Diet-induced alteration of microbiota and development of obesity, nonalcoholic fatty liver disease and diabetes

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

Summary

ID

NL-OMON47711

Source
ToetsingOnline

Brief title
DIAMOND trial

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, insulin resistance

Research involving
Human

Sponsors and support

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

Intervention

Keyword: bariatric surgery, diabetes, microbiota, obesity

Outcome measures

Primary outcome

* Bodyweight, BMI, abdominal circumference, plasma glucose/insulin,

lipidspectrum

* Faecal and intestinal microbiota composition

* Plasma en faecal Short Chain Fatty Acids, Glucagon-like-peptide-1

* Paneth cel typing by determination of luminal en faecal concentrations of

lysozym/HD5/HD6/LL-37/sPLA2/HIP/PAP

* Intestinal protein en mRNA expression and localisation of lysozym/HD5/HD6

* Mucus typing by determination of the number of goblet cells, mucin 2 protein

concentration en glycosylation.

* Volatile Organic Compounds (VOC) in exhailed air

* Fecal calprotectin in obese subjects

Secondary outcome

nvt

Study description

Background summary

Gut microbiota play an important part in the development of obesity-related type 2 diabetes. The composition, localisation and translocation of intestinal bacteria is greatly influenced by antimicrobial proteins which are secreted by Paneth cells in the small intestine, as well as mucin components secreted by goblet cells in the small intestine.

Study objective

The exact mechanism behind these dietary influenced modulations of the composition of gut microbiota is unknown. Our hypothesis is that dietary fat intake indirectly causes alteration of the gut microbiota composition, by affecting the function of Paneth cells and goblet cells.

The objective of this study is to prove a causal relation between dietary fat intake en alterations in gut microbiota composition, by focussing on diet induced alterations in Paneth cell function and the impact of diet induced alterations in goblet cell function and mucin composition.

Study design

Patients will be approached for participation while they are on the waiting list for a laparoscopic gastric bypass. After obtaining informed consent, patients will take a oral glucose toleration test and will be asked to provide a stool sample. As a part of the standard pre-operative screening by the anesthesiologist, blood will be drawn with some additional samples for research. All participants in the obese group will have a sampling of the exhailed air. During the operation a biopsy will be performed of liver tissue, subcutaneous fat, visceral fat, rectus abdominis muscle tissue and jejunal tissue.
The control group will receive the same interventions, but the jejunal tissue will be obtained in a different population. We will be using jejunal biopsies obtained during endoscopy in patients with dysfagia of dyspepsia.

The duration of follow-up is one year, comprising of five routine visits to the outpatient department at 3-6 weeks, 3 months, 6 months, 9 months and 12 months). During these visits, some extra blood will be drawn for research purposes simultaneously to the standard blood sample protocol. After 12 months a new stool sample will be requested and new glucose tolerance test will be performed.

Study burden and risks

For the glucose tolerance test the patient will be asked to come to the hospital without breakfast of any other food intake prior to the test. A baseline bloodsample will be drawn. The patient will be asked to drink a solution of 75 grams of glucose in 200 ml of water. Two hours after ingestion another bloodsample will be drawn. Patients will be asked to provide a stool sample at baseline and at 12 months postoperatively, which will be used for analysis of microbiota composition.

During every routine blood sample drawal about 6ml of blood will be drawn and processed to plasma. The blood necessary for research will be drawn

simultaneously to the routine collection. This adds up to two times 6 ml extra per patient.

The sampling of exhailed air takes about 5 minutes and is risk free.

The biopsies of liver, fat, muscle and jejunum tissue will be performed by the surgeon during laparoscopy. A biopsy of about 0.5cm3 will be taken from the outside of the liver and rectum abdominis muscle. The site of biopsy will be checked for possible bleeding and if necessary cauterisation will be perforemd. Likewise, a biopsy of the omentum majus and subcutaneous fat of the abdominal wall will be performed. These biopsies do not cause inconvenience to the patient, because they will be performed during the gastric bypass surgery. A possible complication could be bleeding from the biopsy site, but previous studies have shown this possible complication to occur very rarely.

The jejunal biopsies of the control population willl be obtained via endoscopy and might cause a slight inconvenience for the patient due to a possible more lengthy procedure. The biopsy itself is not painful and a possible complication might be bleeding of the biopsy site or a perforation, but previous experience has shown that these complications occur very rarely.

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

BMI > 40 kg/m2 or > 35 kg/m2 with comorbidities
Undergoing a laparoscopic gastric bypass
Age between 18 and 65;Control population:
BMI between 20-25 kg/m2
Indication for laparoscopic cholecystectomy
Indication for gastroscopy
Age 18 to 65 years

Exclusion criteria

Both groups:
Type 1 diabetes
Alcohol abuse or drug abuse
Inflammatory illness, such as auto-immune disease
Degenerative disease
Physician prescribed use of corticosteroids and prednisone;Controlgroup
Diabetes type 2
Cachexia

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-02-2016
Enrollment:	228
Type:	Actual

Ethics review

Approved WMO Date:	10-11-2015
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	29-11-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	01-03-2019
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 20944
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL52416.015.15
OMON	NL-OMON20944