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

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To investigate the acute responses occuring in the esophageal mucosa of EoE patients after local allergen provocation

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29465

Bron
NTR

Verkorte titel
LOIRE-trial

Aandoening

Eosinophilic esophagitis

Ondersteuning

Primaire sponsor: Amsterdam UMC, Location AMC
Overige ondersteuning: NWO-TTW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: 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.

Objectives: 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: pathophysiological study

Study population: 12 EoE patients with active disease, aged 18-75 years

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.

Main study parameters/endpoints: 1. Visible response to allergen provocation in the esophagus, defined as early phase response 2. Immune response after allergen injection and flush of allergens, defined as activated immune cells observed in biopsies 3. Immune response to added allergens of esophageal mucosal cells in culture medium, defined as release of cytokines 4. Esophageal motility changes after allergen exposure

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: 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 expectative 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.

Doel van het onderzoek

To investigate the acute responses occuring in the esophageal mucosa of EoE patients after local allergen provocation

Onderzoeksopzet

24 months

Onderzoeksproduct en/of interventie

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. 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.

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	29-05-2019
Aantal proefpersonen:	12
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Toelichting
Anonymized individual primary and secondary outcome measures will be published.

Ethische beoordeling

Positief advies

Datum:	04-06-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7781
Ander register	METC AMC : METC 2019_049

Resultaten

Samenvatting resultaten
N/A