In vivo evaluation of esophageal mucosal permeability in patients with non erosive reflux disease

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We hypothesise that the increased permeability of the esophageal mucosa in GERD patients can be shown using confocal laser scanning fluorescence microscopy. This difference in esophageal permeability may prove a diagnosticum for patients without...

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

Summary

ID

NL-OMON32964

Source
ToetsingOnline

Brief title
permeability and NERD

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
Gastro-esophageal reflux disease (GERD), heartburn

Research involving
Human

Sponsors and support

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

Intervention

Keyword: confocal endomicroscopy, dilated intercellular spaces (DIS), gastro esophageal reflux disease (GERD), non erosive reflux disease (NERD)

Outcome measures

Primary outcome

Primary outcome parameter is the permeability as measusered by fluorescein

diffusion. It is measured by the identifiable layers of epithelium after

certain times of spraying.

Secondary outcome

Secondary outcome variables:

- permeability, as measured in vitro in ussing chambers

- expression of tight junction proteins

- occurence of dilated intercellular spaces

Study description

Background summary

Gastroesophageal reflux disease (GERD) is a very common disorder causing both symptoms (heartburn, regurgitation) and damage of the esophagus (esophagitis). In the majority of patients with reflux symptoms, upper gastrointestinal endoscopy however reveals no abnormalities. Diagnosing GERD then occurs by pH/impedance measurement. When this diagnosis can be made, patients are referred to as having Non Erosive Reflux Disease (NERD). However, there are patients with similar complaints who do not have a relation between their complaints and esophageal reflux. These patients are referred to as having functional heartburn. During endoscopy, there is no possibility to distinguish these two.
Functional and histological analysis show various changes suggestive of reflux induced damage in NERD patients. The basal cell layer is thickened and intra-papillary capillary loops are elongated. More interestingly, in patients with GERD the paracellular permeability of the esophageal mucosa for small molecules is increased. In addition, the intercellular spaces are dilated in

NERD patients compared to healthy subjects. Due to these enlarged intercellular spaces acid in the refluxate can reach the nerve endings in the epithelial layer, giving rise to heartburn, one of the main symptoms of GERD. Dilated intercellular spaces (DIS) were first seen in in vitro experiments, and later proven as a persistent histopathological feature in patients with GERD. Probably they are due to the proteolytic properties of pepsin and trypsin in the refluxate on desmosomes and tight junctions. Both increased paracellular permeability and DIS might prove to be a specific feature in the diagnosis of NERD. Recent evidence suggest that the increase of paracellular permeability precedes the occurrence of DIS.
The recent development of confocal endomicroscopy provides an opportunity to obtain a 3-dimensional optical biopsy in vivo without physically disrupting epithelial integrity.
By incorporating a miniaturized laser scanner with confocal imaging into a conventional endoscope, confocal endomicroscopy can collect high-resolution images from living human epithelium without fixation artefacts. Confocal endomicroscopy has already shown dilated intercellular spaced in vivo. In this study, fluoresceine was applied intravenously, where after it was taken up by the esophageal mucosa.
When fluoresceine is sprayed into the esophageal lumen, this might show us the permeability of the esophageal epithelium, as it diffuses through the intercellular spaces. The aim of this study is to compare the esophageal permeability in GERD patients to that of healthy volunteers, with a focus on the permeability in patients with NERD.

Study objective

We hypothesise that the increased permeability of the esophageal mucosa in GERD patients can be shown using confocal laser scanning fluorescence microscopy. This difference in esophageal permeability may prove a diagnosticum for patients without other evidence of GERD at endoscopy, e.g. for patients with non erosive reflux disease (NERD).

Study design

We will perform a prospective feasibility study comparing esophageal mucosal permeability in patients with endoscopically confirmed GERD, patients with esophageal complaints, to healthy subjects.

Study burden and risks

The risks of the study are limited to the risk of the endscopy and the biopsies. The potential benefit for the group of patients can be that more insight is acquired in pathophysiology of non erosive reflux disease. Furthemore the study might lead to an endoscopic diagnosis of non erosive

reflux disease.

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

Patients:
- Age 18 * 75 years
- Written informed consent
Healthy volunteers:
- Age 18 * 75 years
- Written informed consent

Exclusion criteria

Patients:
- Surgery of the GE-tract other than appendectomy
- Use of PPI, or other medication influencing gastric or GI motility
- patients unable to undergo endoscopy
- Allergy to fluoresceine, midazolam, buscopan
- Renal insuffiency
Healthy volunteers:
- Surgery of the GE-tract other than appendectomy
- Gastro-intestinal complaints, including typical GERD complaints
- Medication influencing gastric motility or GI motility
- Allergy to fluoresceine, midazolam, buscopan
- Renal insuffiency

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:	Pending
Start date (anticipated):	01-06-2009
Enrollment:	50
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	NL26672.018.09