"The role of fat in symptom generation in patients with functional dyspepsia"

Published: 13-05-2008
Last updated: 07-05-2024

Gain insight into the mechanism underlying enhanced mechanoperception of the stomach and duodenal chemoperception in response to fat in patients with functional dyspepsia.

Ethical review	Not approved
Status	Will not start
Health condition type	Gastrointestinal conditions NEC
Study type	Observational invasive

Summary

ID

NL-OMON32048

Source
ToetsingOnline

Brief title
"Fat and dyspeptic symptoms"

Condition

- Gastrointestinal conditions NEC

Synonym
indigestion, upper abdominal complaints

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Astra Zeneca

Intervention

Keyword: Functional dyspepsia, Vet, Visceral hypersensitivity

Outcome measures

Primary outcome

Differences in mRNA expression between FD patients and healthy volunteers of at least a factor 1.5.

Secondary outcome

Significantly different apoA-IV concentrations in plasma and/or mucosal biopsies of FD patients and healthy volunteers.

Significantly different CCK concentrations in plasma and/or mucosal biopsies of FD patients and healthy volunteers.

Correlation mRNA expression, apoA-IV and/or CCK concentration with sensitivity to gastric distension and/or gastric emptying rate.

Study description

Background summary

Functional dyspepsia (FD) is a common condition, with an estimated prevalence of 12% to 15% in developed countries. FD is characterized by chronic or recurrent upper abdominal symptoms in the absence of organic, systemic, or metabolic disease likely to explain these symptoms. Dyspeptic symptoms are frequently induced or exacerbated by food ingestion.
In FD there is only a weak correlation between symptoms and upper gastrointestinal motor abnormalities. More recently, visceral hypersensitivity to mechanical and nutrient stimuli has been recognized as important in the etiology of dyspeptic symptoms. A subgroup of FD patients have lower thresholds for first perception and for discomfort or pain during distension of the proximal stomach when compared with healthy volunteers. Furthermore, intraduodenal infusion of lipid induces greater symptoms in FD patients than in healthy subjects and exacerbates symptoms induced by concurrent gastric distension. These findings show that gastric hypersensitivity to mechanical stimuli and increased small intestinal chemosensitivity to lipid contribute to symptoms in FD emerged.
The effect of duodenal lipid on the generation of dyspeptic symptoms and the perception of gastric distension is mediated by cholecystokinin (CCK)-1

receptors. For inhibition of gastric emptying, another CCK1-mediated effect of duodenal lipid, it has been demonstrated that apolipoprotein A-IV (apoA-IV) is an essential component of the signal transduction pathway involved. ApoA-IV is a component of chylomicrons and is released from enterocytes during lipid absorption. It has been hypothesized that apoA-IV stimulates adjacent endocrine cells to release CCK, which can activate CCK1 receptors on the peripheral terminals of duodenal extrinsic primary afferents. This signal transduction route may also be involved in the CCK1-mediated generation of dyspeptic symptoms during gastric distension upon duodenal lipid load, i.e. postprandial symptoms.
Perception of esophageal stimuli is also enhanced by duodenal lipid. Recently we found that genes implicated in lipid absorption are expressed at higher levels in gastro-esofageal-reflux disease (GERD) patients. This suggests that in GERD patients the chylomicron-apoA-IV-CCK pathway generates more signals, which may induce central sensitisation and thereby heighten the perception of esophageal stimuli. As central sensitisation as a consequence of enhanced stimulation of duodenal extrinsic primary afferents likely heightens the perception of esophageal stimuli in GERD patients, in patients with functional dyspepsia gastric mechanoperception may be enhanced in this way. Furthermore, enhanced stimulation of duodenal extrinsic primary afferents by increased release of CCK may underlie small intestinal chemosensitivity to lipid. Thus the differences in gene expression identified may constitute the mechanism by which fat contributes to symptom generation in FD.
FD is a heterogeneous disorder and it is unknown whether this putative mechanism underlying small intestinal chemosensitivity to lipid correlates with increased mechanosensitivity to gastric distension and/or delayed gastric emptying.

Study objective

Gain insight into the mechanism underlying enhanced mechanoperception of the stomach and duodenal chemoperception in response to fat in patients with functional dyspepsia.

Study design

In view of comparing components of the chylomicron-apoA-IV-CCK pathway between FD patients and healthy subjects, intraduodenal lipid infusion followed by upper GI endoscopy will be performed. A venous cannula will be inserted in the arm for repeated sampling of blood in which ApoA-IV and CCK concentrations will be measured. A manometric catheter will be introduced through the nostril. Lipid will be infused through this catheter into the duodenum. During infusion, patients will score upper abdominal sensations every 15 minutes. After removal of the catheter an upper GI endoscopy will be performed and several biopsies of the duodenum will be collected, which will be used for mRNA expression analysis and apoA-IV and CCK quantification.

To assess the correlation of chylomicron-apoA-IV-CCK pathway components with sensitivity to gastric distension, a gastric barostat test will be conducted. A tube with an adherent small plastic bag will be introduced through the mouth. The plastic bag will be inflated stepwise. During the distension protocol patients will be asked to score upper abdominal sensations.
Determination of gastric emptying rate by 13C octanoic breath test is part of the standard workup of FD patients presenting at our department.
Intraduodenal lipid infusion followed by upper GI endoscopy and the gastric barostat test will be carried out in random order.

Study burden and risks

All participants will be asked to complete two questionnaires prior to the study. During the intraduodenal lipid infusion patients will score upper abdominal sensations every 15 minutes. Also 5 ml blood will be collected 6 times. In general a GI endoscopy is a safe procedure. The occurrence of relative uncommon complications does not increase by taking duodenal biopsies. During the barostat study patients will be asked to complete a questionnaire after each distension step. The barostat study is a safe procedure. In the extremely rare occasion that the balloon comes off the catheter, an endoscopy will have to be performed to remove the balloon from the stomach.
Patients will be asked to discontinue any medication likely to affect gastric-duodeno motility and sensitivity one week prior to both study days.

Contacts

Public
Universitair Medisch Centrum Utrecht

Postbus 85500
3508 GA
Nederland
Scientific
Universitair Medisch Centrum Utrecht

Postbus 85500
3508 GA
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

18-65 years old
Recurrent bothersome postprandial fullness, early satiation and/or epigastric pain
At least 2 days per week for 3 months or more

Exclusion criteria

Esophagitis
Barrett's esophagus
Peptic ulcer disease
Prior gastrointestinal surgery
Pregnancy
Drug- or alcohol abuse

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start

Enrollment:	30
Type:	Anticipated

Ethics review

Not approved

Date:	13-05-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL22433.041.08