Multifocal motor neuropathy: a natural history study on prognosis, disease mechanism and new biomarkers.

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1.To document natural history in this patient group and to establish which factors put patients at risk for an unfavourable outcome. 2.To determine which factors contribute to (reduced) quality of life (QoL) in patients with MMN.3.To investigate the...

Ethical review	Not approved
Status	Will not start
Health condition type	Peripheral neuropathies
Study type	Observational invasive

Summary

ID

NL-OMON40136

Source
ToetsingOnline

Brief title
Multifocal motor neuropathy: a natural history study.

Condition

- Peripheral neuropathies

Synonym
Nerve inflammation by own immune system, periferal motor neuropathy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Reeds beschikbaar geld dat tevoren is verworven. Geen specifieke sponsoring voor deze studie.

Intervention

Keyword: disease mechanism, MRI, Multifocal motor neuropathy, natural history study

Outcome measures

Primary outcome

- the Overall Disability Sum Score (ODSS) ranging from 0 (normal) to 5 for the arms

and to 7 for the legs and Rankin scores;

- the Fatigue Severity Scale (FSS) scores;

- Medical Research Council (MRC) sum scores or myometric scores;

- Time needed to perform the 9-hole peg test;

compared to the data obtained in 2007.

-SF-36 domain scores and physical and mental component scores will be used to document QoL.

Secondary outcome

- Carriership rates of H. Influenzae and the presence of GM1 like stuctures on bacteria.

- We will look for nerve and brachial plexus abnormalities on T1W and STIR (T2W) MR images, in particular for thickening and increased T2W signal that probably reflects, inflammation and compare MMN and MND patients and healthy controls. We will also compare EMG findings in MMN patients with MRI findings to investigate whether we can image the CB.

-HRUS will be performed in all MMN patients and in the MND patients who undergo

MRI of the forearm. HRUS results will be compared to EMG and MRI in the MMN subgroup who underwent all three investigations. Finally, HRUS results will be studied in relation to patient characteristics (i.e. weakness, disability, response to treatment, presence of axonal damage). A subgroup of patients has had US in the past21 to see if HRUS is a biomarker for disease progression the 21 patients who were included will be asked again for HRUS.

-Changes in IVIg concentration before and after treatment and over time in patients who are IVIg naïve and start IVIG maintenance treatment. Next to this parameter, HRUS findings over time (one year) are measured to test its value as a prognostic biomarker for clinical decline and/or response to IVIg.

- Nerve excitability in MMN patients as a pilot study and compare results to former data of excitability on healthy controls. Results include strength duration time constant, threshold electrotonus, recovery cycle and will be compared with the already available data in healthy persons.

Study description

Background summary

Multifocal motor neuropathy (MMN) is a rare immune-mediated disorder characterized by slowly progressive, asymmetrical weakness of limbs without sensory deficits or upper motor neuron signs. More men than women are affected, at a ratio of approximately 3:1. The mean age at onset is 40 years, with a range of 20-70 years. MMN should be distinguished from other lower motor neuron diseases, in particular variants of amyotrophic lateral sclerosis (ALS), because prognosis is better and it is responsive to treatment with intravenous immunoglobulins (IVIg). The diagnosis of MMN may be elusive. The hallmark of

MMN is the phenomenon of conduction block (CB) in nerves, which can be found by means of nerve conduction studies (NCS). Facilities and skills to perform extensive NCS using MMN specific protocols are not widely available. Tools that facilitate diagnosis are therefore urgently needed. Treatment with high-dose (IVIg) is the only established therapy for MMN. There are no alternatives. Prednisone and plasmapheresis may even increase weakness and mycophenolate mofetil was shown not effective. IVIg improves muscle strength within two weeks in the large majority of patients, but treatment effects last only several weeks and maintenance treatment is therefore required. Moreover, disease course is slowly progressive resulting in permanent axonal loss despite IVIg treatment in many patients. At least 20% of patients develop significant disability of the arms in the course of the disease.
Long-term follow up studies with a relatively large number of MMN patients to document the rate of progression have not been performed. Such studies are needed to identify risk factors that are associated with an increased risk of poor outcome. The optimal IVIg dose and treatment frequency for patients with MMN has not been established. Finally, we need more insight in the immune pathogenesis of MMN in order to develop new treatment strategies.

Study objective

1.To document natural history in this patient group and to establish which factors put patients at risk for an unfavourable outcome.
2.To determine which factors contribute to (reduced) quality of life (QoL) in patients with MMN.
3.To investigate the potential of modern high resolution ultrasound (HRUS) and MRI techniques of the brachial plexus and peripheral nerves to facilitate the diagnosis of MMN and test its values as a biomarker for disease progression.
4.To study the pharmacokinetics of IVIg treatment and its relation to treatment efficacy and natural history.
5.To test validation of- and contribution of potassium channels by-excitability tests on EMG in MMN patients.
6.To further investigate the immune pathogenesis of this disorder.
7.To further test the hypothesis that MMN is caused by a chronic infection.

Study design

All the patients with MMN are asked to consent and to fill in quastionnaires.
All the research (interventions) will take place in one extra outpatient clinic vist.
Patients will be asked to draw blood and a throat swab.

After that, there are 4 substudy parts:
1. MRI/US and/or EMG
2. Excitability

3. Long term follow up US
4. IVIg concentration and US followed over time.

Study burden and risks

Patients will visit the outpatient clinic of the department of Neurology/Neuromuscular diseases once. The burden consists of undergoing an interview, physical examination, throat swab and venapuncture. A subgroup of patients will be asked to participate in an MRI, EMG or HRUS study. These studies will take an additional 30 minutes each for MRI, excitability testing and HRUS, and 45 minutes for EMG. The cumulative burden for patients is limited. For venapuncture, transient local pain and blue spots from the injection is mentioned. Throat swabs can sometimes give an unpleasant feeling during the procedure but takes only a short time.
For excitability testing and HRUS, no specific burdens are mentioned and for MRI, scalds are seen sometimes when patients have tattoos containing ferromagnetic components. Prior to MRI all patients are checked for iron containing materials since this can be of harm when magnetized and launched by the MRI.
Patients will feel nerve stimulation during NCS but this is generally well tolerated. NCS are harmless and do not lead to complications.

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

Multifocal Motor Neuropathy

Exclusion criteria

No Multifocal motor neuropathy

Study design

Design

Study type:	Observational 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:	270
Type:	Anticipated

Ethics review

Not approved

Date:	17-02-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL46675.041.13