

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

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

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|-----------------------------|-----------------------|
| Ethische beoordeling | Positief advies |
| Status | Werving gestart |
| Type aandoening | - |
| Onderzoekstype | Interventie onderzoek |

Samenvatting

ID

NL-OMON26566

Bron

NTR

Verkorte titel

Faecal transplatation in patients with refractory IBS

Aandoening

Refractory Irritable bowel Syndrome

Healthy volunteers

Adolescents

Fecal transplantation

Ondersteuning

Primaire sponsor: Academic Medical Center, Amsterdam

Overige ondersteuning: Stichting Kindermotiliteit

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

Bowel lavage with Klean-Prep

Faecal transplantation by nasoduodenal tube infusion

Venapunction

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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 pump 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 Enterobacteriaceae, 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

Onderzoeksopzet

Opzet

| | |
|------------------|-----------------------|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Dubbelblind |
| Controle: | Placebo |

Deelname

Nederland
Status: Werving gestart
(Verwachte) startdatum: 01-03-2017
Aantal proefpersonen: 45
Type: Verwachte startdatum

Ethische beoordeling

Positief advies
Datum: 22-02-2017
Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

| Register | ID |
|----------------|-----------------|
| NTR-new | NL6100 |
| NTR-old | NTR6441 |
| Ander register | METC : 2016_205 |

Resultaten