Quantitative sensory testing and intraepidermal nerve fibre density for improved diagnosis of Fabry disease.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON37662

Source
ToetsingOnline

Brief title
SFN assessment for improverd Diagnosis of Fabry disease

Condition

- Metabolic and nutritional disorders congenital

Synonym
Anderson-Fabry disease, Fabry disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: TI Pharma,farmaceutische industrie,Genzyme,Shire

Intervention

Keyword: Diagnosis, Fabry, Small fiber neuropathy

Outcome measures

Primary outcome

To determine if alterations of intraepidermal nerve fiber density and quantitative sensory testing are present in patients with a possible diagnosis of Fabry disease, but without clinical signs and symptoms of small fiber neuropathy.

Secondary outcome

To evaluate if alterations of intraepidermal nerve fiber density and quantitative sensory testing can contribute to the diagnosis of Fabry disease in patients with a possible diagnosis of Fabry disease, but without clinical signs and symptoms of small fiber neuropathy.

Study description

Background summary

Fabry disease is an X-linked inherited multisystem lysosomal storage disorder with an estimated birth prevalence of classically affected patients of ~1:40,000. Deficient activity of the lysosomal hydrolase alfa-galactosidase A is the primary cause of the disease and as a consequence glycosphingolipids, primarily globotriaosylceramide (Gb3, also named GL-3 or CTH) accumulate. In hemizygous males the first signs or symptoms usually occur during childhood and adolescence. These include acroparesthesia, intolerance to heat, inability to sweat and micro-albuminuria. Later in life cerebrovascular disease, cardiac hypertrophy and progressive kidney disease may develop. Fabry disease may manifest itself in carrier females in a more variable and in general a more attenuated course.
The rarity of the disorder and variability of disease signs and symptoms often cause important diagnostic delays. Although many ethical, legal and social issues remain, several studies on the feasibility of screening for Fabry

disease have already been executed. These initiatives included screening of high risk groups as well as neonatal screening. Surprisingly, the birth prevalence of Fabry disease as diagnosed by newborn screening is around 10 times higher than birth prevalence based upon traditional diagnostic trajectories. This may be explained by a high incidence of individuals with mutations associated with late onset and mild disease manifestations. Whether such individuals will develop Fabry related complications has not been investigated sufficiently.
Sometimes, individuals are identified with a decreased alfa-galactosidase A activity or a genetic variation in the GLA gene. These patients often only present with a single -otherwise unexplained- symptom such as albuminuria, left ventricular hypertrophy, pain in hands or feet, early stroke and/or atypical white matter lesions, *red spots*, fatigue, gastrointestinal symptoms etc. Oligosymptomatic patients are increasingly subjected to screening studies for Fabry disease. These symptoms need not necessarily be causally related to the genetic variations. Thus, there is an increasing need to specify whether in positively sreened patients, specific signs and symptoms are actually caused by Fabry disease or not. Biopsies from affected organ(s), to establish actual storage of GB3, may in those cases be essential for a definite diagnosis.
The aim of the current study is to evaluate the added value of quantitative sensory testing and intraepidermal nerve fiber density in individuals with a AGAL deficiency and/or variation in the GLA gene of unknown clinical significance. These assessments will be incorporated in a general Fabry disease diagnostic algorithm that will explore all organ systems involved in Fabry disease.

Study objective

The aim of the current study is to evaluate the added value of quantitative sensory testing and intraepidermal nerve fiber density in individuals with a AGAL deficiency and/or variation in the GLA gene of unknown clinical significance. These assessments will be incorporated in a general Fabry disease diagnostic algorithm that will explore all organ systems involved in Fabry disease.

Study design

Patients with a mutation or variant of undetermined clinical significance in the AGAL gene or a decreased enzyme activity of *-galactosidase A are eligible for the study; The AMC is the national referral center for Fabry disease. Eligible patients are selected from the AMC Fabry patient cohort. .Quantitative sensory testing and Skin biopsy for intraepidermal nerve fiber density are performed and scheduled with other clinical assessments for Fabry disease after informed consent is obtained.

Study burden and risks

The aim of the study is to delineate the added value of QST and intraepidermal nerve fiber density in the establishment of Fabry disease. This is of extreme importance for adequate counseling and support of patients and especially for appropriate installation of costly treatment. The project has high potential to lead to important clinical benefit when treatment can be more appropriately timed. When patients are better diagnosed, we expect that those who need it can be treated earlier and more effectively. On the other hand individuals may be identified who carry a polymorphism or mild mutation who are asymptomatic or have symptoms that suggest Fabry disease but are in fact caused by another condition. In these cases, burdensome and anxiety causing procedures can be avoided, such as unnecessary counseling, treatment and problems related to eligibility for life insurance or disability insurance.
Fabry disease is one of the first genetic disorders for which the question of disease versus non-disease will be studied in depth, with clear consequences for patients and society.
A general public health goal will be served by avoiding unnecessary treatment and interventions as well as to promote more timely initiation of therapy. Harmonizing the approach to individuals with suspected Fabry disease within the Netherlands supports the principles of equity, evidence and efficiency.
All procedures will be conducted by trained medical professionals only, resulting in a low complication risk.

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

Adult males and females with signs or symptoms possibly attributable to Fabry disease.

Exclusion criteria

Patient is unwilling to participate

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-01-2013
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	17-09-2012
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	NL40011.018.12