Peppermint oil for the treatment of Irritable Bowel Syndrome: optimizing therapeutic strategies using targeted delivery

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1. To assess the efficacy and safety profile of treatment of IBS symptoms with peppermint oil compared to placebo. Thereby superiority of peppermint oil can be scientifically supported, leading to increased recognition of this therapy in IBS.2. To...

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

Summary

ID

NL-OMON45856

Source
ToetsingOnline

Brief title
PERSUADE

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
abdominal pain, altered bowel habits

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: ZonMw,WillPharma

Intervention

Keyword: Abdominal Pain, Irritable Bowel Syndrome, Peppermint oil, Targeted Delivery

Outcome measures

Primary outcome

1. Abdominal pain response rate after 8 weeks of treatment.

a. A responder is defined as a patient who experiences at least a 30 percent decrease in the weekly average of worst daily abdominal pain (measured daily, on an 11 point NRS) compared to baseline weekly average in at least 50 percent of the weeks in which the treatment in given.

2. Degree of relief response rate after 8 weeks of treatment.

a. A responder is defined as a patient who experiences a weekly relief of 1 or 2 (on a 7 point NRS) in at least 50 percent of the weeks in which treatment is given.

Secondary outcome

Global symptom improvement, abdominal discomfort, bloating, regurgitation, nausea, urgency, abdominal cramps (as determined by symptom diary and Irritable Bowel Syndrome Symptom Severity Scale (IBS-SSS), average stool frequency and consistency (measured by the Bristol Stool Form Scale) at baseline and after treatment (number of complete spontaneous bowel movements (CSBMs) for IBS-C, more lumpy stools in case of IBS-D), cost-utility (as determined by calculations with EQ-5D, direct costs MCP, indirect costs PCQ and social tariff), quality of life (as determined by the EQ-5D and IBS-QoL), use of OTC

and rescue medication, number and severity of side effects, responder rates following discontinuation of treatment at 4 and 6 months, different thresholds for the responder analysis of abdominal pain (e.g. 40 and 50 percent improvement). Worst-case-analysis: imputing a non-response day for each day on which the electronic diary entry was missing (due to non-reporting of the patient).

Study description

Background summary

Peppermint oil has shown to be effective in the treatment of IBS symptoms in several meta-analyses. However, the level of evidence is moderate and peppermint oil remains relatively under-used in IBS. Therefore, we plan to conduct a multicenter randomized controlled trial to investigate the effects of an eight-week peppermint oil treatment in IBS patients according to current EMA/FDA guidelines. To improve efficacy and to reduce side effects, we aim to study the use of a new peppermint oil formulation, a colon-targeted-delivery capsule that will release the oil in the (ileo-) colonic region specifically.

Study objective

1. To assess the efficacy and safety profile of treatment of IBS symptoms with peppermint oil compared to placebo. Thereby superiority of peppermint oil can be scientifically supported, leading to increased recognition of this therapy in IBS.
2. To ascertain whether treatment of IBS symptoms with colon-targeted-delivery peppermint oil results in a greater reduction of IBS symptoms and reduction of side effects, compared to enteric-coated capsules delivering the oil in the small intestine.

Study design

a randomized, double blind, placebo-controlled clinical trial with three parallel study arms.

Intervention

group A will receive 8 weeks of daily treatment with enteric-coated peppermint

oil capsules (Tempocol®), group B will receive 8 weeks of daily treatment with colon-targeted-delivery peppermint oil capsules (Tempocol-ColoPulse®), group C will receive 8 weeks of daily treatment with placebo capsules.

Study burden and risks

Subjects may be confronted with certain inconveniences and minor risks. Study participants have to visit the hospital 4 times, including the first visit in which eligible subjects will be screened before participation. The screening will take up to 1 hour and will consist of a simple questionnaire, a general physical exam performed by the physician-investigator and a standard pregnancy test (in women of fertile age, <55 year only). If deemed suitable by the investigator, subjects will enter the run-in period. During this period, patients are asked to report their daily stool and symptom scores to an electronic diary. If after the run-in period, patients meet the in- and exclusion criteria, they will enter the treatment period. If randomized to peppermint oil treatment, the subject may feel relief of IBS symptoms. If randomized to placebo, the subject may experience minor burden due to not receiving treatment (although dietary and lifestyle advice continue). Side effects of peppermint oil include heartburn, esophageal reflux, a burning anal sensation and a headache. During the treatment period, daily symptom and stool scores have to be reported. Moreover, several questionnaires have to be competed at several time-points, taking several hours in total.

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. Age between 18 and 75 years;
2. Diagnosed with Irritable Bowel Syndrome according to the Rome IV criteria:
* Recurrent abdominal pain or discomfort, at least 1 days/week for the last 3 months;
* Symptom onset at least 6 months prior to diagnosis
* Associated with two or more of the following:
1. Pain related with defecation;
2. Pain associated with a change in frequency of stool;
3. Pain associated with a change in form (appearance/consistency) of stool;
3. Based on the medical history and previous examination, no other causes for the abdominal complaints can be defined. Especially no history of:
a. Inflammatory Bowel Disease;
b. Celiac Disease;
c. Thyroid dysfunction (if not well-regulated);
If alarm symptoms (including unexplained rectal blood loss or weight loss) are present, a colonoscopy has been performed and was negative for other causes.
4. Women in fertile age (<55 years old) must use contraception or be postmenopausal for at least two years.
5. Average worst abdominal pain score (on 11-point NRS) of > 3, during the two-week run-in period.

Exclusion criteria

1. Insufficient fluency of the Dutch language;
2. Any previous use (also incidental use) of peppermint oil capsules in the last 3 months prior to inclusion;
3. The inability to stop regular use of medication affecting the gastro-intestinal system (such as Non Steroidal Anti Inflammatory Drugs (NSAID), laxatives, prokinetics, opioids, smasmolytics and anti-diarrhoeal drugs);
a. The use of 1 antidepressant drug is allowed, providing dosing has been stable for > 6 weeks before enrollment;
b. The use of 1 proton pump inhibitors (PPI) is allowed, providing dosing has been stable > 6

weeks before enrollment;
4. Previous major abdominal surgery or radiotherapy interfering with gastrointestinal function:
a. Uncomplicated appendectomy, cholecystectomy and hysterectomy allowed unless within the past 6 months;
b. Other surgery upon judgment of the principle investigator;
5. History of liver disease, cholangitis, achlorhydria, gallstones or other diseases of the gallbladder/biliary system;
6. Pregnancy, lactation;
7. Using drugs of abuse;
8. Known allergic reaction to peppermint.

Study design

Design

Study phase:	3
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):	17-08-2016
Enrollment:	180
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tempocol®
Generic name:	Menthae piperithae aetheroleum/Pepermint Oil
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Tempocol-ColoPulse®
Generic name:	Menthae piperithae aetheroleum/Pepermint Oil

Ethics review

Approved WMO Date:	09-03-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-06-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-05-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-06-2017
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	EUCTR2015-005467-16-NL
ClinicalTrials.gov	NCT02716285
CCMO	NL56000.068.16

Study results

Date completed:	01-11-2018
Actual enrolment:	234