

Effect of Fecal microbiotA Transplantation combined with MEditerranean Diet on insulin sensitivity in subjects with metabolic syndrome

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To study the effect of a Mediterranean diet (MD) followed by lean donor fecal microbiota transplantation (FMT) versus the prescription of Mediterranean diet (MD) followed by autologous (own) FMT in male subjects with metabolic syndrome on peripheral...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON42899

Source

ToetsingOnline

Brief title

FATMED

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Metabolism disorders NEC

Synonym

Metabolic syndrome, obesity

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: ZONMW

Intervention

Keyword: Fecal transplantation, Gut microbiota, Mediterranean diet

Outcome measures

Primary outcome

Primary endpoints are changes in fecal, intestinal (biopsies) and oral microbiota composition and (the relation to) peripheral /hepatic insulin sensitivity (stable isotope based hyperinsulinemic euglycemic clamp and resting energy expenditure) at baseline and 6 weeks.

Secondary outcome

Secondary endpoints are changes in postprandial plasma lipids (mixed meal test) and subcutaneous adipose tissue inflammation (biopsy) at baseline and 6 weeks. Finally, we will study effect on plasma and 24 feces and 24 urine metabolites at baseline, after 3 and 6 weeks

Study description

Background summary

The prevalence of obesity and type 2 diabetes mellitus (DM) is rising at an alarming pace. Although many factors have been identified as partakers in the development of these diseases, the complete pathophysiological pathway is still not completely understood and moreover, effective therapeutic options seem even harder to establish.

Mounting evidence links altered fecal intestinal microbiota composition to the development of obesity, insulin resistance/type 2 diabetes mellitus and even cardiovascular disease. Previous research has shown that faecal microbiota transplantation of lean healthy donors improves insulin sensitivity. Moreover,

we recently published that engraftment of these beneficial bacterial strains from lean donor feces is not equally efficient in all metabolic syndrome subjects, and that this is related to the level of improvement in insulin sensitivity upon allogenic fecal transplantation (LI-Nieuwdorp, Science 2016). It seems that especially the recipient microbiota composition determines whether engraftment of the beneficial donor bacteria takes place. We know that diet is of pivotal importance in gut microbiota composition and changes in diet can rapidly alter gut microbiota composition. In particular the Mediterranean diet has shown many beneficial effects on health in previous research.

Based on these data, we hypothesize that prescription of a beneficial (Mediterranean) diet will enhance engraftment of beneficial donor intestinal bacteria upon lean donor FMT and will thus have a synergistic beneficial effect on (peripheral) insulin sensitivity and intestinal microbiota composition in subjects with metabolic syndrome. Furthermore, this therapeutic intervention study will help us in understanding host-microbiota interactions in human (glucose) metabolism and will hopefully help to dissect progression from benign to malignant (insulin resistant) obesity and eventually type 2 diabetes mellitus.

Study objective

To study the effect of a Mediterranean diet (MD) followed by lean donor fecal microbiota transplantation (FMT) versus the prescription of Mediterranean diet (MD) followed by autologous (own) FMT in male subjects with metabolic syndrome on peripheral insulin sensitivity and (small) intestinal microbiota composition

Study design

This is a double blind randomized single centre trial in which we will randomize 24 male metabolic syndrome patients in 2 treatment arms:

- Mediterranean diet followed by allogenic lean donor FMT (n = 12)
- Mediterranean diet followed by autologous FMT (n = 12)

12 healthy lean male donors will be used for the allogenic donor FMT

Intervention

All patients will adhere to the Mediterranean diet for the total duration of the study with guidance of a dietitian and/or investigator.

Patients will be treated with infusion of either allogenic (lean healthy donor) or autologous (their own) feces transplantation:

1. Morning stool sample (150-250 gram) is collected by recipient & donor and brought to AMC for processing

2. Randomization met syndrom subject for either allogenic or autologous feces transplantation
2. Gastro-duodenoscopy will be performed for positioning of duodenal tube; during the procedure mucosal biopsies from small intestine will be taken. Correct position of the tube is checked with an abdominal X-ray.
3. Thereafter, bowel lavage with 2-3 liters of Clean Prep through the duodenal tube (according to standard protocols) will be performed to ensure complete bowel lavage (duration 2-3 hours)
4. Finally, feces mixed in ~ 500 cc saline (filtered, < 6 hours after processing) will be infused in the duodenum through positioned duodenal tube.

Study burden and risks

Total duration of study will be 14 weeks, during which patients will visit AMC 7 times (total 35 hours and 390 ml blood will be drawn) Moreover, subjects with metabolic syndrome will be asked to follow mediterranean diet for 8 weeks.

- Fecal transplantation: No side effects of faecal transplantation have been reported in our previous trials. Because a strict screening protocol is applied to faeces donors at the AMC, the risk of spreading potential pathogens during faecal transplantation seems negligible and no long term effects have been reported at our clinic since 2007 (>500 faecal transplantations performed).
- Gastroduodenoscopy: The risk of bleeding or perforation of the biopsy site during gastroscopy is regarded as small. The placing of the duodenal tube can be an unpleasant experience for the subjects, but there are no risks involved.
- Hyperinsulinemic clamp: This is regarded as a safe test. The placing of the intravenous cannula in our study can be an unpleasant experience for the subjects and it can cause a minor hematoma, which will resolve spontaneously.
- Discomfort: the participants could experience minor discomfort from placing of the intravenous cannula, blood withdrawal, injection with lidocaine during subcutaneous adipose tissue biopsies or placement of duodenal tube during gastroduodenoscopy.

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

Patients: Male obese (BMI > 30) subjects 21 to 65 years-old

With at least 3 out of 5 metabolic syndrome criteria (fasting plasma glucose * 5.6 mmol/l, triglycerides * 1.7 mmol/l, waist-circumference > 102 cm, HDL-cholesterol < 1.04 mmol/l, blood pressure * 130/85 mmHg). ;Donors: caucasian, age 18 - 65 years old, BMI 18.5 - 25 kg/m²

Exclusion criteria

Patients:

- Use of any medication, including proton pump inhibitors and antibiotics in the past three months
- Cholecystectomy
- A history of cardiovascular event (MI or pacemaker implantation)
- (expected) prolonged compromised immunity (due to recent cytotoxic chemotherapy or HIV infection with a CD4 count < 240).
- Unmotivated or not able to adhere to a specific diet;Exclusion criteria for donors:
 1. diarrhoea
 2. cholecystectomy
 3. HIV, HAV, HBV, HCV, active CMV, active EBV
 4. Unsafe sex practice (questionnaire)
 5. presence of fecal bacterial pathogens (salmonella, Shigella, Campylobacter, Yersinia) or parasites
 6. positive C. difficile stool test

7. any medication use including PPI and antibiotics; Individuals with an increased risk for one of the above conditions (homosexual contacts, recent blood transfusions) will be excluded, and donors are not recruited amongst health care providers.

Study design

Design

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

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	31-10-2016
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO	
Date:	20-07-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	20-02-2017
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	NL57871.018.16