Gastroscopic Esophageal Prick Test in adult Eosinophilic Esophagitis Patients: a pilot study

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26684

Source
Nationaal Trial Register

Brief title
“EPT-trial”

Health condition

Eosinophilic Esophagitis, allergy, sensitizations, clinical trial, pilot study, dietary treatment

Eosinophiele oesofagitis, allergie, sensibilisatie, klinische studie, pilot studie, dieetbehandeling

Sponsors and support

Primary sponsor: Investigator inintiated study, Academic Medical Center Amsterdam
Source(s) of monetary or material Support: This trial is partly funded by a Gastrostart grand

Intervention

Outcome measures

Primary outcome

The primary outcome parameters of our study are: (1) visible mucosal changes within 20 minutes after esophageal allergen injections, the acute response, and (2) visible mucosal changes after 24 hours, the delayed response.

Secondary outcome

Secondly, we will compare the local sensitization patterns identified through EPT with those identified through SPT and serum allergen specific IgE testing. Finally, we will evaluate whether the allergens that tested positive on EPT were in agreement with the reported implicating foods in patients' history.

Study description

Background summary

Background: Skin and serum IgE tests perform poorly as tools to guide elimination diets in eosinophilic esophagitis (EoE). We hypothesize that a test detecting local esophageal sensitization will have better clinical relevance in EoE.
Aim: To investigate the feasibility of testing sensitizations on esophageal tissue by local allergen challenge; the Esophageal Prick Test (EPT).
Methods: In this prospective pilot study we included adult EoE patients and controls. Specific serum IgE and skin prick tests (SPT) were performed for the same allergens as the EPT. During gastroscopy 0.2 mL of 6 diluted allergen extracts (wheat, milk, soy and 3 allergens based on history), a negative control (0.9% NaCl) and a positive control (diluted histamine) were injected at different sites in the esophagus, using a through the scope injection needle. Local reactions were recorded up to 20 minutes and videos were saved. A second gastroscopy was performed after 24 hours to evaluate delayed responses.
Results: We included 8 EoE patients, age 49 (22 – 54) years, of whom 6 (75%) had an atopic background and 3 healthy controls, age 22 (19 – 23) years, of whom 1 (33%) had an atopic background. Skin and serum test were positive for 24 allergens in 6 patients and negative in all controls. No systemic anaphylactic reactions occurred in response to the EPT, but 4/8 patients experienced chest pain after allergen injection. In 5/8 patients an acute response (< 2 min) consisting of complete luminal obstruction and blanching of the mucosa was observed after esophageal injection (soy, banana, apple, oats, hazelnut). During the next endoscopy the obstruction was dissolved. In two other patients an erythematous wheal was visible at the injection site (peach and walnut). The EPT was negative in controls.
Conclusion: This study shows that an allergy test based on esophageal tissue is safe, feasible and may have additional value above conventional allergy tests based on serum and skin. Both acute and delayed responses were observed. The allergens that triggered an acute response on EPT were in agreement with the reported implicating foods but different from those that triggered a delayed response. The EPT deserves further exploration as it can potentially guide elimination diets.

Study objective

The pathophysiology of EoE appears to partly align with other atopic diseases such as asthma and allergic rhinitis. A similar local allergic immune activation occurs in patients with allergic rhinitis. Nasal provocation with house dust mite showed specific locally produced IgE in the nasal secretion, whereas cutaneous and serum IgE testing to the same allergen showed no sensitization. Provocation tests have not only been developed for allergic rhinitis, but also for atopic dermatitis, bronchial asthma and allergic conjunctivitis. For gastrointestinal food allergy a colonoscopic allergen provocation test (COLAP) showed that the injected allergens induced wheal and flare reactions in the cecum and intestinal eosinophil activation. These positive test results correlated with symptoms experienced after ingestion of the same foods whereas results of standard allergy test were not predictive.
We thus hypothesize that the allergic sensitizations relevant to EoE are a local phenomenon different from the systemic allergic sensitization and therefore only tests based on detection of local inflammation can reveal clinically relevant sensitization patterns, on which eventually elimination diets can be based. Therefore we aim to further develop the EPT, an endoscopic test in which the esophageal mucosa is challenged with injected food allergens. This diagnostic approach has never been suggested this far and is entirely novel. This concept is in contrast with the way of thinking in the EoE field where the idea is to improve sensitivity of tests on serum and skin.

The Esophageal Prick Test as proposed in this grant proposal may thus become a very helpful diagnostic tool for assessment of sensitizations in EoE.

Study design

Consented patients will be pre-treated with an elemental or elimination diet in the six weeks preceding the EPT, because severe esophagitis could hamper interpretation of responses. The diet will be guided by a dietician with special expertise in EoE. During the trial patients are not allowed to use any immunosuppressive drugs. Before the initial endoscopy, serum will be collected for analysis of allergen specific IgE and SPTs will be performed for the same allergens as that will be tested with the EPT.
All subjects will undergo two endoscopies; during the first endoscopy allergens will be injected and acute responses will be recorded up to 20 minutes, after 24 hours a second endoscopy will be performed to evaluate delayed EPT responses.

Intervention

We will perform the EPT in adult EoE patients, previously diagnosed with EoE according to the American College of Gastroenterology (ACG) guidelines. In a washout period of at least two weeks prior two the EPT, patients will stop all drugs that can affect immune response such as topical corticosteroids and antihistamines. The allergens that will be used for the EPT are cow’s milk, wheat, soy and egg since these are the most prevalent allergens in EoE. In addition, two other allergens will be added based on patients’ history. Prior to the EPT, in all subjects serum IgE and skin prick testing will be performed for the same allergens. These tests are performed under the standard clinical routine protocol by an allergist with expertise in EoE. Outcomes of these tests will be compared with outcome of the EPT. In order to demonstrate that a response to injected allergens is exclusively found in EoE patients, the

EPT will also be performed in 4 healthy controls.

During gastroscopy, 0.2 ml of 6 diluted allergen extracts, a negative control (0,9% NaCl) and a positive control (diluted histamine) will be injected in the esophageal mucosa using an endoscopically advanced sclerotherapy needle. The injections are done in a pre-specified order at different levels of the esophagus, which guarantees enough space between injections to allow separate readings to different solutions. The mucosal wheal and flare reaction will be classified 20 minutes after injection and scored subsequently by an independent, blinded observer, using pictures and videos taken during the gastroscopy after 20 minutes. It is scored if acute contractions and acute edema occur at the level of the injection of one or more allergens. A second gastroscopy is performed 24 hours later in order to see whether delayed responses to the injected allergens occur. A grading of 0-4 is used for evaluation, where 0 indicates no reaction; 1 questionable reaction, 2 moderate reaction (<1 cm), 3 strong reaction (between 1-2 cm) and 4 very strong reaction (< 2 cm).

Contacts

Public
Research fellow
M. Warners
Department of Gastroenterology and Hepatology Academic Medical Center, room C2-321 Meibergdreef 9
Amsterdam 1105 AZ
The Netherlands
+ 31 (0)20 5665584
Scientific
Research fellow
M. Warners
Department of Gastroenterology and Hepatology Academic Medical Center, room C2-321 Meibergdreef 9
Amsterdam 1105 AZ
The Netherlands
+ 31 (0)20 5665584

Eligibility criteria

Inclusion criteria

- 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

- Macroscopic disease remission or with very mild macroscopic abnormalities after four weeks of treatment with an elemental or elimination diet

- Written informed consent

- Age 18 – 75 years

Exclusion criteria

- 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

- History of GI tract surgery (except appendectomy)

- ASA class III, IV or V

- History of anaphylaxis

- History of a severe systemic reaction to previous allergy tests (grade 3 or 4)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)

Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-01-2016
Enrollment:	12
Type:	Actual

Ethics review

Positive opinion

Date:	07-06-2017
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 42606
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL6197
NTR-old	NTR6361
CCMO	NL54305.018.15
OMON	NL-OMON42606

Study results

Summary results
Digestive disease week 2017 oral presentation