The effect of bile acid binding with colesevelam on postprandial glucose concentrations in patients after RYGB and cholecystectomy : a meal test study

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Objective: Primary : To compare the difference in glucose nadir during the MMT on and off pre-treatment with colesevelam in RYGB-CCx patients with a hypoglycaemia (RYGB-CCx-hypo) in the first MMT Secondary:To evaluate the difference in number of...

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

Summary

ID

NL-OMON50934

Source
ToetsingOnline

Brief title
Colesevelam hypOglycemia Bile acid binding in Rygb: a meAl test study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
post bariatric hypoglycemia hypoglycemia after gastric bypass surgery

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Leeuwarden

Source(s) of monetary or material Support: stichting CON VOLUME research;Wetenschapsfonds MCL

Intervention

Keyword: cholecystectomy, colesevelam, hypoglycemia, RYGB

Outcome measures

Primary outcome

Glucose nadir during the MMT in mmol/L

Secondary outcome

During the MMT :

Number of patients with a hypoglycemic episode (glucose < 3.0 mmol/L)

Glucose Area under the curve between 60 and 180 minutes (glucose AUC60-180min),

Bile acids and derivatives, GLP-1, PPY, FGF-19, and insulin, both as peaks and

as AUC0-60 min .

Glucose kinetics (absorption rate, endogenous glucose production) using stable

isotope dilution of glucose

Study description

Background summary

Rationale:
Postprandial hyperinsulinemic hypoglycaemia often occurs after bariatric surgery and is called PBH.
We previously found that 48% of patients after RYGB developed a hypoglycemic event in a mixed meal test (MMT). In these patients bile acid (BA) concentrations were much higher compared to those without hypoglycemia. Furthermore, more patients with hypoglycemia had undergone a cholecystectomy (CCx). The role of postprandial bile acids in PBH has up till now not been elucidated

Study objective

Objective:
Primary : To compare the difference in glucose nadir during the MMT on and off pre-treatment with colesevelam in RYGB-CCx patients with a hypoglycaemia (RYGB-CCx-hypo) in the first MMT
Secondary:To evaluate the difference in number of RYGB-CCx-hypo patients developing a hypoglycemia (glucose < 3.0 mmol/L) during the MMT on and off pretreatment with colesevelam
To compare differences during the MMT on and off pre-treatment with colesevelam in glucose AUC at different time intervals : 0-60, 60-120, 60-180, bile acids, bile acid subclasses, GLP-1, PPY, and insulin, both as peaks and as AUC0-60 min
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To compare differences during the MMT on and off treatment with colesevelam in glucose kinetics (absorption rate, distribution) using stable isotope dilution of glucose
To compare differences during the MMT on and off treatment with colesevelam in level of satiety, hunger score and dumping complaints
Study design: prospective, non-blinded, intervention
Study population:
Patients between 20 and 60 years who underwent RYGB surgery 2 years or more before and have a history of CCx
Intervention : colesevelam tablets 625mg , 3,750 mg dissolved in water
Main study parameters/endpoints:
Glucose nadir during the MMT
Number of patients developing hypoglycemia during the MMT
Glucose disposal rate and endogenous glucose production during the MMT measured with stable isotope dilution
Changes in bile acids and subclasses during the MMT
Changes in insulin, GLP-1, PYY, FGF19 during the MMT
Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
Patients have to visit the outpatient clinic 2 times max, in fasting condition.
Via an indwelling catheter blood samples will be drawn 11 times to a total amount of 242 mL
The meal can induce dumping complaints and can induce a low blood sugar, which will be monitored and treated if necessary.

Study design

Patients 2-3 years after RYGB with a previous cholecystectomy will start this study with a MMT. After full explanation of the study and written informed consent patients will be admitted in the outpatient clinic between 8 and 9 pm after an overnight fast of at least 10 hours. An indwelling catheter will be placed in an antecubital vein for blood withdrawal. After the first sample is drawn, they will be asked to consume in 10 minutes a liquid mixed meal, consisting of 200mL Ensure® Plus to which 50 mL 2,5% D-[6,6,-2H]-glucose tracer (:1,25 gram) is added, in total volume of 250 mL
Blood samples will be withdrawn, blood pressure and pulse will be measured,

satiety, hunger and dumping scores will be documented at various time points until 180 minutes.
Those patients who develop a hypoglycemic event (glucose < 3.0 mmol/L) during the MMT will repeate the MMT between 7 and 14 days with pretreatment with colesevelam 3750mg dissolved in 25 ml water once dosed shortly before the MMT.

Intervention

Colesevelam tablet 625 mg (Cholestagel®) 3750 mg once dosed dissolved in water

Study burden and risks

1. during the MMT a hypoglycemic event can occur. Patients are under constant observation and an intravenous access is available for administration of glucose in case of clinical signs of neuroglycopenia.
2. insertion of a cannula for venous access can fail leading to a small hematoma.
3. Colesevelam can cause side effects, mainly gastro-intestinal (constipation, nasea, sometimes diarrhea) which can be simply treated by stopping the drug.
4. Colesevelam can reduce the absorption of other drugs. Therefore patients who use drugs could possibly be interfered with by colesevelam are excluded. Also patients will be reminded to contact the investigator when new drugs are prescribed to them during the study

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

patients 20-60 years, 2 years or more after RYGB and with a history of a cholecystectomy

Exclusion criteria

known with post bariatric hypoglycemia
(former) diabetic
hypertriglyceridemia
renal or liver disease
addiction behaviour
medication use that will be interfered ith by colesevelam
pregnancy (planning)
bowel or choledochusobstruction

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-05-2022
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cholestagel
Generic name:	colesevelam
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-10-2021
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	30-11-2021
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	04-04-2022
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

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	EUCTR2021-000667-74-NL
ISRCTN	ISRCTN00009249
CCMO	NL76848.099.21

Study results

Date completed:	25-08-2022
Actual enrolment:	14