Five year follow-up of the phenotype of X-linked adrenoleukodystrophy carriers: a cohort study.

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

Summary

ID

NL-OMON43945

Source
ToetsingOnline

Brief title
Follow-up phenotype X-ALD carriers

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: Geen geldstroom. Reiskosten van

proefpersonen worden gefinancierd uit het budget van de afdeling kinderneurologie.

Intervention

Keyword: adrenoleukodystrophy, carriers, myelopathy, X-linked

Outcome measures

Primary outcome

To conduct a five year follow-up of the X-ALD carriers and evaluate progression

of symptoms by assessing participants* current symptomatic and biochemical

(VLCFA in plasma) status.

Secondary outcome

To validate a new biomarker (26:0-lyso-PC(1-

hexacosanoyl-2-lyso-sn-3-glycero-phosphorylcholine)) amongst X-ALD carriers. To

identify new (diagnostic) biomarkers for X-ALD using lipidomics analysis.

Study description

Background summary

X-linked adrenoleukodystrophy (X-ALD) is the most common peroxisomal disorder, caused by mutations in the ABCD1 gene, biochemically characterized by accumulation of very-long-chain fatty acids and decreased beta-oxidation. Clinically the phenotype in men is highly variable, ranging from exclusively adrenocortical insufficiency, a gradually progressive myelopathy and peripheral neuropathy to a devastating progressive and fatal cerebral demyelinating disease.
Considering X-ALD is an X-linked disease, it was speculated that female carriers would be asymptomatic. However, amongst others, the prospective cross-sectional cohort study conducted in our outpatient clinic in the Academic Medical Centre (AMC) in 46 X-ALD carriers showed that the majority (63%) also develop symptoms of myelopathy and/or peripheral neuropathy, of which the frequency increases with age. In addition the very long-chain fatty acids (VLCFA) in plasma were elevated in 69%, with decreased beta-oxidation in fibroblasts in 60%. Adrenocortical insufficiency and the devastating cerebral

demyelinating disease are rare in carriers.

Study objective

We aim to conduct a five year follow-up amongst the X-ALD carriers and assess their current symptomatic and biochemical status. This data will provide new insights in the progression of the disease in carriers. Moreover we would like to validate a new biomarker (26:0-lyso-PC(1-hexacosanoyl-2-lyso-sn-3-glycero-phosphorylcholine) which is the substrate for the recently validated newborn screening for X-ALD and to identify new (diagnostic) biomarkers for X-ALD with lipidomics analysis.

Study design

This study is the five year follow-up of a prospective cohort study, requiring one visit to the hospital.

Study burden and risks

Participants will have to visit the hospital once and undergo a venapunction. Considering there is very limited data available on X-ALD carriers we believe the burden of this minor intervention outweighs the possible benefits of more knowledge on the phenotype of X-ALD carriers.

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

- Female carriers of X-ALD (confirmed by ABCD1 mutation analysis)
- Age above 18 years
- Willing to visit the hospital
- Informed consent obtained from participant

Exclusion criteria

- Unable to visit the hospital
- Neurological co-morbidity (because this would impede accurate interpretation of the neurological assessment)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-05-2015
Enrollment:	60

Type:	Actual

Ethics review

Approved WMO Date:	22-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-02-2016
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	NL52846.018.15