Randomized controlled trial of escitalopram versus placebo for patients with irritable bowel syndrome and panic disorder.

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PRIMARY OBJECTIVE· 1. To study the effect of escitalopram versus placebo in the treatment of abdominal pain, in IBS patients with panic disorder.SECONDARY OBJECTIVES· 2.1. To assess the effect of escitalopram on gastrointestinal and psychiatric...

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

Summary

ID

NL-OMON43726

Source
ToetsingOnline

Brief title
Escitalopram trial.

Condition

- Gastrointestinal motility and defaecation conditions
- Anxiety disorders and symptoms

Synonym
IBS and anxiety disorder, Irritable bowel syndrome and panic disorder

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: Clinical trial., Escitalopram., Irritable bowel syndrome., Panic disorder.

Outcome measures

Primary outcome

Gastrointestinal Symptom Rating Scale (GSRS): Self-assessment questionnaire

for gastrointestinal symptoms.

Secondary outcome

A. OTHER MEANS OF ASSESMENT OF GASTROINTESTINAL AND PSYCHIATRIC SYMPTOMS.

·State Trait Anxiety Inventory (STAI)

.Hospital Anxiety and Depression Scale (HADS).

.Cognitive Scale for Functional Bowel Disorders (CS-FBD).

·Symptom diary.

·Experience Sampling Method (ESM).

B. QUALITY OF LIFE.

·Rand-36-item Healthy Survey (SF-36).

C .RECTAL BAROSTAT.

D. SUGAR PERMEABILITY TEST.

E. IMMUNE ACTIVATION AND INFLAMMATION.

·Circulating cytokines/chemokine profiles and faeces calprotectine.

F. NEURO-HORMONAL AND NEURO-TRANSMISSIONAL REGULATORY MECHANISMS.

·Corticotropin releasing factor (CRF) and adrenocorticotropic hormone (ACTH).

·Markers of the serotonergic system, such as serotonin (5-HT), 5-HIAA,

5-hydroxytryptophan and kynuramine.

·Activities of circulating enzymes involved in the breakdown of ATP, such as

adenosine deaminase and xanthine oxidase.

·Concentrations of ATP metabolites.

G. DNA FOR POLYMORPHISM ANALYSIS.

H. EPIGENETIC DIFFERENCES.

Study description

Background summary

More recently, patients that fail on standard IBS therapy are treated with antidepressants. In a recent meta-analysis of Ford et al. (1) thirteen randomized controlled trials were reviewed on antidepressants. Twelve trials compared antidepressants with placebo, and one compared both psychological therapy and antidepressants with placebo. The study quality was generally good. Ford et al. therefore concluded that antidepressants were effective in the treatment of IBS: the relative risk of IBS symptoms persisting with antidepressants versus placebo was 0.66 (95% CI, 0.57 to 0.78), with similar treatment effects for both tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRI*s). The number needed to treat was 4. We found no trials on the SSRI escitalopram. However, two of the trials in the meta-analysis of Ford et al. dealt with citalopram, an SSRI we use frequently in our clinical practice, and which is familiar to escitalopram: one trial (Tack et al., 2) found an improvement in IBS symptoms and the other (Talley et al., 3) did not. Overall, it should be taken into account that these trials included small numbers of patients, studied IBS patients with heterogeneous psychiatric diagnoses, treated patients with low dosages of SSRI, and did not treat initial side effects of the SSRIs, resulting in extensive dropout. We propose a larger, randomized controlled trial comparing the SSRI escitalopram with placebo not in a heterogenous, mixed IBS group but in IBS patients with associated panic disorder. In our population of the Medical Psychiatric Centre Maastricht a high proportion of IBS patients, approximately 40%, has a panic disorder as defined by DSM-IV. Besides selecting patients with the same psychiatric diagnosis, we use a study design with a higher dosage of SSRI, reflecting panic disorder treatment guidelines, and treat side effects of the SSRI with a low dosage of benzodiazepines in the first two weeks of treatment.

This restriction is necessary to get an impression what the maximum efficacy in the case of adequate treatment indication and treatment procedure will be. Until now, studies only have been proposed in very heterogeneous IBS populations and side effects have not been prevented adequately.

1.Ford AC, Talley NJ, Schoenfeld PS, et al. Efficacy of antidepressants and psychological therapies in irritable bowel syndrome: systematic review and meta-analysis.Gut 2009; 58: 367-78.
2.Tack J, Broekaert D, Fischler B, et al. A controlled crossover study of the selective serotonin reuptake inhibitor citalopram in irritable bowel syndrome. Gut 2006; 55: 1095-1103.
3.Talley NJ, Kellow JE, Boyce P, et al. Antidepressant therapy (imipramine and citalopram) for irritable bowel syndrome: a double-blind, randomized, placebo-controlled trial. Dig Dis Sci 2008; 53: 108-15.

Study objective

PRIMARY OBJECTIVE
· 1. To study the effect of escitalopram versus placebo in the treatment of abdominal pain, in IBS patients with panic disorder.

SECONDARY OBJECTIVES
· 2.1. To assess the effect of escitalopram on gastrointestinal and psychiatric symptoms as measured with State Trait Anxiety Inventory (STAI), Hospital Anxiety and Depression Scale (HADS), Cognitive Scale for Functional Bowel Disorders (CS-FBD), Symptom diary, and Experience Sampling Method (ESM), in IBS patients with panic disorder.
· 2.2. To assess the effect of escitalopram on quality of life, in IBS patients with panic disorder.
· 2.3. To assess the effect of escitalopram on visceral perception by the rectal barostat method, in IBS patients with panic disorder.
· 2.4. To assess the effect of escitalopram on intestinal permeability by the sugar permeability test, in IBS patients with panic disorder.
· 2.5. To assess the effect of escitalopram on immune status, neurohormones, purinergic signalling and (epi)genetic changes, in IBS patients with panic disorder.

Study design

This study will be executed according to a randomized double-blind placebo-controlled trial with two parallel groups, treated over the period of 6 months.

Intervention

Treatment with escitalopram or placebo.

Study burden and risks

No special risks involved: research involving normal patient care with only additional questionaires, symptom diary, blood and faeces sampling, ECG, rectal barostat and sugar permeability test.

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

1) IBS will be diagnosed according to the Rome III criteria1 *:Recurrent abdominal pain or discomfort at least 3 days per month in the last 3 months associated with 2 or more of the following:· Improvement with defecation.· Onset associated with a change in frequency of stool.· Onset associated with a change in form (appearance) of stool.*Criteria have to be

fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.*Discomfort means an uncomfortable sensation not described as pain. In pathophysiological research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation is an indication for subject*s eligibility.2) Subtyping of IBS patients will be performed using the following classification according to the Rome III criteria: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M) or unsubtyped IBS (IBS-U). 3) Based on the medical history and previous examination, no other causes for the abdominal complaints can be defined.4) A panic disorder will be diagnosed based on DSM IV criteria. 5) Age above 18 years and under 70 years.6) Given written informed consent.

Exclusion criteria

1) Inability to stop medication that can influence gastrointestinal motility or perception (like loperamide, butylscopolamine, duspatal, metoclopramide, domperidon, erytromycine), serotonin metabolism (like carbidopa, food supplementation), or epigenitics (like valproic acid), or containing Sint-Janskruid (Hypericum perforatum).2) Administration of investigational drugs in the 180 days prior to the study.3) Major abdominal surgery interfering with gastrointestinal function (uncomplicated appendectomy, cholecystectomy and hysterectomy allowed, and other surgery upon judgement of the principle investigator), epilepsy or (hypo)manic episodes.4) Pregnancy and lactation. 5) Excessive alcohol consumption (>20 alcoholic consumption per week) or drug abuse.6) Co-intervention or other treatment for IBS or anxiety, with the exception of initial co-intervention with benzodiazepines (alprazolam) contrasting side effects due to SSRIs during the first two weeks of administration or during the first two weeks of dose elevation. 7) Known prolongation of QT-interval or long-QT-syndrome, other cardiac disease, or use of medication with known prolongation of QT-interval.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-01-2012
Enrollment:	35
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lexapro
Generic name:	escitalopram
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Xanax
Generic name:	alprazolam
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	05-07-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	31-03-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	28-12-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

Approved WMO

Date:	12-01-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	05-12-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-12-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-07-2016
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
EudraCT	EUCTR2010-020906-14-NL
CCMO	NL32908.068.10

Study results

Date completed:	08-06-2016
Actual enrolment:	32