PLEASE NOTE: This trial has been registered retrospectively.

**Trial Description**

**Title**
Fecal microbiota transplantation in irritable bowel syndrome: a double blind, placebo controlled trial.

**Trial Acronym**
/

**URL of the trial**
http:///

**Brief Summary in Lay Language**

Irritable bowel syndrome (IBS) is a functional disorder of the gastrointestinal tract, which is determined by chronic recurrent abdominal pain with irregular bowel movements. Depending on the stool behavior IBS is divided into 3 subgroups: diarrhea-dominant irritable bowel syndrome (IBS-D), constipation-dominant irritable bowel syndrome (IBS-C) and IBS with alternating stool passage (IBS- U = unsubtyped). The causes of this disorder, which concerns up to 20% of the population, are to some extend psychogenic, however, the composition of the individual intestinal bacteria (= intestinal microbiome) of patients seems to play a central role. IBS often occurs after infections, surgery, but also after antibiotic therapies.

Stool transplantation (also known as fecal microbiota transplantation, FMT) is a method to treat an altered intestinal microbiome, also called dysbiosis, by transplanting stool of a healthy person in the gut of a patient. Donor stool will be prepared in the laboratory and applied via a probe or colonoscopy to the gut. FMT has up to now only been established for antibiotic associated bacterial infections of the colon.

The aim of this work is to evaluate the clinical benefit of FMT on the symptoms of the IBS.

36 patients with IBS-D and 36 patients with IBS-O will receive a total of 3 FMTs in 14-day intervals via colonoscopy after antibiotic pretreatment. Since this is a double-blind randomized controlled trial, half of the patients will receive their own stool (autologous stool), the other half receives stool of a healthy donor (= allogeneic stool).

The allocation is made randomly through a computer system, wherein neither the patient nor the medical team is informed of the allocation (= double-blind).

To assess the effects on the symptoms and the changes of the intestinal microbiome during the observation period of 90 days, patients will answer a questionnaires, blood-, stool-, urine-, saliva- and mucosal samples from the rectum will be collected and breath tests carried out during overall 5 visits.

**Brief Summary in Scientific Language**
Irritable bowel syndrome (IBS) is a functional disorder of the gastrointestinal (GI) tract. IBS is diagnosed according to the Rome III criteria. Depending on stool passage (diarrhea, constipation or alternating stool passage) 3 subgroups of equal frequency can be distinguished: IBS-D (diarrhea) IBS-C (constipation) and IBS-U (unsubtyped).

IBS is triggered by psychogenic factors, can occur in 10-20% after intestinal infections, especially after infections with Campylobacter jejuni, but also after surgery. Food intolerances, especially of FODMAPs (fermentable oligo-, di- and monosaccharides and Polypeptide) are often associated with IBS. Catecholamines released in stressful situations are known to affect also abundance and pathogenicity of gram-negative intestinal bacteria. To date, studies of the intestinal microbiota in IBS provide conflicting results, however, decrease of Bifidobacteria and Bacteroidetes seem to play a possible role. The intestinal metabolome of IBS patients produced less butyric acid, but significantly more sulphides; H2S is an important neurotransmitter in the pathogenesis of visceral hypersensitivity.

Fecal microbiota transplantation (FMT) is a new interventional procedure for the treatment of intestinal dysbiosis by delivering stool of a healthy person in the intestines of a patient. Donors are selected according to national and international guidelines, their stool homogenized, diluted and filtered. Fecal administration can be performed via a nasogastric tube in the upper GI tract, or during colonoscopy in the terminal ileum and right colon. To date, recurrent Clostridium difficile infection is the only established indication for FMT. However, some case reports describe a positive effect even with RDS.

The aim of this study is to observe clinical response by improvement in a clinical score (IBS-SSS) of FMT in IBS. Secondary objectives include the change in stool frequency, stool consistency (Bristol Stool Scale), the intestinal microbiome, the methane production of the microbiota and the subgroup analysis according to IBS diarrhea-dominant and constipation-dominant subgroups. This study will be performed as a single-center, randomized, double-blind study. A total of 72 patients (36 patients with IBS-D and 36 patients with IBS-C) receive antibiotic pretreatment with rifaximin (3x400mg over 10 days) before randomization in a 1:1 ratio with the IT program at the Medical University Graz "randomizer" (http://www.randomizer.at). Half of the patients receives their own stool (autologous transplantation), the other half stool from a healthy donor (allogeneic transplantation). A total of 3 FMTs will be performed in 14-day intervals during a colonoscopy or sigmoidoscopy. Blood-, urine-, saliva- and blood samples will be collected during all of the 5 study visits, mucosa samples will be taken in the context of all 3 FMTs for further analysis. A lactulose breath test will be repeatedly performed. The entire study extends over 90 days.
Secondary IDs

Health condition or Problem studied

- Free text: Irritable Bowel Syndrom (IBS)
- ICD10: K58.9 - Irritable bowel syndrome without diarrhoea

Interventions/Observational Groups

- Arm 1: 36 patients with IBS (18 with IBS-D and 18 with IBS-C) receive after antibiotic pretreatment 3 allogeneic FMTs via colonoscopy or sigmoidoscopy. Changes of clinical symptoms is elicited using the IBS-SSS and Bristol stool scale. Blood-, stool-, urine- and saliva samples as well as mucosal samples from the rectum are collected during 5 timepoints within 90 days to assess the impact on the intestinal microbiome.

- Arm 2: 36 patients with IBS (18 with IBS-D and 18 with IBS-C) receive after antibiotic pretreatment 3 autologous FMTs via colonoscopy or sigmoidoscopy. Changes of clinical symptoms is elicited using the IBS-SSS and Bristol stool scale. Blood-, stool-, urine- and saliva samples as well as mucosal samples from the rectum are collected during 5 timepoints within 90 days to assess the impact on the intestinal microbiome.

Characteristics

- Study Type: Interventional
- Study Type Non-Interventional: [---]*
- Allocation: Randomized controlled trial
- Blinding: [---]*
Study Type: Interventional
Study Type Non-Interventional: [---]*
Allocation: Randomized controlled trial
Blinding: [---]*
  - Who is blinded: patient/subject, investigator/therapist, assessor, data analyst
  - Control: Placebo
  - Purpose: Treatment
  - Assignment: Parallel
  - Phase: N/A
  - Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): N/A

Primary Outcome

The primary objective is to evaluate whether allogeneic FMT has a positive impact on clinical scores in IBS after 90 days.

Secondary Outcome

- Improvement of stool frequency and consistency of the Bristol-stool-scale.
- Change in intestinal microbiota
- Change the methane content of the exhaled air in the lactulose / CH4 breath test
- Subgroup analysis IBS-D and IBS-O.

Countries of recruitment

- AT Austria

Locations of Recruitment

- University Medical Center Klinische Abteilung für Gastroenterologie und Hepatologie, Graz

Recruitment

- Planned/Actual: Actual
- (Anticipated or Actual) Date of First Enrollment: 2016/03/16
- Target Sample Size: 72
- Monocenter/Multicenter trial: Monocenter trial
- National/International: National
Inclusion Criteria

- Gender: Both, male and female
- Minimum Age: 18 Years
- Maximum Age: 80 Years

Additional Inclusion Criteria

Patients with IBS, aged between 18 and 80 years, informed consent

Exclusion criteria

- Secondary gastrointestinal motility disorder,
- Major abdominal surgery,
- Pregnant and lactating women,
- Medication under another clinical trial,
- Serious chronic diseases such as neoplasia, autoimmune disorders or metabolic disorders.

Addresses

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Sources of Monetary or Material Support

- Institutional budget, no external funding (budget of sponsor/PI)

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Status

- Recruitment Status: Recruiting ongoing
- Study Closing (LPLV): [---]*

Trial Publications, Results and other documents

* This entry means the parameter is not applicable or has not been set.
*** This entry means that data is not displayed due to insufficient data privacy clearing.