Local Responses to Food Allergens in Eosinophilic Esophagitis: Mechanisms and Clinical Application

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1. To investigate different modes of allergen administration to the esophageal wall, by testing the effect on visible mucosal changes2. To investigate which immune cells become activated after allergen provocation 3. To investigate whether the...

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

Summary

ID

NL-OMON49025

Source
ToetsingOnline

Brief title
LOIRE-trial

Condition

- Gastrointestinal inflammatory conditions
- Allergic conditions

Synonym
allergic esophagitis, Eosinophilic esophagitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: allergen provocation tests, Eosinophilic esophagitis, high resolution manometry, pathophysiological study

Outcome measures

Primary outcome

Visible response to allergen provocation in the esophagus, defined as early

phase response

Secondary outcome

1. Immune response after allergen injection and flush of allergens, defined as

activated immune cells observed in biopsies

2. Immune response to added allergens of esophageal mucosal cells in culture

medium, defined as release of cytokines

3. Esophageal motility changes after allergen exposure

Study description

Background summary

Eosinophilic esophagitis (EoE) is an inflammatory disease of the esophagus that leads to progressive narrowing of the lumen and symptoms of dysphagia and food impaction. There is a huge increase of EoE prevalence in the last 10 years and for many patients an acceptable treatment is lacking. Food allergy plays an important role in eosinophilic esophagitis, but it is unclear which mechanisms are responsible for this local food-induced immune response in individual patients. We recently developed an innovative esophageal allergen injection method, that provides us with the opportunity to investigate the acute immune response after allergen provocation and may allow identification of local sensitization in individual patients.

Study objective

1. To investigate different modes of allergen administration to the esophageal wall, by testing the effect on visible mucosal changes

2. To investigate which immune cells become activated after allergen provocation
3. To investigate whether the abnormal response to causative allergens can be simulated in vitro.
4. To investigate the esophageal motility changes induced by allergen provocation.

Study design

Pathophysiologcial study

Intervention

EoE patients will undergo two gastroscopies with allergen provocation tests. In one gastroscopy patients undergo esophageal allergen injections as described in our pilot study (NL54305.018.15 / METC 2015_195) and in the other gastroscopy the esophagus is flushed with 50-100 ml of fresh allergens. The order of the two gastroscopies is randomized. The acute response to allergen provocation will be registered up to 20 minutes after allergen provocation. Before the allergen provocation, biopsies from esophageal mucosa are taken for in vitro allergen provocation and for immune profiling of baseline conditions. After provocation, biopsies are taken from sites with visible response to allergen exposure and from sites where no response was seen after exposure to allergens. Six weeks after the second gastroscopy patients will undergo a High Resolution Manometry during which allergen provocation is performed by drinking a mixture of allergens that induced a visible response during the earlier gastroscopies. In addition, patients undergo a skin prick test and a vena puncture for serum IgE testing at the start of the study. For the validation of the in vitro allergen provocation method biopsies are taken from patients that undergo a gastroscopy for other indications than esophageal complaints. These biopsies will be used in the in vitro allergen provocation experiments.

Study burden and risks

The risk of the performed procedures consists of the risk of the gastroscopies with allergen provocation and the High Resolution Manometry. The risks of gastroscopies and manometry, such as bleeding and perforation, are very rare and can be treated expectatively or endoscopically. Anaphylactic reactions to allergen provocation are very rare in EoE, however any patient with a history of such reactions will be excluded from participation and these reactions also were not seen in our pilot study. Nonetheless, medications for management of acute anaphylactic will be present during and after endoscopy. The study will evaluate the effect of a local allergen provocation and lead to new insights into pathophysiology. This could eventually contribute to a new diagnostic approach and might serve as guidance for dietary therapy in eosinophilic

esophagitis.

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

Eosinophilic esophagitis patients
- Previous diagnosis of active EoE confirmed by histopathology e.g. presence of > 15 eosinophilic granulocytes per high power field (hpf) in mid or proximal esophageal biopsies
- Written informed consent
- Age 18-75 years

Non- eosinophilic esophagitis patients
- Patients that undergo a gastroscopy for other indications than esophageal

complaints
- Written informed consent
- Age 18 * 75 years

Exclusion criteria

Eosinophilic esophagitis patients
- Inability to stop topical corticosteroids
- Inability to stop beta-blockers and ACE inhibitors
- Use of oral or systemic antihistaminics, oral cromoglicates, systemic corticosteroids, leukotriene inhibitors, or monoclonal antibodies, in the month preceding the study
- Proven gastroesophageal reflux disease or other cause for esophageal eosinophilia
- History of peptic ulcer disease
- History of Barrett*s esophagus
- History of GI cancer
- ASA class III, IV or V
- History of anaphylaxis
- History of a severe systemic reaction to previous allergy tests (grade 3 or 4)

Non- eosinophilic esophagitis patients
- Symptoms of esophageal dysfunction
- History of esophageal diseases

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	14-08-2019
Enrollment:	18
Type:	Actual

Ethics review

Approved WMO Date:	24-05-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-06-2020
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

No registrations found.

In other registers

Register	ID
CCMO	NL68871.018.19