Unravelling the etiology of chronic idiopathic axonal polyneuropathy

Published: 29-07-2008
Last updated: 07-05-2024

Objectives1. Achieve a complete ascertainment of incident CIAP patients in the middle of the Netherlands during a three-year period and determine the frequency of CIAP.2. Establish whether CIAP is associated with the metabolic syndrome, and if so,...

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

Summary

ID

NL-OMON32297

Source
ToetsingOnline

Brief title
Etiology of CIAP

Condition

- Peripheral neuropathies

Synonym
Chronic idiopathic axonal polyneuropathy, cryptogenic axonal polyneuropathy, polyneuropathy without an identifiable cause

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Prinses Beatrix Fonds

Intervention

Keyword: Case-control studies (MESH), Epidemiological studies (MESH), Etiology (MESH), Polyneuropathies (MESH)

Outcome measures

Primary outcome

- Determine the incidence of CIAP in the middle of the Netherlands (province of Utrecht).

- Establish by means of odds ratios if and to what extent CIAP is associated with the metabolic syndrome and which of is components are the most important determinants.

- Establish by means of odds ratios if other prevalent conditions such as COPD, cardiovascular disease, environmental and nutritional factors contribute to the risk of CIAP.

- Establish by means of Cox regression analysis if there is an association between clinical features such as age at onset, gender, disease duration, neurological symptoms and identified significant risk factors.

Secondary outcome

Not applicable.

Study description

Background summary

Polyneuropathy is the most common neuromuscular syndrome. There are many causes of polyneuropathy, but after extensive investigations no cause can be found in about one-third of patients: 'chronic idiopathic axonal polyneuropathy' (CIAP). Althoug CIAP runs a benign and slowly progressive course, it can have a marked impact on daily functioning and quality of life.

Pathological examination of nerve biopsies from patients with CIAP have shown endoneurial microvascular changes. A possible pathogenetic mechanism could be an association with the metabolic syndrome, which is an important determinant of microvascular disease. Other common etiologies to be considered are chronic obstructive pulmonary disease (COPD), cardiovascular disease, environmental and nutritional factors (such as exposure to toxins or alcohol, subtle vitamin B12 deficiency, vitamin B6 toxicity).
However, there is no conclusive evidence that these conditions are importantly associated with CIAP because most previous studies were small, not population-based, or uncontrolled.

Hypothesis
CIAP may be caused by microvascular, hypoxic or toxic nerve damage that can be linked to the metabolic syndrome or other prevalent conditions such as COPD, cardiovascular disease, environmental or nutritional factors.

Study objective

Objectives
1. Achieve a complete ascertainment of incident CIAP patients in the middle of the Netherlands during a three-year period and determine the frequency of CIAP.
2. Establish whether CIAP is associated with the metabolic syndrome, and if so, which of its components appear to be the most important determinants.
3. Investigate whether prevalent conditions such as COPD, cardiovascular disease, environmental and nutritional factors contribute to the risk of developing this disease.

The study may help identify etiological links between chronic idiopathic axonal polyneuropathy (CIAP) and the metabolic syndrome or other prevalent conditions in the population, as well as target treatment of this disease that has a negative influence on quality of life. For example, lifestyle adjustments or treatment aimed at prevention similar to those in (pre)diabetes and cardiovascular disease should be considered if the metabolic syndrome plays a role. Similarly, more rigorous treatment or eradication of other conditions may also reverse or positively influence the disease course of CIAP. Consequently the effects of interventions on CIAP could be studied or CIAP could be included as an outcome parameter in studies on lifestyle interventions.
The study may facilitate the diagnostic process in the large group of patients with a chronic axonal polyneuropathy, and provide further insight whether CIAP should still be considered as a singular entity with variable clinical expression or indeed represents a heterogeneous group of conditions with specific so far unrecognized etiologies.

Study design

A prospective, population-based, case-control study in the middle of the

Netherlands (province of Utrecht). Validated up-to-date questionnaires, clinical and laboratory (blood) investigations will be used to collect data and assess risk factors. All analyses will be adjusted for possible confounders.

Study burden and risks

Burden:
-for patients routine evaluation at the outpatient clinic (conform CBO guideline 'Polyneuropathie': clinical neurological and neurophysiological examination, fasting venapuncture), for controls fasting venapuncture (if not yet done).
-fill out questionaire at home.

Risk:
The risk of the venapuncture is negligible (haematoma at the site of puncture). The venapuncture will be done at the UMC Utrecht and performed by qualified personnel (physicians, nurses, laboratory technicians).

In view of the minor burden and negligible risk of the venapuncture this study is justifiable, because of the effect of CIAP on activities of daily living and quality of life, the prevalence of possible associated conditions and potential henceforthcoming therapeutic consequences.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
3584 CX Utrecht
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
3584 CX Utrecht
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion criteria for patients with CIAP are: (1) patient age 45 years or older; (2) presence of distal symmetrical sensory or sensorimotor symptoms and deficits. These impairments should have begun distally in the legs, and have evolved slowly over months; (3) exclusion of any recognized cause of polyneuropathy such as diabetes mellitus, renal insufficiency, liver disease, alcohol abuse, medication, thyroid disease, vitamin deficiency, malignancy, polycythaemia, paraproteinaemia, systemic autoimmune or connective tissue disease, inflammatory bowel disease, metabolic storage disease, sarcoidosis, amyloidosis; (4) no indication of hereditary polyneuropathy; (5) electrophysiological investigations in agreement with axonal polyneuropathy without demyelinating features.
Inclusion criteria for controls are: (1) age 45 years or older; (2) absence of symptoms suggestive of polyneuropathy; (3) absence of any recognized cause of polyneuropathy.

Exclusion criteria

Exclusion criteria for patients with CIAP are: (1) age younger than 45 years; (2) presence of asymmetrical or multifocal symptoms and deficits suggestive of a multifocal neuropathy; (3) (sub)acute onset and rapid progression of the neuropathy to a nadir within 12 weeks; (4) presence of any recognized of polyneuropathy, including hereditary neuropathy; (5) electrophysiological evidence of a demyelinating neuropathy according to established electrophysiological criteria.
Exclusion criteria for controls are: (1) age younger than 45 years; (2) presence of symptoms suggestive of polyneuropathy; (3) presence of any recognized cause of polyneuropathy.

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):	22-04-2009
Enrollment:	948
Type:	Actual

Ethics review

Approved WMO

Date:	29-07-2008
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	NL21385.041.08