Oesophageal acid perception in patients with Barrett*s oesophagus.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Observational invasive

Summary

ID

NL-OMON35534

Source
ToetsingOnline

Brief title
Acid perception in Barrett

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
Barrett, Barrett's oesophagus

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Acid perception, Barrett, Oesophageal permeability, Tissue Impedance

Outcome measures

Primary outcome

Oesophageal permeability.

Secondary outcome

Tissue impedance spectrum of the oesophageal epithelium.

Sensitivity to oesophageal acid perfusion.

Study description

Background summary

Barrett*s oesophagus
Oesophageal adenocarcinoma is one of the fastest rising malignant diseases in the western world, with a four-fold increase in the past few decades (1). A premalignant condition associated with an increased risk of development of adenocarcinoma is Barrett*s oesophagus (BO), defined as a replacement of the normal squamous epithelium with columnar epithelium, or intestinal metaplasia (2). The BO to adenocarcinoma pathway develops slowly through a well defined sequence of intestinal metaplasia, low-grade intraepithelial neoplasia, high grade intraepithelial neoplasia and finally early adenocarcinoma (3). The disorder is thought to be a complication of longstanding chronic gastro-oesophageal reflux disease (GORD) and it has been shown that there is increased acid exposure in the oesophagus of Barrett patients compared to healthy controls and symptomatic GORD patients (4). Approximately 10% of GORD patients have shown to have a BO, however, recent studies suggest even higher prevalence for short segment Barrett oesophagus, as defined as a segment of Barrett epithelium < 3cm. A population based study in Sweden reports a total prevalence of 1.6% (5).
Severity of oesophageal acid exposure is partly dependent on oesophageal acid clearance, of which the main mechanism is pharyngeal swallowing (6). It has been shown that the swallowing frequency increases in response to increased oesophageal acid exposure in GORD patients (7). Furthermore, this increase is most likely due to an increase in perception of reflux episodes (7). Patients with BO are less sensitive to oesophageal acid exposure than GORD patients (8,9). This could lead to decreased perception of reflux episodes and to a

decreased oesophageal clearance. Thereby it could contribute to the development of intestinal metaplasia. Furthermore, a decreased sensitivity to oesophageal acid could delay a physician consultation and delay adequate acid inhibition, thereby leading to an excessive exposure of the oesophageal mucosa to acid and the development of intestinal metaplasia.
A study currently performed at the Motility Centre in the AMC focuses on the mechanisms of oesophageal acid sensitivity and permeability of oesophageal tissue in GORD patients (MEC 10/275), with the hypothesis that oesophageal permeability changes are thought to facilitate acid diffusion towards the sensory nerves. In vivo measurements of tissue impedance (TIM) and ex vivo Ussing experiments are performed to assess oesophageal permeability.
In the present study we hypothesize that oesophageal permeability changes mediate the decreased acid sensitivity and perception in BO patients compared to GORD patients and healthy volunteers.

Tissue impedance measurement (TIM)
Tissue impedance measurement is a new method to assess in vivo impedance of tissue using an electrical current. It has previously been demonstrated that with tissue impedance measurements is it possible to separate precancerous from normal tissue in the cervix (10,11). In vitro work showed the possibility to distinguish oesophageal squamous epithelium from metaplastic columnar epithelium (12). The concept depends on inherent properties of the electrical current, where high frequencies pass through the cells in the tissue while low frequencies tend to pass between cells (13). By examining a range of frequencies, the relative composition of the tissue can thus be examined. A new probe designed to fit into the working canal of a gastroscope has been designed in order to allow impedance evaluation of the distal oesophagus during routine endoscopic examination. In animal experiments the probe has been demonstrated to have an acceptable inter- and intraindividual variability of the main parameters.

Study objective

Key objective: the hypothesis that will be tested
Our hypothesis is that the decreased oesophageal acid sensitivity is mediated by oesophageal permeability changes. Furthermore we hypothesize that the electrical tissue impedance of oesophageal tissue in BO patients is altered compared to normal oesophageal squamous epithelium, in both areas of intestinal metaplasia and non-affected mucosa situated above these mucosal regions.

Aim
To investigate the oesophageal sensitivity to acid and the mechanism underlying acid sensitivity changes in BO. Oesophageal permeability will be assessed functionally by Ussing experiments on oesophageal biopsies and morphologically by electron microscopy.

Study design

The study has an observational prospective design. One group of subjects will be included, consisting of patients with BO without neoplastic changes.
The METC of the AMC Amsterdam has previously granted permission for the inclusion of GORD patients and healthy volunteers in a similar protocol (MEC 10/275). While the analyses are similar, the healthy controls will serve as control populations.

Study burden and risks

The risk of the performed procedures consists of the risk of oesophageal biopsies, namely bleeding and perforation. The Bernstein test is a safe procedure, only associated with discomfort during placement of the perfusion catheter. There is no additional risk involved with the tissue impedance measurements. The impedance measurements and obtaining 6 jumbo biopsies prolong the time of a regular endoscopy with approximately 7 minutes. The study will contribute to better understanding of the condition and possibly offer new diagnostic tools.

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

-Barrett*s oesophagus patients with Barrett segment > 1cm
-Age >18 years
-Proton pump inhibitors (PPI) use longer than 4 weeks
-Written informed consent

Exclusion criteria

-Previous invasive treatment of Barrett oesophagus, e.g. endoscopic resection, radiofrequency ablation.
-Presence of dysplasia
-Surgery of the GI tract other than appendectomy or cholecystectomy
-Motility disorders of the GI tract leading to delayed gastric emptying or altered intestinal motility
-Inability to stop the use of medication influencing GI motility for 3 weeks
-Inability to stop the use of proton pump inhibitors for 3 weeks

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2012

Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	01-11-2011
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	NL38089.018.11