Prospective and cross-sectional multicentre cohort study nerve sonography in polyneuropathy

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peripheral neuropathies
Study type	Observational non invasive

Summary

ID

NL-OMON47420

Source
ToetsingOnline

Brief title
PROZEP

Condition

- Peripheral neuropathies

Synonym
generalised disease of the nerves

Research involving
Human

Sponsors and support

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

Intervention

Keyword: nerve, polyneuropathy, sonography

Outcome measures

Primary outcome

Sonographic neural abnormalities (nerve hypertrophy, fascicle enlargement and hypervascularisation), clinical findings (ie pattern and degree of sensory disturbance and muscle weakness (medical research council (MRC) sum-score), results of electrodiagnostic studies, laboratory and CSF analysis, treatment response in treated cases, nerve biopsy, family history and DNA analysis.

Secondary outcome

not applicable

Study description

Background summary

A polyneuropathy is a prevalent disorder of the peripheral nerves, that has a wide spectrum of underlying pathology. The starting point of diagnosing a polyneuropathy, is to classify it as either axonal or demyelinating The potential causes and treatments differ among axonal and demyelinating polyneuropathies. The differentiation between axonal and demyelinating polyneuropathies is at present based on clinical features and electrodiagnostic studies. However, this diagnostic sensitivity of clinical and electrodiagnostic findings is poor due to coinciding clinical presentations of the various polyneuropathy subtypes and the modest discriminating power (sensitivity and specificity) of electrodiagnostic studies. High resolution sonography (HRUS) of the peripheral nervous system may have an additive value in this discrimination. It evaluates nerve parameters different from electrodiagnostic studies and has recently established its place in the diagnostic guidelines of mononeuropathies. Current literature suggests, that in demyelinating polyneuropathies HRUS reveals more abnormalities as compared to axonal polyneuropathies. It was never studied, whether HRUS is of additional value to clinical and electrodiagnostic parameters in discriminating axonal from demyelinating polyneuropathy. Such a finding would have practical implications

for polyneuropathy diagnosis, and is the main objective of this study.

Study objective

1.The first objective is to determine the nature and spatial distribution of sonographic abnormalities in demyelinating and axonal polyneuropathies of different etiologies.

2.On the basis of the findings in objective 1, we define a standardized HRUS research protocol that has the highest discriminative value between demyelinating and axonal polyneuropathies.

3.To determine whether this standardized HRUS protocol is of additional value to clinical and electrodiagnostic parameters in discriminating axonal from demyelinating polyneuropathies in a consecutive group of patients suspected of polyneuropathy. If HRUS is of additional value, a prediction rule for demyelinating polyneuropathy will be defined.

4.To evaluate whether the additive value of this prediction rule holds true in common neurological practice, it is validated in a new cohort of consecutive patients suspected of polyneuropathy.

Study design

To study objective 1, nerve sonography will be performed in clearly defined, hereditary and acquired, demyelinating (chronic inflammatory demyelinating polyneuropathy, Charcot-Marie-Tooth type 1, multifocal motor neuropathy (MMN), hereditary neuropathy with liability to pressure palsies and anti-Mag associated polyneuropathy) and axonal (chronic idiopathic axonal polyneuropathy, spinal muscular atrophy, vasculitis associated polyneuropathy) polyneuropathies. It will encompass extensive sonographic measurement in multiple nerves in both arms and legs. Various sonographic parameters will be evaluated (e.g. nerve and fascicle size, vascularisation). This study results in a description of the nature and distribution of the sonographic abnormalities for each of the investigated polyneuropathies.

To investigate objective 2, the demonstrated nature and spatial distribution of the sonographic abnormalities will be further categorized. By selecting the parameters and nerves with the highest discriminating power between axonal and demyelinating polyneuropathies, the extensive HRUS protocol will be reduced to a standardized HRUS protocol.

To evaluate objective 3, a group of consecutive patients clinically suspected of a polyneuropathy (derivation set) will undergo clinical and electrodiagnostic evaluation, as well as the standardized HRUS protocol. We will determine whether this standardized HRUS protocol is of additional value

to clinical and electrodiagnostic parameters in discriminating axonal from demyelinating polyneuropathies Since there is no gold standard for polyneuropathy diagnosis, we will apply the use of consensus diagnosis as outcome variable. Consensus diagnosis is based on combined clinical information consisting of clinical presentation and course, treatment response in treated cases, results from electrodiagnostic studies, analysis from blood and CSF, nerve biopsy, family history and DNA analysis. If HRUS is of additional value, a prediction rule for demyelinating polyneuropathy will be defined.

Finally, to study objective 4, the prediction rule will be tested in a validation set in a prospective multicentre cohort study of consecutive patients clinically suspected for polyneuropathy. Consensus diagnosis is used as outcome variable, as mentioned under objective 3.

Study burden and risks

Clinical examination, laboratory results and electrodiagnostic studies are part of the standard clinical evaluation of patients clinically suspected for polyneuropathy. A short history and neurologic examination are standardized. Nerve sonography is the only additional burden that is required for the purpose of this study. This has proven to be safe, reliable, effective, non-invasive and is usually well tolerated.

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

high clinical suspicion of polyneuropathy (based on history and findings at neurological examination), age 18- 80 years.

Exclusion criteria

age <18 or >80 years, prior history of polyneuropathy, physically unable to undergo electrodiagnostic or HRUS of the peripheral nervous system (e.g. cast, recent pelvic fracture or prosthetic operation, extensive reconstructive surgery on the extremities).

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-02-2015
Enrollment:	350
Type:	Actual

Ethics review

Approved WMO Date:	12-09-2013
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-03-2014
Application type:	Amendment
Review commission:	METC St Elisabeth Ziekenhuis (Tilburg)
Approved WMO Date:	01-12-2015
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-05-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	NL42895.008.12