Molecular studies in a multigenerational family with gastro-esophageal reflux disease (GERD)

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

Summary

ID

NL-OMON35981

Source
ToetsingOnline

Brief title
Molecular studies in a family with GERD

Condition

- Gastrointestinal tract disorders congenital
- Gastrointestinal motility and defaecation conditions

Synonym
GERD, heartburn

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Stichting

Kindermotiliteit

Intervention

Keyword: family, Genetic, GERD, Molecular

Outcome measures

Primary outcome

The primary outcome is linkage to one or more chromosome regions and

idenfication of associated gene(s) in the GERD family.

Secondary outcome

The secondary outcome will consist of a thorough description of the clinical

characteristics, the phenotype, of patients with GERD in this family.

Study description

Background summary

Gastro-esophageal reflux disease (GERD) is a common disease in adults and chilren. The pathophysiology of GERD is largely unknown and is probably multifactorial. However, the reported familial clustering and high prevalence of GERD in twins indicate that genetic factors are likely to play a role as well in its pathophysiology. In families with GERD only a few linkage studies have been performed aiming to identificate genes that are associated with a GERD phenotype. Linkage analysis in a family with pediatric GERD by Hu et al. showed a linked region on chromosome 13q14.Subsequently conducted studies, did not succeed in replication of linkage to this region nor in identification of a susceptibility gene for GERD in this region. More recently, genome wide linkage analysis in four different patient cohorts followed by an association study and protein analysis identified COL3A1, a gene located on chromosome 2 and responsible for the synthesis of the protein collagen type 3, as a susceptibility locus for GERD.
No replication studies have yet been performed to confirm this possible association. To conclude, up till now no genes have been confirmed to be associated with GERD.
Performing molecular analyses in well-defined large families may allow identification of genes associated with GERD, especially if linkage and sequencing studies are combined. This should lead to increased insight in the

pathophysiology of this common disease.

Study objective

To identify chromosomal regions associated with the GERD-phenotype in a large multigenerational family with multiple affected members. Subsequently these regions will be sequenced to detect causative gene(s). The second aim is to describe the clinical characteristics of GERD within this family (the phenotype).

Study design

Linkage analysis will be performed in one large multigenerational family. Suggestive chromosomal regions identified in this way will be further investigated by sequencing, either Sanger sequencing or Next Generation Sequencing, depending on number and size of the identified regions. Furthermore, clinical information will be obtained by a questionnaire and from files.

Study burden and risks

Participating patients will not be subjected to invasive investigations. Filling out the questionnaire will take about 10 minutes of their time. Peripheral blooddrawing or taking saliva samples does not bring along noteworthy risks.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

- Affected family members and all adult unaffected family members will be asked to participate. Family members are considered to be affected either if a diagnosis of GERD has been made by a physician (usually a [pediatric] gastroenterologist), if additional investigations such as pH/impedance measurements or gastroesophageal endoscopies show evidence for GERD, or if anti-reflux surgery has been performed in the past. GERD is considered as a dichotomous trait in this study.
- Informed consent is needed to be included. Informed consent will be asked for by the parents when children are under the age of 12 years. At present there is only a single affected child (8 yrs) in this family.

Exclusion criteria

Insufficient understanding of the purpose and risks of the study.

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:	Recruitment stopped
Start date (anticipated):	05-02-2012
Enrollment:	23
Type:	Actual

Ethics review

Approved WMO

Date:	17-01-2012
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	NL36521.018.11