Effects of the gut flora on serum LDL cholesterol concentrations in slightly hypercholesterolemic subjects

Published: 19-03-2012
Last updated: 26-04-2024

To study the effects of the gut flora on serum LDL-cholesterol concentrations in slightly hypercholesterolemic subjects. The minor objective is to study the effects of gut flora on other parameters related to lipid and lipoprotein, and to parameters...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON37583

Source
ToetsingOnline

Brief title
Gut flora and lipid metabolism

Condition

- Lipid metabolism disorders

Synonym
hypercholesterolemia / increased serum cholesterol concentration

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: antibiotics, gut flora, LDL cholesterol, lipid metabolism

Outcome measures

Primary outcome

The main study parameter is the change in fasting serum LDL-cholesterol concentrations.

Secondary outcome

Secundary study parameters are changes in concentrations of HDL cholesterol, triacylglycerol and glucose. Changes in ex vivo and in vitro lipolysis in abdominal subcutaneous adipose and in skeletal tissue will be measured in a subgroup.

Study description

Background summary

There is substantial evidence from in particular animal studies that the gut microbiota is related to lipid and lipoprotein metabolism. It is not known however to what extent modulation of the gut microbiota in humans changes lipid and lipoprotein metabolism.

Study objective

To study the effects of the gut flora on serum LDL-cholesterol concentrations in slightly hypercholesterolemic subjects. The minor objective is to study the effects of gut flora on other parameters related to lipid and lipoprotein, and to parameters related to glucose metabolism.

Study design

Using a randomized, double-blind, placebo-controlled parallel design, subjects will receive for 7 days a broad spectrum antibiotic (Amoxicillinum Gb; daily 3x500 mg) or placebo.

Intervention

During the experimental period, subjects will receive daily 6x250 Amoxicillinum Gb or placebo for 7 days. Placebo capsules will be filled with gelatine, cellulosum microcristallinum PH102. Blood samples will be taken at regular intervals.

Men and women aged between 18-70 years and with a BMI >18.5 kg/m2 will be asked if they are willing to collect an abdominal adipose tissue biopsy and skeletal muscle biopsy.

Study burden and risks

Before the start of the study subjects will be screened to determine eligibility during two 15-minute visits. During these visits, body weight, height and blood pressure will be measured and a blood sample (4.5 mL) will be drawn by means of venapunction. During the study, subjects will receive a broad-spectrum antibiotic or placebo for 7 days. At days 1, 4, 8, 12 and 16, a fasting blood sample will be drawn (20 mL at each occasion) and (in a subgroup) on days 1 and 8 biopsies of subcutaneous adipose and skeletal tissue. Subjects will be asked to fill out a 3-day food record two times and to keep a study-diary throughout study. On rare occasions, blood sampling / taking biopsies might cause bruises or hematoma. Amoxicillin can cause gastrointestinal complaints like diarrhea or stomach ache. Additionally allergic skin reactions, interstitial nephritis and blood disturbances like hemolytic anemia and thrombocytopenia may occur. These effects, however, have been reported scarcely. Total time investment for the subjects will be approximately 4 hours and 6 hours for those who are willing to participate in the sub-study to collect biopsies.

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

- aged between 18-70 years
- mean serum total cholesterol concentrations between 5.0 - 8.0 mmol/L

Exclusion criteria

- mean serum triacylglycerol > 3.0 mmol/L
- use of oral anticonceptives (OAC)
- pregnant or breastfeeding women
- subjects with kidney insufficiencies (defined as creatinine clearance <30 mL/min).
- unstable body weight (weight gain or loss >2 kg in the past 3 months)
- known allergy to antibiotics
- indication for treatment with cholesterol-lowering drugs according to the Dutch Cholesterol Consensus
- use of medication or a medically prescribed diet known to affect lipid or glucose metabolism
- active cardiovascular disease like congestive heart failure or recent (<6 months) event (acute myocardial infarction, cerebro vascular accident)
- severe medical conditions that might interfere with the study such as epilepsy, asthma, chronic obstructive pulmonary disease, inflammatory bowel diseases and rheumatoid arthritis
- abuse of drugs
- more than 21 alcohol consumptions per week for men and 14 consumptions for women
- not or difficult to venipuncture as evidenced during the screening visits
- use of an investigational product within the previous 30 days
- not willing to stop the consumption of products rich in plant stanol or sterol esters 3 weeks before the start of the study
- not willing to give up being a blood donor (or having donated blood) from 8 weeks before the start of the study and during the study

- use of gastric acid inhibitors, laxantia, prebiotica, probiotica and antibiotica for at least one month before the start of the study and during the study

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-04-2012
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	19-03-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	04-06-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-08-2012

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
ClinicalTrials.gov	NCT-
CCMO	NL39874.068.12