Oesophageal epithelial permeability changes in patients with eosinophilic oesophagitis

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To show that in eosinophilic oesophagitis gastro-oesophageal reflux-induced epithelial barrier dysfunction facilitates passage of food-antigens through the epithelial barrier and subsequent increased exposure of antigens by dendritic cells activates...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON36166

Source
ToetsingOnline

Brief title
Oesophageal epithelial permeability changes in EoE

Condition

- Gastrointestinal inflammatory conditions
- Allergic conditions

Synonym
idiopathic allergic oesophagitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: eosinophilic, oesophagitis, osophageal, permeability

Outcome measures

Primary outcome

- Oesophageal intercellular spaces are dilated in EoE patients compared to healthy subjects.

- Mucosal permeability to small molecules is increased in EoE patients compared to healthy subjects.

- Tissue impedance measurement is affected in EoE patients compared to healthy subjects.

- Dilated intercellular spaces correlate with affected tissue impedance and increased mucosal permeability to small molecules in EoE patients.

- Affected tissue impedance correlates with increased mucosal permeability to small molecules in EoE patients.

- Numbers of oesophageal intraepithelial eosinophils are increased in EoE patients compared to healthy subjects.

- Numbers of oesophageal intraepithelial mast cells are increased in EoE patients compared to healthy subjects.

Secondary outcome

- Tissue impedance, dilation of intercellular spaces, increased mucosal permeability to small molecules, and numbers of oesophageal intraepithelial mast cells and eosinophils are reversible by 8 weeks administration of 40 mg esomeprazole twice daily.

- The composition of inflammatory cells present in the esophageal biopsies

- The number of reflux episodes

Study description

Background summary

Eosinophilic oesophagitis (EoE) is a recently recognized disorder characterized by symptoms of dysphagia and oesophageal food impaction. Long-term presence of the disorder leads to fibrotic strictures and diffuse narrowing in the oesophagus that require endoscopic dilatations.
The pathophysiology is largely unknown, a potential allergic pathway in the pathophysiology of this disorder is suggested. Furthermore, it is reported that patients with EoE are hypersensitive to acid. Current standard treatment uses topical or systemic corticosteroids to suppress the immune system, a therapy that is accompanied with various side-effects and therefore less suitable for long-term use. The search for better therapy is complicated by the lack of knowledge of the pathophysiology.
Recent data shows that in patients with EoE the periostin gene is overexpressed and expression of the filaggrin gene is down regulated. Periostin is an extracellular matrix molecule that regulates eosinophil adhesion while filaggrin is a protein that is important for maintaining the epithelial barrier. In the skin, it has been shown that a loss of function of filaggrin is associated with increased skin permeability and susceptibility to atopic dermatitis. It has been suggested that the atopic dermatitis is the result of the increased penetration of antigens through the epithelium.
The esophageal biopsy specimens of EoE patient are characterized by a Th2-type inflammatory process, with increased numbers of eosinophils, mast cells and lymphocytes. The interplay between these cells remains largely unknown.
We hypothesize that in EoE a similar process of impaired epithelial barrier function plays an important role. The impaired epithelial barrier could result in a penetration of food antigens and subsequent uptake by epithelial cells followed by activation of an inflammatory Th2 response. In gastro-oesophageal reflux disease an impaired epithelial barrier function has been linked to hypersensitivity to acid, and hence, this could explain the observed hypersensitivity to acid in patients with eosinophilic oesophagitis as well.

Study objective

To show that in eosinophilic oesophagitis gastro-oesophageal reflux-induced epithelial barrier dysfunction facilitates passage of food-antigens through the epithelial barrier and subsequent increased exposure of antigens by dendritic cells activates the Th2 immune response (increased numbers of eosinophils and mast cells). Epithelial barrier dysfunction is defined as affected oesophageal tissue impedance, dilated intercellular spaces and increased oesophageal

mucosal permeability.
Furthermore, we wish to widely investigate the composition of inflammatory cells present in the esophageal biopsies of EoE patients and characterize them.

Study design

Prospective observational non-randomised study. 2 groups: EoE patients and healthy subjects.

Study burden and risks

For this study patienten with EoE will receive once a pH-impedance measurement en twice a gastroscopy (with biopsy taking). The risks consist of a bleeding or perforation due to biopsy taking. These complications need to be treated immediately, endoscopically or even surgically. The risk for these complications, however, is small.
Preceding these interventions participating patients will be asked to stop the use of topical corticosteroids. Participating patients will refrain from use of topical corticosteroids for approximately 3 months.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Previous diagnosis of eosinophilic oesophagitis confirmed by histopathology e.g. presence of >15 eosinophilic granulocytes per high power field in mid-oesophageal biopsies before the start of any therapy
2. Written informed consent
3. Age 18 * 75 years

Exclusion criteria

1. Inability to stop topical corticosteroids
2. Inability to stop PPI, H2-receptor antagonist or prokinetic drug for 8 weeks
3. Use of systemic corticosteroids, leukotriene inhibitors, or monoclonal antibodies, in the 2 month period preceding the study
4. Use of oral anticoagulants
5. Use of NSAIDs
6. History of peptic ulcer disease
7. History of Barrett*s oesophagus
8. History of GI cancer
9. History of GI tract surgery (except appendectomy)

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):	02-09-2011
Enrollment:	22
Type:	Actual

Ethics review

Approved WMO Date:	19-07-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-01-2012
Application type:	Amendment
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

ID: 28827
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL36704.018.11
OMON	NL-OMON28827