Bile acid composition and diabetes

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To investigate the effects of colesevelam (bile acid sequestrant) on bile acid composition, glucose metabolism and composition of faecal flora in patients with an impaired glucose tolerance or newly diagnosed type 2 diabetes

Ethical review	Approved WMO
Status	Will not start
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON33057

Source
ToetsingOnline

Brief title
Bile acid composition and diabetes

Condition

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

Synonym
bile acid metabolism, diabetes

Research involving
Human

Sponsors and support

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

Intervention

Keyword: colesevelam, faecal flora, glycemic control, type 2 diabetes mellitus

Outcome measures

Primary outcome

The primary endpoints are changes in bile acid composition

Secondary outcome

Secondary endpoints are changes in hepatic and peripheral insulin resistance (assessed by hyperinsulinemic euglycemic clamp and stable isotopes at baseline and after 12 weeks), metabolic parameters (lipid profile, glycemic control) as well as changes in faecal microbiota, glucose and lipid content (assessed by analysing faeces samples). Finally, muscle and adipose tissue samples will be obtained to assess D2 mRNA and activity and phosphorylation status of the insulin signalling cascade.

Study description

Background summary

Colesevelam is a bile acid sequestrant that has been approved for use as a cholesterol-lowering agent. Surprisingly, treatment with colesevelam not only improves lipid parameters, but also improves glycemic control in patients with type 2 diabetes, with a reduction in HbA1c of 0,5 % and a concomitant decrease in postprandial plasma glucose values. The exact mechanisms behind these glucose lowering effects remain unclear; however they are likely multifactorial.

Study objective

To investigate the effects of colesevelam (bile acid sequestrant) on bile acid composition, glucose metabolism and composition of faecal flora in patients with an impaired glucose tolerance or newly diagnosed type 2 diabetes

Study design

Double blind randomized controlled single center trial

Intervention

Patients will be randomised to either colesevelam treatment or placebo treatment for a period of 12 weeks

Study burden and risks

Stable isotopes are harmless. Muscle biopsies and fat aspirate can cause hematoma: a minimal invasive biopsy and pressure bandage are used in order to minimalize this risk. Patients can however experience a bruising feeling. During clamp, insulin is infused at 20-60 mU per m2 per minute. Insulin infusion involved the risk of a hypoglykemia. In order 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 levels every 5 to 10 minutes.

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 subjects with an impaired fasting glucose or newly diagnosed type 2 diabetes (fasting plasma glucose> 6.0), 18 to 55 years-old and body mass index (BMI) >30 kg/m2.

Exclusion criteria

- Patients with medication known to interfere with glucose metabolism or gut microbiota composition (antibiotics, sequestrants, chenodiole, ursochol)
- Patients with severe hypertriglyceridemia or any other primary lipid disorder.
- Patients who practice intensive sports (>three times weekly endurance exercise)
- Patients with thyroid diseases (TSH is measured at screening)

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	24
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	cholestagel

Generic name:	Colesevelam
Registration:	Yes - NL outside intended use

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
EudraCT	EUCTR2009-011972-31-NL
CCMO	NL27774.018.09
Other	NTR-5545