Genetic modifiers of cardiac electrophysiology in a large Dutch family with the SCN5A 1795insD mutation

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In the present study we aim to identify the genetic modifiers in this family which underlie differences in severity and type of phenotype by means of linkage analysis.

Ethical review	Approved WMO
Status	Pending
Health condition type	Cardiac arrhythmias
Study type	Observational invasive

Summary

ID

NL-OMON30585

Source
ToetsingOnline

Brief title
Genetic modifiers of cardiac electrical phenotype

Condition

- Cardiac arrhythmias
- Chromosomal abnormalities, gene alterations and gene variants

Synonym
primary arrhythmia syndromes - heritable heart rhythm disorders

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Nederlandse Hartstichting;Foundation Leducq

Intervention

Keyword: Brugada syndrome, Conduction disease, Genetic modifiers, Long QT syndrome

Outcome measures

Primary outcome

The discovery of genetic modifiers which are associated with the cardiac electrical phenotype and SCD may allow improved risk stratification and individualised tailoring of preventive and therapeutic treatment not only for the SCN5A 1795insD family but also for other populations at risk for SCD.

Secondary outcome

Not applicable.

Study description

Background summary

A large Dutch family carrying the SCN5A 1795insD mutation which encodes for the cardiac sodium (Na+) channel is characterised by a high number of nocturnal sudden cardiac death (SCD) and multiple arrhythmia syndromes. We documented an extensive variability in the type and severity of symptoms in this family. We have shown that these symptoms could in part be attributable to the biophysical properties of a multi-dysfunctional mutant Na+ channel. Here we hypothesize that genetic background plays a significant role in determining the ultimate cardiac phenotype. In support of this hypothesis, studies we carried out on transgenic mice of two different inbred genetic strains both carrying the murine equivalent of the SCN5A 1795insD mutation, demonstrated that the phenotype is more severe in one genetic background compared to the other.

Study objective

In the present study we aim to identify the genetic modifiers in this family which underlie differences in severity and type of phenotype by means of linkage analysis.

Study design

After obtaining informed consent, the participants will provide; for genotyping: 27 ml of blood (taken by venapuncture) or saliva (in a 10 ml tube); for phenotyping: a single baseline ECG and a follow up ECG after at least one year. The phenotype and genotype of the subjects in this study will be used for linkage analyses. Comparing genotype and phenotype from mutation carriers and non-mutation carriers will identify genes that are associated with the cardiac electrical phenotype and SCD.

Study burden and risks

The burden for the participants is the provision of their time, blood or saliva and ECG, with a possible risk for a haematoma following venapuncture. Benefit; with this research we will be more informed on a selection of candidate genes and have better chance to discover genes which confer risk for SCD, which may not only ameliorate SCD risk stratification for their children, family and future offspring, but also for other populations at risk for SCD.

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

Having conceived 1 or more children carrying the SCN5A 1795insD mutation with someone who is also carrying this mutation (i.e. the individual is a spouse and parent of a mutation carrier)

Exclusion criteria

No informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2007
Enrollment:	70
Type:	Anticipated

Ethics review

Approved WMO

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	NL16269.018.07