Symptom perception in patients with functional dyspepsia: involvement of the TRPV-1 neuropeptide pathway

Published: 22-04-2015
Last updated: 21-04-2024

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

Summary

ID

NL-OMON55610

Source
ToetsingOnline

Brief title
Functional dyspepsia and symptom perception

Condition

- Gastrointestinal conditions NEC

Synonym
Functional dyspepsia, functional stomach complaints

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Functional dyspepsia, Healthy volunteers, Symptom perception, TRPV-1 neuropeptide pathway

Outcome measures

Primary outcome

The primary objective of the present study is to assess the involvement of the duodenal TRPV-1 neuropeptide pathway in symptom perception in FD patients compared to healthy controls.

Secondary outcome

Symptoms:

- To assess whether there are differences in gastrointestinal symptoms, psychological symptoms and quality of life between FD patients and healthy controls by using retrospective questionnaires.

- To evaluate the number of FD patients with comorbid diagnosis of IBS.

Gastric and duodenal tissue:

- To assess the difference in transcription of genes encoding for proteins involved in intestinal barrier function (e.g. tight junction proteins) and symptom perception (e.g. TRPV-1), as well as protein expression of these proteins in both stomach and duodenum between FD patients and healthy controls.

- To compare serotonin metabolism in mucosal tissue (e.g. 5-HT, 5-HIAA) between FD patients and healthy controls.

Predominant symptoms

- To assess whether there are differences in parameters involved in the TRPV-1 neuropeptide pathway (e.g. TRPV-1 mRNA transcription, neuropeptide concentrations) between (1) patients with predominant pain symptoms and (2) patients with predominant symptoms of epigastric fullness and bloating.

Study description

Background summary

Functional dyspepsia is a common gastrointestinal disorder with a negative impact on daily functioning and quality of life. The pathophysiology of FD remains largely unknown, although a multifactorial pathophysiology is suggested. Previous investigations found evidence for both mechanical and chemical visceral hypersensitivity in FD patients compared to healthy controls. Patients with FD demonstrate chemical hypersensitivity to capsaicin ingestion compared to healthy controls. Capsaicin is a chemical agonist of TRPV-1 receptors which are present on afferent sensory nerves in the gastrointestinal mucosa. Activation of TRPV-1 sensitive neurons leads to release of neuropeptides including substance P and somatostatin. It is suggested that activation of this TRPV-1 neuropeptide pathway is involved in symptom perception in FD patients. Moreover, several publications found evidence for involvement of the duodenum in the pathophysiology of functional dyspepsia with an impaired duodenal permeability in FD patients compared to healthy controls. The primary focus of the present study is the duodenal TRPV-1 neuropeptide pathway. However, serotonin is another important neurotransmitter involved in local processes in the gastrointestinal tract (e.g. secretion, motility) as well as in pain perception. Up till now, studies evaluating serotonin metabolism in FD patients are limited with one study describing a decreased plasma serotonin level in FD patients compared to healthy controls. Information about serotonin metabolism in gastrointestinal mucosa is lacking.

Study objective

The primary objective of the present study is to assess the involvement of the duodenal TRPV-1 neuropeptide pathway in symptom perception in FD patients compared to healthy controls. The present study has several secondary objectives with regard to intestinal permeability and serotonin metabolism.

Study design

The study design conforms to a case-control study with inclusion of both FD

patients and healthy controls. All participants will undergo an upper gastrointestinal endoscopy with biopsy taking from stomach and duodenum. Symptoms will be assessed using retrospective questionnaires.

Study burden and risks

Healthy controls and FD patients will undergo an upper gastrointestinal endoscopy with multiple biopsy taking from stomach and duodenum. Endoscopy will be performed by experienced gastroenterologists and this is a standard diagnostic procedure that takes about 20 minutes. A diagnostic endoscopy is a safe procedure and one large investigation in the USA described an overall complication rate of 0.13% and associated mortality of 0.004%. The most important complications are perforations and significant hemorrhages, which, however are rarely seen (0.0009% and 0.002%, respectively). A recent publication evaluated the safety of multiple biopsy taking during endoscopic procedures (with a mean of 35 biopsies per procedure) for research purposes and they found no association between the number of biopsies taken and the occurrence of complications. After endoscopy, side effects are not often reported. Participants can complain about a sore throat or bloated feeling, which usually disappear short after the endoscopy. FD patients participating in the present study have all a medical indication for upper endoscopy and they receive this investigation as part of regular patient care. For study purposes, (additional) biopsies will be taken.

Assessment of symptoms with retrospective questionnaires is safe and no problems are expected.

In case of unexpected findings during endoscopy of healthy controls, these will be reported to the participant and to his/her general practitioner. As FD patients will undergo endoscopy as part of regular care to exclude organic diseases, the referring physician (general practitioner and/or specialist) will be informed about the findings during endoscopy.

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

Healthy controls <= No gastrointestinal symptoms or history of gastrointestinal disease, especially not meeting criteria for functional dyspepsia and IBS (according to the ROME III criteria), Functional dyspepsia patients <= Patients referred for upper gastrointestinal endoscopy by either general practitioners or doctors from the gastroenterology outpatient clinic, meeting ROME III criteria for functional dyspepsia

Exclusion criteria

Healthy volunteers and functional dyspepsia patients:
1. Inability to stop the intake of NSAIDs within 14 days prior to endoscopy.
2. Inability to stop the intake of medication affecting gastrointestinal function (e.g. proton pump inhibitors, prokinetics, laxatives) within 5 days prior to endoscopy
3. Current use of antidepressants
4. Medical history of diabetes mellitus
5. Medical history of coeliac disease
6. Organic disease at upper gastrointestinal endoscopy (i.e. erosive esophagitis, Barrett*s esophagus, benign esophageal stricture, Schatzki ring, esophageal carcinoma, esophageal candidiasis, gastric ulcer, gastric erosions, gastric cancer, duodenal erosions or duodenal ulcer).
7. First-degree family members with diabetes mellitus type I, coeliac disease, Crohn*s disease or ulcerative colitis

8. Medical history of food allergy or anamnestic evidence of food allergy
9. Presence of coagulation disorders or use of anticoagulants
10. Dieting
11. Pregnancy or lactation
12. Smoking
13. Excessive alcohol use (>20 alcoholic consumptions/week) and inability to avoid use of alcohol in the 2 days prior to endoscopy

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-08-2015
Enrollment:	70
Type:	Actual

Ethics review

Approved WMO Date:	22-04-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-05-2017
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL51112.068.14