Magnetic Resonance Spectroscopy in Acid Sphingomyelinase Deficiency

Published: 19-01-2023
Last updated: 14-03-2025

To assess the ability of MRI techniques to detect early stages of lipid accumulation in the liver of ASMD patients with the chronic visceral subtype compared to values of age-, sex- and BMI-matched healthy subjects.

Ethical review	Approved WMO
Status	Completed
Health condition type	Inborn errors of metabolism
Study type	Observational invasive

Summary

ID

NL-OMON53399

Source
ToetsingOnline

Brief title
MONACO

Condition

- Inborn errors of metabolism

Synonym
acid sphingomyelinase deficiency, Niemann-Pick disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: werkbudget onderzoeksgorep

Intervention

Keyword: acid sphingomyelinase deficiency, magnetic resonance elastography, magnetic resonance spectroscopy

Outcome measures

Primary outcome

Fat fraction in volume percentage (%) measured with MRS of ASMD patients

compared to values of healthy subjects.

Secondary outcome

- to assess whether MRS is able to specifically distinguish SM accumulation

from lipid accumulation in liver tissue.

- to assess the effect of therapy on the fat fraction and liver stiffness in

the patients that are eligible to start treatment.

- to identify patients with liver involvement of ASMD by assessing the

correlation between the fat fraction and liver stiffness and markers of liver

involvement of ASMD.

- to assess the correlation of the fat fraction and liver stiffness with other

biomarkers for ASMD.

Study description

Background summary

Acid sphingomyelinase deficiency (ASMD) is a rare lysosomal storage disorder caused by a deficiency of sphingomyelinase resulting in accumulation of the sphingolipid sphingomyelin in the liver, spleen and lungs. Enzyme replacement therapy (ERT, olipudase alfa, Sanofi Genzyme) is currently investigated in a phase 2/3 trial and is expected to get market approval in the second half of 2022. Accumulation of sphingomyelin in the liver leads to liver fibrosis in a subset of ASMD patients. As ASMD is a slowly progressive disease, detection of

early stages of sphingomyelin storage in the liver might aid in identifying patients at risk for major manifestations who would benefit from therapy. Two magnetic resonance (MR) based techniques might be of interest: MR Spectroscopy (MRS) to measure lipid accumulation (steatosis) and MR Elastography (MRE) to measure liver stiffness (fibrosis).

Study objective

To assess the ability of MRI techniques to detect early stages of lipid accumulation in the liver of ASMD patients with the chronic visceral subtype compared to values of age-, sex- and BMI-matched healthy subjects.

Study design

Cross-sectional pilot study in which MRS and MRE measurements of ASMD patients will be compared to values of age-, sex- and BMI-matched healthy subjects. All ASMD patients who participate will undergo an MRI during their yearly assessments. Patients eligible for therapy will also undergo an MRI after one year of treatment. Healthy subjects will undergo one MRI.

Study burden and risks

The MRI procedure yields no risk: at most patients might feel uncomfortable lying in tight space. Patients will not directly benefit from participation in the study. The results of the study may improve clinical care in the future.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Patients:
- The patient has biochemically proven ASMD (preferably genetically confirmed)
- The patient is >= 18 years of age
- The patient is willing and able to provide written informed consent prior to the study-related procedure.

Healthy controls:
- The individual is willing and able to provide written informed consent prior to the study-related procedure
- The individual is >= 18 years of age
- General good health as determined by medical history

Exclusion criteria

ASMD patientes and healthy controls:
- Inability to adhere to the study protocol
- Inability to undergo an MRI procedure

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:	Completed
Start date (anticipated):	05-05-2023
Enrollment:	34
Type:	Actual

Medical products/devices used

Generic name:	software patch MRE
Registration:	No

Ethics review

Approved WMO

Date:	19-01-2023
Application type:	First submission
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	NL80644.018.23