Peripheral neuropathy in MLD patients: possible pathomechanisms, dynamic biomarkers and clinical relevance

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

Summary

ID

NL-OMON48491

Source
ToetsingOnline

Brief title
Neuropathy in MLD

Condition

- Neurological disorders congenital

Synonym
hereditary white matter disorder, metachromatic leukodystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Stichting Metakids;via een contract

Intervention

Keyword: Biomarkers, Metachromatic leukodystrophy, Neuropathy

Outcome measures

Primary outcome

The primary study parameters will be the:

Total pmTNS score (between 0 * 32) and nerve conduction velocities (m/s) of the radial nerve, ulnar nerve, tibial nerve and common peroneal nerve in MLD patients at three different time points, and the changes in the total pmTNS score and NCV over time.

Correlation between levels of different sulfatide species and biomarkers (protein level) in CSF and blood and the severity of peripheral neuropathy in MLD patients at three different time points and over time.

Changes in size, vascularity and echogenicity of the radial nerve, ulnar nerve, tibial nerve and common peroneal nerve in MLD patients over time.

Secondary outcome

The secondary study parameters will be the:

Calculated differences in total pmTNS scores and nerve conduction velocities at baseline between different MLD patient subgroups.

Absolute levels of sulfatide and elevated or lowered biomarkers in CSF and blood in MLD patients at three different time points and the calculated differences with these levels in CSF and blood in healthy controls.

Correlation between size, vascularity and echogenicity of the radial nerve, ulnar nerve, tibial nerve and common peroneal nerve and different stages of the

disease.

Study description

Background summary

Metachromatic leukodystrophy (MLD) is a lethal metabolic disease characterized by deficient enzyme activity of arylsulfatase A (ASA) and accumulation of sulfatides in the nervous system. A part of the Dutch MLD patients is currently treated with hematopoietic stem cell transplantation (HCT), but this treatment mainly impacts the brain white matter whereas the peripheral neuropathy shows no or limited response to HCT. In our experience, peripheral neuropathy contributes significantly to morbidity in MLD patients but scientific data about the etiology, severity, and predictive biomarkers in these patients are lacking.

Study objective

The goals of this study are to examine the aetiology and daily impact of peripheral neuropathy in MLD patients over time, and to identify dynamic biomarkers that correlate with the severity of peripheral neuropathy over time, and might predict peripheral neuropathy progression after treatment.

Study design

It is a multi center study that uses a longitudinal cohort study design. The cohort consists of 40 pediatric and adult MLD patients (aged 4 * 50 years). Data collection will take place during a period of three years. Each year, the research participants will undergo the same procedures: examination according to the Pediatric-modified Total Neuropathy Score (pmTNS), ultrasound and electromyography (EMG) of the peripheral nerves, and cerebrospinal fluid (CSF) and venous blood sampling. In this manner we can observe changes in levels of (lyso)sulfatide and different biomarkers in CSF and blood, and in electrophysiological and morphological characteristics of the peripheral nerves over time. We will use historical data providing information on these characteristics of (age-matched) healthy controls for comparison.

Study burden and risks

The procedure includes one hospital visit per year for three years, combined with the standard follow-up appointments. There is no direct benefit for the participants; there is only benefit for the patient population by increased knowledge. Risks and burdens of the study will be minimized by collecting

samples and data from standard care procedures as much as possible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Diagnosis of MLD confirmed by demonstrating a deficiency of ASA activity in leukocytes, increased urinary sulfatide levels and/or pathogenic ARSA mutations.

Exclusion criteria

No informed consent (IC) given by the participant or given by parents/legal representative if necessary

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-12-2019
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	26-07-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	07-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL69005.029.19