FATLOSE 2 study *Single versus multiple fecal transplants harvested from lean volunteers on lipid and glucose metabolism in subjects with metabolic syndrome; the FATLOSE 2 trial (Fecal Administration To LOSE insulin resistance)*

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In this follow-up study we would like to compare the effect of single versus multiple (2x) duodenenal tube infused allogenic versus autologous feces (as controls) on insulin resistance, cholesterol and (shortchain) free fatty acid metabolism in...

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

Summary

ID

NL-OMON35735

Source
ToetsingOnline

Brief title
FATLOSE2

Condition

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

Synonym

gut microbiota, metabolic syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: fecal transplant, gut microbiota, metabolic syndrome, SCFA

Outcome measures

Primary outcome

The primary endpoint changes in fecal flora composition and shortchain fatty

acid metabolism in fecal samples after 3, 6, 10, 13, 16 and 20 weeks.

Secondary outcome

Secondary endpoints are changes in insulin resistance/fatty acid metabolism

(assessed by hyperinsulinemic normoglycemic clamp and stable isotope

glucose/palmitate infusion) and postprandrial lipidmetabolism (mixed meal test)

at baseline and after 10 and 20 weeks). Finally, changes in gutregulatory

hormones in plasma (leptin, adiponectin and GLP-1) will be assessed.

Study description

Background summary

The Metabolic Syndrome (MS) is characterised by a constellation of cardiovascular risk factors, which include elevated triglyceride (TG) levels, reduced high-density lipoprotein cholesterol (HDL-C) and increased fasting glucose levels. According to the National Cholesterol Education Program*s (NCEP*s) Adult Treatment Panel (ATP III) definition, MetS is identified by having three or more metabolic abnormalities in terms of elevated triglycerides, decreased HDL-Cholesterol and increased fasting blood glucose

levels, abdominal obesity and elevated blood pressure (1). A most disturbing consequence of the steady increase in MetS prevalence (2, 3) is the concomitant rise in the incidence of both diabetes and cardiovascular disease in these subjects (4, 5). In an effort to limit these detrimental sequelae, therapeutic strategies are focussing at a comprehensive lowering, or even *normalizing* these risk factors. In summary, these risk factors as mentioned above catalyze the process of atherosclerosis and cardiovascular disease in type 2 diabetes mellitus.
Recent research shows that obesity is associated with changed bowel flora composition with a relative abundance of the two dominant bacterial divisions, the Bacteroidetes and the Firmicutes (6). Interestingly, this specific bacteria associated condition is transmissible: colonization of obese mice with an *leanmicrobiota* results in a significantly greater decrease in total body fat (-30%) than colonization with a *obese microbiota* (+5%). In addition, Bacteroidetes species are decreased and Firmicutes increased in feces of obese people compared to lean people (7). We recently finished the FATLOSE trial, in which we studied the therapeutic effect of donor feces infusion from screened volunteers, after 6 weeks, on insulin resistance (hyperisulinemic clamp with stable isotopes) in male patients with metabolic syndrome (MEC 07/114, see 8). We found a 50% reduction in both periferal and hepatic insulin resistance implicating substantial effects of whole body glucose metabolism. Moreover, we found significant reductions in fasting lipidprofiles after allogenic fecal therapy, which are in line with previously published data suggesting a direct effect between duodenal lipid uptake and glucose production orchestrated by gutmicrobiota driven brain-gut axis (9). The efficacy of fecal therapy is explained by enhanced production of specific short chain free fatty acid butyrate produced by the infused lean donor feces, which probably restores normal fecal physiology by implantation of missing lean-figure flora components (10,11). In collaboration with dr Zoetendal and prof de Vos (WUR), we confirmed by HITCHIP that the butyrate producing bacterial phylum Bacteroidetes is specifically increased after allogenous feces transplantation (12).

Study objective

In this follow-up study we would like to compare the effect of single versus multiple (2x) duodenenal tube infused allogenic versus autologous feces (as controls) on insulin resistance, cholesterol and (shortchain) free fatty acid metabolism in obese male subjects with metabolic syndrome.

Objectives

To investigate the pathophysiological role of changes in fecal flora composition on insulin resistance in patients with metabolic syndrome

I Changes in caloric intake (diet lists and weight) in relation to fecal flora composition and
shortchain fatty acid metabolism in fecal samples at baseline and

after 3,6, 10, 13, 16 and 20 weeks in a group of uncomplicated male MS patients receiving either single or twice allogenic or autologic feces transplantation after total bowel lavage (n=10 per group).

II Longterm changes in fecal flora and insulin resistance (hyperinsulinemic, normoinsulinemic clamp and glucose disappearance rate Rd) and lipidmetabolism (mixed
meal test) before and 10 and 20 weeks after intervention with fecal infusion

III Investigate the interaction between longterm changes in gutmicrobiota and inflammation
and plasma markers of metabolic control (plasma GLP-1, adiponectin and leptin levels)

Study design

This is a double blind randomized controlled single center trial.

Intervention

Patients will be treated with infusion of allogenic or autologous feces by duodenal tube after bowel lavage

Patients will be randomized by sealed envelopes to the following 6 treatment arms:
1. single (at baseline) allogenic lean donor feces
2. single (at baseline) allogenic obese donor feces
3. multiple (at baseline and 10 weeks) allogenic lean donor feces
4. multiple (at baseline and 10 weeks) allogenic obese donor feces
5. single autologous (own) feces
6. multiple (at baseline and 10 weeks) autologous (own) feces

Study burden and risks

Subjects are submitted to a hyperinsulinemic normoglycemic clamp. To compensate for the insulin infusion, glucose 20% is infused to maintain blood sugar levels between 5 and 5.5 mmol/l, The rate of glucose infusion is determined by checking the blood sugar level every 5 minutes.
Because strict conditions are there for donors, the risk of spreading potential pathogens during faecal transplantation seems nil.

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

Male obese subjects with metabolic syndrome, age 21-65, BMI 30-43 kg/m2

Exclusion criteria

cardiovascular event (MI or pacemaker implantation), use of medication including PPI and antibiotics, (expected) prolonged compromised immunity (due to recent cytotoxic chemotherapy or HIV infection with a CD4 count < 240).

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):	11-12-2011
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
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	NL35474.018.11
Other	NTR-8966