Postprandial FGF-19 response after fat challenge in patients with cholestatic liver disease

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Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON34548

Source
ToetsingOnline

Brief title
Postprandial FGF-19 response in cholestatic liver disease

Condition

- Gastrointestinal inflammatory conditions
- Hepatic and hepatobiliary disorders

Synonym
primary biliary cirrhosis and primary sclerosing cholangitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Maag Lever en Darm Stichting (MLDS)

Intervention

Keyword: FGF19, Inflammatory bowel disease, Primary biliary cirrhosis, Primary sclerosing cholangitis

Outcome measures

Primary outcome

Plasma levels of FGF-19, plasma markers of bile acid synthesis (as a measure

of suppression of Cyp7A1, a hepatic target gene of FGF19)

Secondary outcome

n.a.

Study description

Background summary

PBC and PSC are disorders of unknown etiology. The protective effect of FGF-19 on the liver might be lacking or insufficient in these diseases. A suboptimal production of FGF-19 could be the cause of insufficient suppression of bile acid synthesis in the liver, which is particularly harmfull in cholestasis, like in PSC and PBC. With this research we want to study the intestinal production of FGF-19 in patients with PBC and PSC after a standardized oral fat challenge. Moreover, we will analyze the effect of this FGF19 production on bile acid synthesis in the liver.

Study objective

Hypothetically, in patients with PBC or PSC the FGF-19 production or -response could be altered. The goal of this research is to study the FGF19 production after a standardized oral fat challenge and the effect of this FGF19 production on bile acid synthesis in the liver, in patients with PBC or PSC.
We postulate that PBC or PSC are the result of insufficient intestinal FGF19-production or hepatic resistance to FGF19.

Study design

Study design: Observational study with invasive measurements.

Patients with PSC, PBC, IBD without PSC or PBC and healthy volunteers (n=12 per

group) will be invited to participate in our study. These patients will be recruted from the Hepatology outpatient clinic of the AMC (PSC, PBC) or from the Inflammatory Bowel Disease outpatient clinic of the AMC (IBD without PSC or PBC). Only patients will be included with an established diagnosis via liver biopsy (PBC), MRI (PSC) or by a clinicians judgement based on medical history, colonoscopy and laboratory findings (IBD). Diagnostics will not be part of this study.

To include patients in our study from the outpatient clinics, collaborating physicians will be informed about this study and will be asked to provide information about this study to patients that could be potential participants. Naturally, it will be stated that the information is provided free of obligations and that refusing the request of participation in this study does not have any consequences for their treatment in the AMC.
Healthy subjects will be recruited from the public squares in the AMC via a written announcement. If this will not lead to recruitment of enough subjects, placing an advertisement in a local newspaper will be considered.

Participants in this study will be administered a standardised oral fat challenge: 30 gram fat per square meter body surface, in the form of cream containing 35 gram fat/100 ml.
Blood sampling will be performed at hourly intervals until 8 hours after the oral fat challenge (8 a.m. until 4p.m.) and will be drawn from an indwelling venous cannula that is placed for this purpose. The blood samples will be analysed for FGF19 and C4 (precursor of bile acid synthesis) in our laboratory. The results of these tests will not have clinical consequences for the subjects since this is a pilot study.

Study burden and risks

Patients are expected to fast overnight (no food after 0.00 hrs a.m) until 4 p.m. on the day of the study. This means they are not allowed to eat nor drink, except from drinking water. A standardized oral fat challenge (30 gram fat per square meter body surface, in the form of cream containing 35 gram fat/100 ml) will be administered. Blood sampling will be performed at hourly intervals until 8 hours after the oral fat challenge (08.00-16.00) via an indwelling venous cannula. The risks of this study are related to the use of this indwelling canula during the 8 hours of the study; hematoma, recurring haemorrhage and phlebitis 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 18-75 years old. Primary biliary cirrhosis (12), primary sclerosing cholangitis (12) diagnosed preliminary and independent of this study by liverbiopsy (PBC) or MRI (PSC) and 12 patients with IBD without PSC/PBC. 12 healthy subjects.

Exclusion criteria

Exclusion of other liver diseases, defined as:
- HBsAg and HCV-antibodies positive
- autoimmune hepatitis (ANA, SMA and AMA positive)
- hemochromatosis (abnormal iron-saturation)
- no Wilson's disease (abnormal ceruloplasmine)
- alcohol intake >2 units/day.
Previous ileocecal resection.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2010
Enrollment:	48
Type:	Anticipated

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
CCMO	NL32356.018.10