HSPG expression in non alcohol steatosis hepatitis in type II diabetes

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Assessment of hepatic HSPG*s in NASH associated dyslipidemia in 8 subjects with DM2 associated NASH (insulin resistant, n=8) vs NASH in FHBL (non insulin resistant, n=8) and control subjects (hemochromatosis, n=8)

Ethical review	Approved WMO
Status	Pending
Health condition type	Hepatic and hepatobiliary disorders
Study type	Observational invasive

Summary

ID

NL-OMON33031

Source
ToetsingOnline

Brief title
HSPG in NASH

Condition

- Hepatic and hepatobiliary disorders
- Diabetic complications

Synonym
diabetes, glucose intolerance

Research involving
Human

Sponsors and support

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

Intervention

Keyword: HSPG, hypertriglyceridemia, liverbiopsy, NASH, type 2 diabetes

Outcome measures

Primary outcome

HSPG expression will be altered (HS synthesizing enzymes: EXT/NDST/OST

decreased and HS degrading enzymes: SULF2 and heparinase increased) in DM2

Secondary outcome

Second Objective: HSPG expression is linearly correlated with increased levels

of triglyceride rich lipoproteins in non-fasting blood samples

Third objective: HSPG expression is inversely correlated with insulin

resistance

Study description

Background summary

Nonalcoholic steatosis hepatitis (NASH) is one of the most common causes of chronic liver injury in many countries. Currently there is no therapeutic intervention to reduce or cure NASH associated dyslipidemia. NASH is frequently seen in patients with type 2 diabetes mellitus (DM2) and tends to be associated with insulin resistance. However, patients with familial hypobeta lipoproteinaemia (FHBL) are also characterized by NASH yet were recently characterized NOT to have insulin resistance. Thus, different genetic factors driving different pathophysiological mechanisms are likely to be important for the development of NASH. Animal studies have indicated a role for heparansulphate proteoglycans (HSPG) in the development of NASH associated dyslipidemia and insulin resistance. We would therefore like to investigate whether changes in expression of HSPG synthesizing and degrading enzymes are associated with presence of dyslipidemia and insulin resistance in NASH

Study objective

Assessment of hepatic HSPG*s in NASH associated dyslipidemia in 8 subjects with DM2 associated NASH (insulin resistant, n=8) vs NASH in FHBL (non insulin

resistant, n=8) and control subjects (hemochromatosis, n=8)

Study design

Case control study

Study burden and risks

Liverbiopsy and fibroscan performed by experienced hepatologist, venapuncture for lipidprofile and determination in insulinresistance (HOMAr) will be performed. A liverbiopsy is routine test performed at dept of Hepatology for patientcare and is associated with a very low complication risk. As we only aim to include patient who will need liverbiopsy for clinical staging of liverdisease, the benefit for the patient will be accurate information on stage of liverdisease as well as prognosis. Moreover, from a scientific point of view this observational study will help us identify the role of heparansulfates in development of DM2 associated NASH vs non insulin resistant stages (FHBL). We believe that the information gathered from this study as well as potential therapeutic insights for NASH outweigh the burden of the interventions.

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

Caucasian males aged between 18 and 60 years of age with either type 2 diabetes mellitus or FHBL AND presence of ultrasound confirmed NASH in conjunction with elevated liverfunction tests. Subjects with stable hereditary hemochromatosis (treated with venesection therapy) who need a liverbiopsy for staging of disease will be used as controls

Exclusion criteria

Use of medication which is known to influence cholesterol metabolism, an active malignancy or presence of a contraindication for liver biopsy

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):	01-09-2009
Enrollment:	24
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	NL29252.018.09