Phenotype prediction in patients with X-linked adrenoleukodystrophy: a prospective study.

Published: 17-02-2015
Last updated: 21-04-2024

The primary objective is to study if quantitative (3- and 7-Tesla) MRI protocols (MRI perfusion, diffusion tensor imaging (DTI), and chemical shift imaging (CSI)) are able to detect phenotype conversion earlier than conventional MRI. Results will be...

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

Summary

ID

NL-OMON45041

Source
ToetsingOnline

Brief title
Phenotype prediction in X-ALD.

Condition

- Neurological disorders congenital
- Congenital and peripartum neurological conditions

Synonym
Schilder's disease, X-ALD, X-linked adrenoleukodystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: VENI beurs aan hoofdonderzoeker

Intervention

Keyword: Lipidomics, MRI, X-ALD, X-linked adrenoleukodystrophy

Outcome measures

Primary outcome

The main study parameter is conversion to cerebral ALD.

Secondary outcome

Natural history of X-ALD.

Study description

Background summary

Patients with X-linked adrenoleukodystrophy (X-ALD) develop adrenocortical insufficiency (80% during childhood) and a progressive myelopathy (in adulthood). In most patients (sub)clinical hypogonadism is present. Many (40% before the age of 18 years) develop rapidly progressive cerebral demyelination (cerebral ALD; cALD). cALD can be treated with haematopoetic cell transplantation (HCT) in early stage disease. To detect cALD in an early pre-symptomatic stage children with X-ALD undergo MRI of the brain every 6 months and adults every 12 months. If there were methods to stratify patients according to risk for cerebral ALD follow-up could be individualized and unnecessary examinations reduced.

Recently the Spinoza Centre, a new research facility for MRI neuroimaging research at high field strength (7-Tesla) was established. This offers the possibility to implement groundbreaking novel MRI imaging techniques in the care for X-ALD patients. Acquiring data at a field strength of 7-Tesla enables measuring at unprecedented level of detail, with a spatial resolution of 0.5 mm. I aim to perform additional MRI sequences at 7-Tesla, parallel to the prospective cohort study, to evaluate if quantitative MRI protocols (MRI perfusion, DTI and CSI) are able to detect phenotype conversion earlier than 3-Tesla imaging techniques.

To gain power for quantitative MRI sequences on both 3- and 7- Tesla I will recruit healthy-age matched-volunteers to participate in this study.

Study objective

The primary objective is to study if quantitative (3- and 7-Tesla) MRI protocols (MRI perfusion, diffusion tensor imaging (DTI), and chemical shift imaging (CSI)) are able to detect phenotype conversion earlier than conventional MRI. Results will be correlated to MRI images of healthy age matched controls. We will also search for new prognostic biomarkers with lipidomics analysis in plasma and cytokine profiles in CSF (optional). We will quantify quality of life, disability and signs of hypogonidsm.
The secondary objective is to validate known genetic biomarkers for the occurrence of cerebral ALD.

Study design

The study is a longitudinal cohort study for a period of 3 years, with visits to the hospital every 6 or 12 months (depending on age). Healthy volunteers will visit the AMC once.

Study burden and risks

Currently, patients with X-linked adrenoleukodystrophy visit the hospital at least once a year for neurological examination, a MRI scan of the brain and endocrinological tests. The frequency of hospital visits will not change, the only differences are:
- Longer neurological history and examination, with questionnaires and scales (SF-36, ALDS, CIS, ICIQ, SSPROM, mJOA, 6MWT, Timed Up and Go test, MMSE)
- Longer MRI protocol (70 minutes versus 45 minutes)
- Extra laboratory tests (additional blood for lipidomics analysis, isolation of extracellular vesicles, DNA storage)
- Lumbar punction (optional)
- Single measurement of testicular volume by ultrasound (optional)

Healthy volunteers will visit the AMC once for:
- Screening for neurological disease and/or cardiovascular risk factors (Structured history and physical examination)
- 3-Tesla MRI protocol (quantitative DTI, MRS/CSI, ASL) for controls between 12 and 18 years and for controls aged 18 years or older, including intravenous gadolinium for controles aged 18 years or older and/or
- 7-Tesla MRI protocol (quantitative DTI, MRS/CSI), solely for controles aged 18 years or older.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1019TH
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1019TH
NL

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

Patients:
- male patients with X-ALD (confirmed by ABCD1 mutation analysis)
- age for which follow-up is normally recommended (2 years and older)
- willing to undergo regular follow-up visits (twice yearly if < 12 years and yearly if > 12 years) with blood sampling and MRI scan of the brain.
- Informed consent obtained from participant or legal guardian in case of a minor;For the additional MRI sequences at 7-Tesla participants must meet these additional criteria:
- Age 18 years or older
- Supplementary informed consent procedure;Subjects eligible to participate as healthy controls must meet all of the following criteria:
- Willing to visit the hospital
- 12 years or older
- For administration of gadolinium: age 18 years or older
- Informed consent obtained from participant

- Informed consent obtained from participant or legal guardian in case of a minor

Exclusion criteria

Patients:
- unable to visit the hospital for follow-up (for instance, due to advanced disease)
- co-existing neurological disease making interpretation of acquired data difficult (for instance, multiple sclerosis);A potential healthy control who meets any of the following criteria will be excluded from participation in this study:
- neurological disease (because this would impede accurate interpretation of the MRI imaging data)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-06-2015
Enrollment:	125
Type:	Actual

Ethics review

Approved WMO

Date:	17-02-2015
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-06-2016
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	NL51345.018.14