Effect of amitriptyline in functional heartburn

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To assess the effect of amitriptyline on gastro-esophageal symptom severity and on esophageal sensitivity to acid perfusion and balloon distension in patients with documented functional heartburn.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal motility and defaecation conditions
Study type	Interventional

Summary

ID

NL-OMON38685

Source
ToetsingOnline

Brief title
amitriptyline and heartburn

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
functional heartburn, pyrosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: amitriptyline, heartburn, pyrosis, reflux

Outcome measures

Primary outcome

GERD symptom score improvement after an 8 week treatment with amitriptyline

(GERDQ questionnaire, RDQ questionnaire)

Secondary outcome

Esophageal sensitivy to acid perfusion (perfusion-related symptom score).

Time to symptoms during esophageal acid exposure and balloon distension

Symptom severity during esophageal acid exposure and balloon distension (visual

analog scale or VAS)

Psychological state and anxiety assessment (HADS and SF12 questionnaire)

Study description

Background summary

Treatment of gastroesophageal reflux disease (GERD) fails in a small proportion of patients. As GERD is one of the most prevalent chronic disorders in the western world, this small proportion of therapy-resistant patients encompasses a substantial part of the patient population.
Many of the patients presenting with typical reflux symptoms who do not respond to the current standard of care (i.e. proton pump inhibition), do not have gastro-esophageal reflux disease. Functional heartburn is an important differential diagnosis in this respect, and can be confirmed or excluded by performing a 24h pH/impedance recording: patients with functional heartburn do not have pathological acid reflux and the symptom-reflux association analysis is typically negative.
The management of functional heartburn is often challenging as evidence-based pharmacological options are not available. The use of visceral pain modulators such as tricyclic antidepressants is generally accepted, even though the clinical trials to support their use are likewise lacking.
Antidepressants are generally used in the treatment of pain-predominant

functional gastro-intestinal disorders such as functional dyspepsia and irritable bowel syndrome. Their use is defended by the assumption that antidepressants have central analgesic actions, and there is increasing evidence of central nervous system dysfunction in functional gut disorders. In addition, antidepressants could reduce the severity of psychological symptoms such as anxiety and depression. These are thought to exacerbate the symptoms in FGD, although this assumption is controversial and the antidepressant dose used for visceral analgesia is considered to be too low to have significant effects on the psychological state.

Study objective

To assess the effect of amitriptyline on gastro-esophageal symptom severity and on esophageal sensitivity to acid perfusion and balloon distension in patients with documented functional heartburn.

Study design

Double blind placebo controlled, randomized cross-over design

Intervention

treatment with placebo or amitriptyline 25-50 mg daily for 6 weeks in a crossover design, with an 8 week washout period in between

Study burden and risks

discomfort associated with the esophageal sensitivity test
side effects from the use of amitriptyline. The most common side effects are dry mouth, constipation, blurred vision, palpitations, weight gain, drowsiness, dizziness, tremors, headache, nausea, sweating, and low blood pressure.

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

* Minimum age: 18 years
* Documented functional heartburn
* Negative esophagogastroduodenoscopy and no history of reflux esophagitis
* Negative 24h pH/impedance recording (physiological acid exposure time) and negative symptom association probability

Exclusion criteria

* Surgery of the esophagus
* Motility disorders of the GI tract leading to delayed gastric emptying or altered intestinal motility
* Use of any medication with a potential effect on upper gastrointestinal motility and/or sensitivity that can not be stopped for the duration of the study. If this medication can be stopped, it should be discontinued for at least 2 weeks before the start of the study.
* Severe and clinically unstable concomitant disease (e.g. liver, cardiovascular or lung disease, neurological or psychiatric disorders, cancer or AIDS and other endocrine disorders)
* Pregnancy or lactation. A pregnancy test will be carried out prior to inclusion in the study. Female patients who are premenopausal and have a negative pregnancy test should be on an anticonceptive.;* Medication-related
* Contra-indications for amitriptyline use: epilepsy, organic central nervous system disorders, prostate hypertrophy, pyloric stenosis, cardiovascular disease, hyperthyroidism, liver- and kidney function impairment.
* Interaction can occur with barbiturates, carbamazepine, ketoconazol and ritonavir . Concommitant use of MAO-inhibitors is contra-indicated.

* Hypersensitivity to the active substance or to any of the excipients.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-01-2014
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	amitriptyline
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	30-08-2013
Application type:	First submission
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

ID: 20475
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-000099-13-NL
CCMO	NL43405.018.13
OMON	NL-OMON20475