The role of genetics in the pathophysiology of gastro-oesophageal reflux disease.

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To identify genetic risk factors associated with GERD.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Observational invasive

Summary

ID

NL-OMON35951

Source
ToetsingOnline

Brief title
Genetics in GORD

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
gastro-oesophageal reflux disease, reflux disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: DNA, genetics, genome, GORD

Outcome measures

Primary outcome

The information obtained will contain all coding regions (exones) of each participant. Not all variants in all exones will be evaluated: the results in patients will be compared to one another in order to find variants in genes they have in common.

Secondary outcome

Severity and frequency of reflux symptoms

Quality of Life

Study description

Background summary

Gastro-oesophageal reflux disease
Gastroesophageal reflux disease (GERD) is a condition in which reflux of gastric content into the oesophagus results in mucosal injury and/or bothersome symptoms. Approximately 15-20% of the general population experiences typical reflux symptoms as heartburn and/or regurgitation at least weekly (1). The presence of GERD symptoms is accompanied by a decrease in health-related quality of life and an increase of healthcare costs due to frequent specialist visits and prescription of chronic medication (2). GERD can be subdivided in patients with mucosal abnormalities such as oesophagitis, so called erosive reflux disease (ERD), and patients with no mucosal abnormalities at upper endoscopy, so called non-erosive reflux disease (NERD).

Pathophysiology
The pathophysiology of GERD is multifactorial. Factors predisposing to an excessive amount of gastroesophageal reflux have been identified, such as alteration of the esophagogastric junction by the presence of a hiatus hernia (3), which is in turn influenced by obesity (4). Independent of severity of esophageal acid exposure, patients report a wide range of symptom severity and

symptom frequency suggesting changes at the mucosal level influencing the perception of reflux. Possible important factors are the presence of visceral hypersensitivity (5), and dilated intercellular spaces (6). However, the exact mechanisms of symptom generation remain to be elucidated.

Genetics in GERD
Epidemiologic studies suggest a genetic component in the pathophysiology of GERD. The presence of typical reflux symptoms is higher among family members of GERD patients (7,8). Additionally, twin studies show an increased concordance of GERD among monozygotic compared to dizygotic twins and estimated that heritability accounted for up to 30% of the liability to GERD in that population (9,10). A recent study found an association between GERD and the heterozygous genotype of the C825T allele of the G-protein B3 subunit, coding for a receptor frequently present in the neural brain-gut axis which is associated with intracellular signal transduction (11). The polymorphism had previously been associated with visceral hypersensitivity in functional dyspepsia, suggesting a possible general genetic susceptibility for visceral hypersensitivity.
These findings support further research aimed at identifying genetic abnormalities underlying the pathophysiology of GERD, thereby possibly generating new targets for therapy.

Study objective

To identify genetic risk factors associated with GERD.

Study design

The study design is prospective and observational. DNA of subjects will be obtained by drawing one sample of whole blood.

Study burden and risks

Venapuncture:
A single venapuncture for the withdrawal of whole blood is a safe procedure and very frequently performed in the clinical setting. There is no serious risk attached. A small complication is a puncture haematoma, for which no treatment is necessary. Patients can respond to venapuncture with a vasovagal collaps, therefore blood shall be drawn in a special chair in semirecumbent position.

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

Patient inclusion criteria:
-Subjects undergoing a 24-hour esophageal pH-measurement with the indication heartburn/reflux.
-Subjects undergoing a control upper endoscopy for reflux oesophagitis.
-Written informed consent
-Age >18

Exclusion criteria

History of disease/surgery affecting gastrointestinal motility

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	500
Type:	Anticipated

Ethics review

Approved WMO

Date:	26-01-2012
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	NL37239.018.11