Triglyceride clearance in subjects with heterozygous FH and triglyceride-linked SNPs in heparan sulphate biosynthesis

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Assessment of triglyceride clearance in a FH population with variations in heparan sulfate biosynthesis.

Ethical review	Approved WMO
Status	Pending
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Observational invasive

Summary

ID

NL-OMON34723

Source
ToetsingOnline

Brief title
Twitter

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
hypertriglyceridemia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: heparan sulfate, triglyceride

Outcome measures

Primary outcome

Triglyceride clearance

Secondary outcome

LPL binding capacity

Urine albumin and glycosaminoglycan profile

Study description

Background summary

Hypertriglyceridemia is an independent risk factor for cardiovascular disease and can be caused by decreased clearance of triglyceride-rich lipoproteins(TRLs) in the liver. In this protocol we will focus on a recently discovered pathway in which TRLs are cleared through heparan sulfate proteoglycans (HSPGs)-assisted endocytosis in the liver. Animal research has elucidated many of the steps in this process but human relevance still remains to be determined. Our hypothesis is that HSPGs are instrumental in the removal of TRLs from the circulation in humans. We hypothesize that HSPGs are instrumental in the clearance of TRLs from the circulation in humans. An important gene in this proces, NDST, codes for N-deacetylase/ N-sulfotransferase, which determines sulfation of heparan sulfate, a glycosaminoglycan that is present throughout the human body. Patients with FH have a mutation in the LDL receptor, and therefore can clear the TRLs less well. Because clearance in this situation is more dependent on HSPGs, genetic variation might result in clearance variation. We would like to investigate whether individuals with a decrease in HSPG sulfation show a decrease triglyceride clearance.

Study objective

Assessment of triglyceride clearance in a FH population with variations in heparan sulfate biosynthesis.

Study design

In the current study we want to evaluate the triglyceride clearance in a population of FH individuals characterized by the NDST tag SNP:
TT (10 individuals wildtype)
GT (10 individuals heterozygous allele)
GG(10 individuals homozygous allele)

* Oral fat loading test (OFLT) to investigate lipid clearance
* LPL test to determine LPL binding
* Standard CV risk biochemistry panel(incl. Cholesterol/crp/hba1c). Also plasma/urine samples for determination of total glycosaminoglycan concentration/sulfation.

Intervention

1. Fat loading test with subsequent blooddrawing
2. LPL-test using heparin

Study burden and risks

Fat loading test is a routine test in our department which requires repetitive blood sampling from an indwelling venous catheter after the consumption of cream and Vitamin A. The low dose of heparin used for the LPL test will not cause any side effects. We believe the information gathered from this study outweighs the burden of these 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

Heterozygous mutation in LDL receptor (heterozygous Familial Hypercholesterolemia)

Exclusion criteria

diabetes

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):	01-04-2010

Enrollment:	30
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	NL31380.018.10