Fecal microbiota tRAnspLantation uSed TO improve postpraNdial bacterIAl translocation;
the RALSTONIA study.

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To investigate whether changes in (small) intestinal microbiota composition regulate postprandial bacterial translocation into plasma and visceral and subcutaneous adipose tissue. Moreover, we will study whether single lean donor feces...

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

Summary

ID

NL-OMON47262

Source
ToetsingOnline

Brief title
RALSTONIA study

Condition

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

Synonym
insulin resistance, metabolic syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NWO Vidi-beurs 2013 toegekend aan M. Nieuwdorp.

Intervention

Keyword: bacterial translocation, fecal transplant, gut microbiota, metabolic syndrome

Outcome measures

Primary outcome

To investigate whether an oral fat load induces translocation of intestinal bacteria including Ralstonia picket and whether lean donor fecal transplantation affects this.

Secondary outcome

To investigate whether changes in (small) intestinal gut microbiota are related to postprandial bacterial translocation. Moreover, we will investigate changes in visceral and subcutaneous adipose tusse and plasma. Furthermore, we will study changes in 24h feces (triglyceride excretion) and 24h urine (TMAO and oxalic acid).

Study description

Background summary

De prevalence of obesity and related conditions such as metabolic syndroom and type 2 diabetes mellitus continues to rise world wide. The rol of the gut microbiota in metabolic disorders has recently been identified. Obesity has been associated with changes in the composition of the gut microbiota and the obese gut microbiota seems to be more efficient in harvesting energy from the diet. The potential causal relationship between metabolism and the gut microbiota was recently implied in the FATLOSE-1 trial, where men with metabolic syndrome showed a marked improvement of insulin sensitivity after

infusion of lean donor feces. Moreover, in the IMAGE-trial we showed that visceral fat tissue of obese, insulin resistant subjects contained bacterial DNA, notably Ralstonia pickettii. The amount of Ralsonia pickettii DNA in this fat tissue correlated with the amount in feces and with inflammatory parameters. Bacterial translocation, especially after a high fat meal, from the intestines into plasma and fat tissue may be a crucial factor in the development of inflammation and insulin resistance.

In the RALSTONIA study we would like to investigate whether and to what extend patients with metabolic syndrome show postprandial bacterial translocation into plasma and fat tissue and whether we can improve this by lean donor fecal transplantation. By relating the results to differences in (small) intestinal gut microbiota, we could contribute to the growing knowledge about the relationship betweet the gut microbiota and type 2 diabetes mellitus.

Study objective

To investigate whether changes in (small) intestinal microbiota composition regulate postprandial bacterial translocation into plasma and visceral and subcutaneous adipose tissue. Moreover, we will study whether single lean donor feces transplantation influences bacterial translocation compared to autologous fecal transplantation.

Study design

Randomized, double blind, controlled, single center, intervention study.

Intervention

Patients will be randomised to receive either single allogenous donor feces (n=12) or single autologous feces (n=12).

Study burden and risks

De screening contains filling out a questionnaire, a physical examination and taking a blood sample (60ml). On the first study day, patients will will visit the AMC to do a mixed-meal test, where they will receive a standardized meal and blood will be taken from a cannula 5 times (140ml). Prior to this, a subcutaneous fat biopsy will be taken. The visit will take 8 hours. On the second study day, a gastroscopy will be performed, with small intestinal biopsies and placement of a probe, followed by a fecal transplant. This visit will also take 8 hours. 3 weeks later, the mixed-meal test and gastroscopy with small intestinal biopsies will be repeated. However, this time no subcutaneous biopsy and fecal transplant will be performed. During the study, patients will twice keep track of their diet for a week, twice collect 2x24h feces and twice collect 1x24h urine. All together, the visits will take 25 hours.

For the donors the burden contains filling out a questionnaire, followed by providing a fecal sample to test for transmissible diseases. If the tests come back negative, a single venous sample (25ml) will be taken to screen the blood of the potential donor for viruses. Suitable donors will then receive a single mixed-meal test (with drawing of 140ml blood) with subcutaneous biopsy. During the study, the donors will keep track of their diet for a week once and once collect 2x24h feces and 1x24h urine. All together, the visits will take 5 hours.

In theory there may be a risk for transmitting unknown diseases via feces (as has been described with blood transfusion). However, by screening the donors thoroughly, we aim to minimise this risk.

Gastroscopy: this is a standard procedure.1 in 1000 procedures are complicated by bleeding or a small tear in the gut. This can often be treated immediately (through the endoscope). Sometimes surgery is necessary. The risk of this procedure is considered minimal. Inspecting the stomach and duodenum has the added advantage of being able to visualise and treat abnormalities of the stomach or duodenum (e.g. ulcer) immediately.

The subcutaneous biopsy will be taken under local anesthesia and will thus not be painful. However, after the procedure a bruise may appear and the puncture site may be painful.

Mixed-meal test: patients will receive a standardized meal, which is not associated with risks. Oral vitamin A has not ben associated with risks.

The harvesting of fat tissue after the fecal transplant has a minimal risk of bleeding. Because harvesting will be done during an already planned procedure, direct action can be taken when this happens. Thus, the added risk is minimal.

Although there is no direct benefit for participating in the study, this research may provide important knowledge about the concept of bacterial translocation and its rol in the development of insulin resistance. Thus, this study may help us in the future to develop new treatment modalities for insulin resistance and type 2 diabetes mellitus.

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

Metabolic syndrome patients:
- Caucasian
- BMI >25 kg/m2
- At least 3 out of 5 NCEP 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
- Scheduled for laparoscopic cholecystectomy or laparoscopic gastric bypass;Lean donors:
- BMI 18,5-25 kg/m2

Exclusion criteria

Metabolic syndrome patients:
- A history of cardiovascular event (cerebrovascular accident, myocardial infarction or pacemaker implantation)
- Use of any medication including proton pump inhibitors and antibiotics in the past three months
- (Expected) prolonged compromised immunity (due to recent cytotoxic chemotherapy or HIV infection with a CD4 count < 240/mm3)
- Type 2 diabetes mellitus
- Smoking;Lean donors:

- Use of any medication including proton pump inhibitors and antibiotics in the past 3 months
- Type 2 diabetes mellitus
- Diarrhea
- Cholecystectomy
- HIV, HAV, HBV, HCV, active CMV, active EBV
- Unsafe sex practice (questionnaire)
- Illicit drug use
- Smoking
- Presence of fecal bacterial pathogens (Salmonella, Shigella, Campylobacter, Yersinia) or parasites
- Positive C. difficile stool test

Study design

Design

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):	28-12-2015
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO

Date:	26-02-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	02-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2016
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	NL52150.018.15