FAIS trial; Faecal transplantation in Adolescents with refractory Irritable bowel Syndrome

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26566

Source
NTR

Brief title
Faecal transplatation in patients with refractory IBS

Health condition

Refractory Irritable bowel Syndrome
Healthy volunteers
Adolescents
Fecal transplantation

Sponsors and support

Primary sponsor: Academic Medical Center, Amsterdam
Source(s) of monetary or material Support: Stichting Kindermotiliteit

Intervention

Outcome measures

Primary outcome

To investigate the effect of repetitive healthy donor faeces infusion (allogeneic) in comparison to infusions with own faeces (autologous) on decrease in IBS complaints, assessed with the pain component of the Irritable Bowel Syndrome Severity Scoring System (IBS-SSS) score

Secondary outcome

To investigate the effect of two healthy donor faeces infusion (allogeneic) in comparison to two infusions with own faeces (autologous) on:

1. Intra-individual changes in faecal gut microbiota composition

2. Safety of faecal microbiota transplantation in patients with irritable bowel syndrome

3. Decrease in IBS complaints, assessed by abdominal pain frequency and intensity, after 6 and 12 months

4. Total IBS-SSS score

5. Health-related quality of life (HRQOL)

6. Depression and anxiety scores

7. Adequate relief

8. Absence of school or work, use of health care resources and additional costs
9. Safety parameters

Study description

Background summary

Double-blind randomised placebo-controlled pilot study as well as a reversed translational part.

Study Population: Patients with refractory IBS, defined as a failure to improve after standard medical treatment, at least 6 sessions of a psychological therapy and absence of response to at least 1 pharmacological agent (aged 16-21 years, male/female, no concomitant medication, non-smoking), will be recruited by their (paediatric) gastroenterologist at the Academic Medical Centre (Amsterdam, the Netherlands) and patients from other hospitals will be enrolled. Donors: relatives or volunteers will serve as faeces donor, potential donors will be thoroughly screened.

Treatment: After bowel lavage with Klean-Prep, patients will be treated with faecal

transplantation at t=0 and t=6 weeks, processed for duodenal tube infusion. Faeces will be collected from a healthy donor (allogeneic) as well as the patient him/herself (autologous), in which their own faeces will be used as a placebo.

Outcome measures: The primary outcome is the proportion of patients with > 50% reduction of their abdominal pain intensity and pain frequency at t=12 weeks after the first faecal transplantation. Secondary outcomes are intra-individual changes in faecal gut microbiota composition. Moreover, additional outcome measures are the proportion of patients with > 50% reduction in pain intensity and pain frequency after 6 and 12 months, changes in quality of life, in depression/anxiety, in school absenteeism and in adequate relief. Furthermore, safety parameters are assessed.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: It seems plausible that patients have benefit from donor faeces of strictly selected healthy donors. Duodenal tube positioning with Cortrak magnetic device has a very small risk of complications. According to our experience in this center with human faecal transplantation in therapy resistant Clostridium difficile associated colitis as well as from the pilot trial studying the effects of faecal transplantation on ulcerative colitis no serious side effects were observed.

Sample size calculation: Since this is a pilot study a reliable sample size calculation is not feasible. It is recommended that pilot studies ideally recruit a total of approximately 30-50 participants. In accordance to this, a minimum of 15 patients per treatment group will be included. In addition, based on accumulated evidence with HITChip analysis, a sample size of 20 individuals per group is normally enough to detect relevant differences in the microbiota, especially with pair-wise comparison. Hence, a total sample size of N=30 seems adequate.

Patients are randomly assigned to allogeneic or autologous fecal transplantation at a 1:1 ratio, thus with 30 IBS patients, 15 healthy faecal donors are needed.

Study objective

Faecal transplantation from a healthy donor can restore the dysbiosis present in adolescents with refractory IBS, thereby inducing improvement of the IBS complaints.

Study design

At t=0, t=6, t=12 wks, and t=6 and t=12 months patients will visit the AMC for assessments.

At t=3 and t=16 patients will be followed by telephone.

Abdominal pain will be assessed at t=0, t=3, t=6, t=12 and t=16 wks, and 6 and 12 months.

Intra-individual changes in faecal microbiota composition will be assessed at t=6 and t=12 weeks and t=6 months.

Patients will be screened for AE’s at t=3, t=6, t=12 and t=16 weeks and at 6 and 12 months.

Intervention

Bowel lavage with Klean-Prep
Faecal transplantation by nasoduodenal tube infusion
Venapunction

Contacts

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Eligibility criteria

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

o Before inclusion, all patients undergo routine laboratory testing to exclude underlying

organic disorders:
complete blood cell count, C-reactive protein, celiac screening (anti-transglutaminase antibodies and IgA), and faecal calprotectin. The need for further diagnostic testing is left to the discretion of the treating physician.

• According to a recently published guideline by the Rome Foundation for the design of pharmacological clinical trials in adolescents, patients are required to have an average daily pain rate of at least 30mm on the pain component scale 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 fibre intake and a decrease in gas producing foods

• Absence of response to a minimum of six sessions of psychological treatment (i.e. cognitive behavioural 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 ≥18 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

• 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 cultures for Clostridium difficile, 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 known malignant disease and/or patients who are receiving systemic anti-neoplastic agents

• Known psychiatric disease (depression, schizophrenia, autism, Asperger’s syndrome)

• Known 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 or known exposure within recent 12 months, 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, 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

• Known 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 type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2017
Enrollment:	45
Type:	Anticipated

Ethics review

Positive opinion

Date:	22-02-2017
Application type:	First submission

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
NTR-new	NL6100
NTR-old	NTR6441
Other	METC : 2016_205

Study results