Fecal Transplantation in adolescents with refractory Irritable Bowel Syndrome

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

Summary

ID

NL-OMON47555

Source
ToetsingOnline

Brief title
Fecal transplantation in patients with IBS

Condition

- Gastrointestinal motility and defaecation conditions

Synonym
Irritable bowel syndrome; functional abdominal pain

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Stichting Kindermotiliteit;Emma Kinderziekenhuis;AMC

Intervention

Keyword: Adolescents, Efficacy, Fecal transplantation, Irritable bowel syndrome

Outcome measures

Primary outcome

The proportion of patients with > 50% reduction of their abdominal pain intensity and pain frequency at t=12 weeks after the first faecal transplantation, assessed by the pain component of the Irritable Bowel Syndrome Severity Scoring System (IBS-SSS) score.

Secondary outcome

- Intra-individual changes in faecal gut microbiota composition at baseline, 6 weeks, 12 weeks, 24 and 48 weeks after faecal transplantation
- Adverse events (AE)
- Decrease in IBS complaints, assessed by abdominal pain frequency and intensity, after 6 and 12 months
- Total IBS-SSS score
- Health related quality of life
- Depression and anxiety
- Absence of school or work, health care resources and costs
- Adequate relief
- Safety parameters
- To find patient and microbiota characteristics that predict a positive response to faecal microbiota transplantation.

Study description

Background summary

Irritable bowel syndrome (IBS) is a chronic disorder characterized by abdominal pain or discomfort associated with a change in stool form or frequency, in the absence of a biochemical or structural explanation for these symptoms. The prevalence of IBS in the general adult population is 9.8-12.8%, which is in accordance to the prevalence of IBS in children and adolescents (6.2%-11.9%). It is suggested that a peak prevalence exists at adolescence. The recently established Rome IV criteria are used as diagnostic criteria for IBS. Patients with IBS report a decreased quality of life, high work or school absence, and are more at risk than healthy controls of developing depressive and anxiety disorders. Consequently, the healthcare costs are substantial; annual costs of care for adults with IBS in the USA are estimated to be over $20 billion. Total annual costs per pediatric IBS patient in the Netherlands are estimated to be ¤2500.
Although the pathophysiology of IBS has not been fully elucidated, pathophysiological abnormal gastrointestinal motility, visceral hypersensitivity, altered brain-gut function, low-grade inflammation, psychosocial disturbance and intestinal microbiota characteristics have been proposed to contribute to the pathophysiology. Current treatment focuses on abnormal gastrointestinal motility, altered brain-gut function and psychosocial disturbances. However, a significant amount of IBS patients has remaining symptoms, despite these treatment regimens. These patients are considered to be therapy-resistant, also called refractory. Treatment focusing on other components of the underlying pathophysiology, such as the intestinal microbiota, might therefore lead to new therapeutic successes in this group of patients.
In this light, being able to modify the intestinal microbiota inrefractory IBS patients could have beneficial effects on symptoms. Fecal transplantation, a relatively new treatment regimen which enables modifying the microbiome, has been shown to be highly effective in treating Clostridium difficile infections and also yielded promising results in patients with other diseases such as diabetes. Thus, in this study protocol we will study the effect of allogenic fecal transplantation compared to autologous fecal transplantation on decrease of IBS symptoms and on intra-individual changes in fecal microbiota composition.

Study objective

In this study we would like to investigate whether fecal transplantation, administered through a nasoduodenal tube, from either allogenic or autologous donors, has beneficial efffects on IBS symptoms such as abdominal pain intensity and frequency, measured with the IBS-SSS score, and on changes in fecal gut microbiota composition. Parallel objectives are to administer the

safety of fecal microbiota transplantation, to assess the proportion of patients with > 50% reduction in pain intensity and pain frequency after 6 and 12 months, to measure total IBS-SSS score, quality of life, depression and anxiety, school or work absenteeism, adequate relief, safety parameters

Study design

This is a double-blind randomized placebo-controlled pilot study with a subsequent reversed translational part. This study (treatment) will be done at the AMC, nevertheless patients from other hospitals can be enrolled for the study too.

Patients will be randomized by a computerised random-number generator for concealment to the following 2 treatment arms:
1. Two allogeneic (healthy donor) faecal infusions at baseline and after 6 weeks.
2. Two autologous (own) faecal infusions at baseline and after 6 weeks.

Intervention

Fecal transplantation

Study burden and risks

There is a burden for patients in this study, i.e. two times placement of a nasoduodenal tube with the Cortrak magnetic device, bowel lavage with Klean-Prep and the administration on (donor) feces.
However, participants suffer from refractory IBS, which means that the current treatment options are insufficient in these patients. Participating in this study might well result in relieve of symptoms or maybe even clinical remission. Additionally, besides the personal benefit, subjects also contribute to the current knowledge in the field of functional abdominal disorders.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients:
• Age 16-21 years
• Non-smokers
• Ability to give informed consent
• Established irritable bowel syndrome diagnosis according to the Rome IV criteria for children or adults
• Average daily pain rate of at least 30mm on the pain component of the IBS-SSS
• Symptoms are present for >= 12 months
• The patient has received adequate explanation and reassurance for his/her symptoms
• Appropriate dietary interventions have occurred, including the normalisation of the insoluble fiber intake and a decrease in gas producing foods
• Absence of response to a minimum of six sessions of psychological treatment (i.e. cognitive behavorial therapy and/or hypnotherapy)
• Absence of response to an adequate dose of at least one IBS specific pharmacological agent tried for a minimum of 6 weeks (like Mebeverine or peppermint oil capsules);Donors:
• Age >=16 years
• Non-smokers
• Ability to give informed consent
• BMI 18-25 kg/m2
• Regular stool pattern

Exclusion criteria

Patients:
• Current treatment by another health care professional for abdominal symptoms
• Known concomitant organic gastrointestinal disease
• Known diagnosis of inflammatory bowel disease (i.e. Crohn*s disease or ulcerative colitis)
• Known diagnosis of an autoimmune disease (e.g. hypo- or hyperthyroidism, celiac disease, rheumatoid arthritis)
• Known diagnosis of cystic fibrosis
• Known diagnosis of porphyria
• Anxiety or depression disorder
• Current use of drugs which influence gastrointestinal motility, such as erythromycin, azithromycin, butyl scopolamine, domperidone, peppermint oil capsules, and Iberogast
• Known pregnancy or current lactation
• Condition leading to profound immunosuppression
o For example: HIV, infectious diseases leading to immunosuppression, bone marrow malignancies
o Use of systematic chemotherapy
• Life expectancy < 12 months
• Use of concomitant medication, including proton pomp inhibitors (PPI), with the exception of pain medication
o Pain medication in the form of Paracetamol or NSAIDs is allowed
• Use of systemic antibiotics in preceding 6 weeks
• Use of probiotic treatment in preceding 6 weeks
• Positive stool culture for Helicobacter pylori
• Positive Dual Faeces Test for Giardia lamblia, Dientamoeba fragilis, Entamoeba histolytica
• XTC, amphetamine or cocaine abuse
• History of surgery:
o Hemicolectomy (defined as: surgery resulting in a resection of > 0.5 of the colon)
o Presence of a pouch due to surgery
o Presence of stoma
• Known intra-abdominal fistula
• Vasopressive medication, ICU stay
• Signs of ileus, diminished passage
• Allergy to macrogol or substituents, e.g. peanuts, shellfish
• Insufficient knowledge of the Dutch language;Donors:
• Abnormal bowel motions, abdominal complaints or symptoms indicative of irritable bowel syndrome
• An extensive travel behaviour
• Unsafe sex practice (questionnaire)
• Use of any medication including PPI
• Antibiotic treatment in the past 12 weeks
• A positive history/clinical evidence for inflammatory bowel disease (Crohn*s disease or ulcerative colitis) or other gastrointestinal diseases, including chronic diarrhoea or chronic constipation
• A positive history/clinical evidence for autoimmune disease (type 1 diabetes, Hashimoto

hypothyroidism, Graves hyperthyroidism, rheumatoid arthritis, celiac disease) and/or patients receiving immunosuppressive medications
• History of or present malignant disease and/or patients who are receiving systemic anti-neoplastic agents
• Psychiatric disease (depression, schizophrenia, autism, Asperger*s syndrome)
• Chronic neurological/neurodegenerative disease (e.g. Parkinson*s disease, multiple sclerosis)
• Predisposing factors for potential transmittable diseases (e.g. regular sexual contact with prostitutes/promiscuity)
• Positive blood tests for the presence of: HIV, HTLV, lues, Strongyloides, amoebiasis
• Active hepatitis A, B-, C- or E-virus infection, acute infection with cytomegalovirus (CMV) or Epstein-Barr virus (EBV)
• Positive faecal tests for the presence of:
o Bacteria:
* Clostridium difficile, Helicobacter pylori
* Salmonella spp., Shigella spp., pathogenic Campylobacter spp., Yersinia enterocolitica, Aeromonas spp., Plesiomonas shigelloides
* Antibiotic resistant bacteria: Extended spectrum beta-lactamase (ESBL)-producing Enterobactereacceae, VRE (vancomycin resistant enterococ)
o Viruses (faecal PCR-test)
* Norovirus Type I and II, Astrovirus, Sapovirus, Adenovirus type 40/41, Rotavirus, Enterovirus, Adenovirus non-41/41
o Parasites:
* Giardia lamblia, Cryptosporidium spp., Entamoeba histolytica, Dientamoeba fragilis, Microsporidium spp., Blastocystis hominis only if microscopically many or very many blastocysts are seen, Isospora spp.
* More than 1 of the following non-pathogenic parasites:
• Entamoeba gingivalis, Entamoeba hartmanni, Entamoeba coli, Entamoeba polecki, Endolimax nana, Iodamoeba bütschlii, Entamoeba dispar, Entamoeba moshkovskii
• If a donor turns out positive for only 1 of the above mentioned non-pathogenic parasites, inclusion is acceptable
o Parasitic worm eggs, larvae, protozoan cysts and oocysts
• Chronic pain syndromes (e.g. fibromyalgia)
• Major relevant allergies (e.g. food allergy, multiple allergies)
• Recent (gastrointestinal) infection (within last 6 months)
• Tattoo or body piercing placement within last 6 months
• Risk of Creutzfeldt Jacob*s disease
• History of current use of IV drugs
• History of treatment with growth factors
• Untreated infection with: Treponematoses, TBC, Herpes virus

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-11-2017
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	26-10-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-03-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	09-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-05-2020
Application type:	Amendment
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

No registrations found.

In other registers

Register	ID
CCMO	NL48420.018.16