Multifocal motor neuropathy: a study on immunological mechanisms and natural history

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To identify (clinical) features of MMN patients that predict a poor clinical disease course. Moge agressive IVIg regimen can be established is this subgroup to maintain functional status of the patient. To find domains in quality of life in MMN...

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

Summary

ID

NL-OMON44983

Source
ToetsingOnline

Brief title
MAIN study

Condition

- Demyelinating disorders

Synonym
disease of motor nerves, inflammatory demyelinating peripheral motor neuropathy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: Eerder verkregen geld dat nu beschikbaar is wordt ingezet voor dit onderzoek

Intervention

Keyword: immunology, Multifocal motor neuropathy, natural history

Outcome measures

Primary outcome

Natural history:

Clinical disease course is determined by questionnaires and a neurological

examination taken in 2007 and in the current study. Special (clinical) features

is looked for in patients that have poor prognosis.

Quality of life scores compared to the standardized Dutch scores.

Immunological part:

Anti-GM1 IgM titers and HLA haplotyping in MMN and controles

-FcuR status on (subsets of) leukocytes is compared with controls.

- Bacterial cultures that can express GM1 (like) epitopes is compared with

controls.

Secondary outcome

not applicable

Study description

Background summary

Multifocal motor neuropathy (MMN) is probably an immune mediated disease with progressieve paresis of muscles, mainly the hands and to a lesser extend the feet and arms. Diagnosis may be elusive and the origin of the disease is unknown. It clinically mimics ALS, but it has a better prognosis and is treatable with immunoglobulins (IVIg) with a good response. Despite maintainance therapy, slowly progressive paresis is seen on average. However,

progressive paresis can lead to severe disability in an estimated number of 20%. This is probably due to irreversible axonal degeneration. It is not known what factors/features this subgroup with a poor clinical outcome has.
Debut of onset is 20-70 year which means that it affect people in their 'active' years, in social as well as in working means.

The origen of MMN is not known. However, there are strong arguments that it is an immune mediated disease. One of these arguments is the presence of anti-GM1 antibodies in around half of the patients. GM1 is a protein that is abundantly expressed on peripheral nerves. Binding of the antibody to GM1 leads to complement activation and forming of the membrane attack complex that damages the nerve and results in local inflammation. The origin of these antibodies in snot elucidated yet.

Study objective

To identify (clinical) features of MMN patients that predict a poor clinical disease course. Moge agressive IVIg regimen can be established is this subgroup to maintain functional status of the patient.
To find domains in quality of life in MMN patients in which MMN patients perform worse than the 'normal values' of the Dutch population.
To unravel the origin of the anti-GM1IgM. Possibilities are an endogenous origin (as a result af deficient IgM receptors on (subsets of) leukocyts or a linkage with HLA-DRB1*15 haplotype). Another possibility is that it is a result of an exogenous pathogen, that is able to express GM1 (like) epitopes on its cell surface and by molecular mimicry the antibodies are produced.

Study design

The goals will be:
- a longitudinal observational study. 88 patients seen in 2007 (METC number 05/273) are re-seen and re-scored by questionnaires (ODSS, FSS, SES) and neurological examination (MRC sum score) as in 2007.
- studying QoL in a cross sectional setting by taking the sf-36 and USER-P questionnaires of 120 MMN patients and these results are compared with validated scores of the Dutch population.
- Disease mechanism in a case cohort study in which bacterial cultures (especially H. Influenzae) is tested for the presence of GM1 epitopes on their cell surface. expression of the FcuR is tested on leukocytes of MMN patients and controls.
Blood samples of MMN patients and controls is further tested for antibody level and HLA haplotyping.

A second venipuncture will performed to test leukocyte subsets (iNKT cells and plasmablasts, for more detailled information see the added information in the introduction in the WMO protocol) in MMN patients and controls.

Study burden and risks

The burden consists of a trip to the hospital and back home, taking questionnaires (that are estimated of low psychological impact) and a clinical examination that focusses on the strength, sensitivity and reflexes of the limbs.
A venapuncture can give local transient pain and/or hematoma, a throat swab can sometimes give an unpleasant feeling that will last only seconds.

For controls, the burden consist of the throat swab and to draw one extra tube in an already planned venapuncture

The total time in the hospital will be around 1,5 - 2h for the MMN patients.

Cumulative burden is estimated low and the risk is neglegible.

Concerning the second venipuncture the same burdens as described above are applicable, except that patients do not come to the hospital for the venipuncture alone, but they will be asked at their regular appointment at the outpatient clinic. Total extra time cost is estimated 5 minutes.

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

Patients are subjects who fullfil the diagnostic consensus criteria for MMN (see protocol, page 40)
Controls are people who visit the neuromuscular outpatient clinic for diseases other than MMN.
All subjects are older than 18 year, are not mentally incapacitated and fully understand the given information for the study

Exclusion criteria

An MMN patient who meets any of the following criteria will be excluded from participation in this study:
- Doubts about the diagnosis MMN
- Relevant concomitant illnesses (i.e. haematological or immunological diseases) that may interfere with any part of the study
A control will be excluded when any of the following criteria is met:
- having MMN as a diagnosis in the history
- under 18 years old.
- not capable of understanding the given information or giving consent.

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:	Recruitment stopped
Start date (anticipated):	22-05-2015
Enrollment:	320
Type:	Actual

Ethics review

Approved WMO Date:	10-12-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-04-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-05-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-04-2017
Application type:	Amendment
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	NL50354.041.14