Effects of a high-fat and a low-fat diet on early biomarkers of metabolic stress in blood and gene expression in the small intestine of healthy subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolism disorders NEC
Study type	Interventional

Summary

ID

NL-OMON31635

Source
ToetsingOnline

Brief title
Effects of high-fat and low-fat diet on the gut

Condition

- Metabolism disorders NEC

Synonym
disturbed fat and glucose metabolism, metabolic syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht

Source(s) of monetary or material Support: Top Institute Food and Nutrition (TIFN) is de subsidieerende partij en NUTRIM is de verrichter.

Intervention

Keyword: early biomarkers, high-fat and low-fat diet, metabolic syndrome, small intestine

Outcome measures

Primary outcome

Potential early biomarkers of the metabolic syndrome in blood and gene

expression profiles in the small intestine.

Secondary outcome

Parameters of the metabolic syndrome in blood, gene expression profiles in PBMC

and gut permeability.

Study description

Background summary

The prevalence of the metabolic syndrome is strongly increasing in developed countries. The role of the small intestine seems important in the development of the metabolic syndrome. Although it is known that a high-fat Western-style of diet has deleterious effects on (post-prandial) lipidemia and glucose homeostase, effects of such a diet on the small intestine is not known. To elucidate the role of the small intestine on the early development of the metabolic syndrome, the effects of a high-fat (HF) and a low-fat (LF) diet will be examined on gene expression in the small intestine and early biomarkers in blood of healthy subjects.

Study objective

The objective of this study is to compare in healthy subjects the effects of a HF diet (40 En% fat) with those of a LF diet (20 En% fat) on early biomarkers and parameters of metabolic stress in blood and on expression of genes in the small intestine. Additional research objectives are:
- To compare the diet-induced changes in transcriptome profile of the small intestine with more easily accessible peripheral blood mononuclear cells (PBMC)
- To establish effects of HF and LF diet on basal gut permeability and after a

chenodeoxycholic acid (CDCA) load (second hit).

Study design

Randomised crossover design. The duration of the experimental periods (HF and LF diet) will be 28 days, separated by a wash out period of at least 3 weeks. At day 21 of each intervention period a postprandial test will be performed and duodenum biopsies will be taken. At day 25 and 28 of each intervention period, respectively, basal gut permeability and gut permeability after a CDCA load will be determined with a sugar recovery test.

Intervention

Subjects will consume in random order a) a HF diet (40 En% fat, 45 En% carbohydrates and 15 En% proteins) and b) a LF diet (20 En% fat, 65 En% carbohydrates and 15 En% proteins).

Study burden and risks

At the screening visit a blood sample (15 mL) will be taken, and blood pressure and body weight will be measured. During the study six blood samples (300 mL) and two duodenum biopsies (at day 21 of each experimental period) will be taken. At the end of each experimental period the subjects will have to collect urine for 24 hours (day 24) and on two occasions they will have to collect urine for 5 hours after ingestion of a beverage containing sugar probes, once for a basal gut permeability test (day 25), and once after a CDCA load (day 28). Three weeks after the diet intervention once again basal gut permeability will be measured to determine basal gut permeability under standard dietary conditions. During the study subjects will have to record their daily fat intake during the intervention periods and two weeks after the last intervention period in diaries. At each visit body weight will be measured.
Total time investment for the subjects will be 88 hours.
Blood samples might cause bruises or haematoma. Obtaining duodenum biopsies by standard flexible gastroduodenoscopy induces local discomfort in the pharynx only during the procedure, which takes about 10 minutes, and causes a theoretical risk for perforations (1:1000) and an infection risk of 1:1.800.000. A single CDCA load is not known to have major side effects; some diarrhea might occur.

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

age between 18 and 65 years
body mass index (BMI) between 18 and 30 kg/m2

Exclusion criteria

- BMI <= 18 and >= 30 kg/m2
- Smoking
- Serum Total cholesterol > 8.0 mmol/L
- Fasting glucose > 7.0 mmol/L
- Use of any medication
- Active cardiovascular diseases like congestive heart failure or recent (<6 months) event (acute myocardial infarction, CVA)
- Gastrointestinal diseases (like celiac disease, inflammatory bowel disease, irritable bowel disease and food allergies) or a history of any gastrointestinal disorders or complaints
- Pre-existing gallbladder disease
- Diabetes mellitus
- Familial hypercholesterolemia

- Severe medical conditions that might interfere with the study such as epilepsy, asthma, COPD and rheumatoid arthritis.
- Unstable body weight (weight gain or loss > 3 kg in the past three months)
- Impairment of renal function, as evidenced by increased serum creatinine >150 mmol/L
- Hepatic diseases as manifested by ALT, AST, GGT, total bilirubin or ALP > 2 times the upper limit of normal
- CRP values > 8.0 mg/mL
- Abuse of drugs and/or alcohol
- Participation in another biomedical study within 1 month prior to the start of this study
- Having donated blood (as blood donor) within 1 month prior to start of this study

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-01-2008
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Chenofalk
Generic name:	chenodeoxycholic acid (CDCA)
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	15-10-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-12-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-02-2008
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-06-2008
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
EudraCT	EUCTR2007-005527-15-NL
ClinicalTrials.gov	NCT00561626
CCMO	NL19635.068.07