL) in patients
with MS and autonomic dysfunction
versus patients with MS without autonomic complaints.

Study design

Patients with MS according to defined criteria will be eligible, and will be divided into 3 groups, subgroup 1 (30 patients) with a relapsing-remitting course, subgroup 2 (30 patients) with a secondary progressive course and subgroup 3 (30 patients) with a primary progressive course. Each group is divided into patients with patients with possible and without ANS dysfunction. Possible ANS dysfunction and/or SFN is defined as at least one of the following symptoms, not otherwise explained: burning pain in extremities, dry mouth or eyes, changes in sweating, flushes, gastro-intestinal dysfunction (constipation or diarrhoea), cardiac complaints (palpitation, dizziness at standing up), uro-genital dysfunction (sexual dysfunction like impotence, incontinence).
The following outome measures will be applied:
* Skin biopsy for determination of IENF density
* Nerve conduction studies
* MRI brain and spinal cord.
* neurological examination (MRC sumscore, INCAT sensory sumscore, EDSS)
* A set of questionnaires will be completed: SFN screening list (SIQ), mdCompass, VAS, PI-NRS, NPS, FSS, SF-36,

EuroQoL

Study burden and risks

The most important burden for patients will be time investment. Patients will visit the hospital once. A skin biopsy is a routine diagnostic procedure and is a minimal invasive procedure. There is a small risk of getting an infection and most people get a small scar conform the size of the punch biopsy (3 mm).

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

Inclusion criteria

- age: 18 years and older
- clinical definite MS according to the revised McDonald criteria.
- Brain MRI fulfilling the revised McDonald criteria.
- a clinical stable condition.
A clinical stable condition is defined as:
a) a clinical state without any new significant symptoms and/or signs as declared by the patient to the best of his/her knowledge
over 3 months prior to the study or
b) No clear objective changes at neurological examination by the researcher when compared with recorded findings over three
month before study entry (if available)
c) No methylprednisolone treatment within 3 months before study entry
- written informed consent
- patients should be ambulant (Expanded Disability Status Scale (EDSS) score of < 5.5). The latter was chosen to avoid possible IENFD reduction and autonomic impairments due to inactivity.

Exclusion criteria

- patients not meeting the inclusion criteria
- use ofmedication that would interfere with ANS assessment, or use of medication that is known to possibly cause peripheral neuropathy
- Other illnesses that might cause autonomic impairment (e.g., parkinson(ism), peripheral neuropathy, diabetes mellitus, alcohol abuse [arbitrarily defined as daily consumption of 5 IU or more], renal dysfunction, systemic illnesses)

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-02-2010

Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	15-12-2009
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	NL25959.096.09