Glycosylation Defects causing DYslipidemia

Published: 14-01-2014
Last updated: 23-04-2024

To characterize the dyslipidemias and their consequences in carriers of mutations in glycosylation genes.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and hereditary disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON38669

Source
ToetsingOnline

Brief title
GiDDY

Condition

- Congenital and hereditary disorders NEC
- Lipid metabolism disorders

Synonym
cholesterol disturbances, Dyslipidemia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Congenital-Disorders-of-Glycosylation, Dyslipidemia, Glycosylation, Heterozygosity

Outcome measures

Primary outcome

Correlation between genetic glycosylation defects and lipid profile.

Secondary outcome

- Correlation between genetic glycosylation defects and postprandial

triglyceride clearance

- Correlation between genetic glycosylation defects and fat percentage found

at 1H-MR spectroscopy of the liver.

- Difference between vessel wall dimensions (total wall volume, mean wall area,

mean wall thickness, normalized walll index measured by MRI), wall shear stress

(measured by MRI) between subjects with genetic defects in glycosylation and

healthy non-affected family members or healthy control subjects

Study description

Background summary

Dyslipidemia is a major driver of atherosclerotic cardiovascular disease (CVD), the leading cause of death worldwide.Recently, we identified an entirely new group of dyslipidemias: those caused by defective glycosylation of proteins involved in lipid metabolism.
Our studies have identified a variety of aberrant lipid profiles in CDG patients. For example, we found severe hypocholesterolemia and hypobetalipoproteinemia in a series of nineteen type 1 CDG patients.
Given the severe phenotype in CDG patients generally including mental retardation, it is not possible to study whether the dyslipidemias observed in these patients affect postprandial lipid profiles, hepatic lipid storage and the development of atherosclerotic cardiovascular disease. Yet such studies are feasible in heterozygous family members of these patients, who do not display a

severe phenotype, are otherwise healthy, but in whom alterations in plasma cholesterol concentrations have been reported (OMIM #601785). Furthermore, a pilot study of six obligate heterozygous parents of patients with ALG6-CDG showed the same phenotype as in the CDG patients: extremely low values for total cholesterol and low-density lipoprotein (LDL) cholesterol (below the 5th percentile for age and gender) and low apolipoprotein B.

Study objective

To characterize the dyslipidemias and their consequences in carriers of mutations in glycosylation genes.

Study design

This study will focus on (pre- en postprandial) cholesterol profiles, hepatic lipid storage and atherosclerosis in individuals with genetic defects of glycosylation and their family members. The results obtained in genetically affected subjects are compared with non-affected family members that are matched for relevant parameters. If an insufficient number of non-affected relatives volunteer, we will complement the control group with unrelated matched controls recruited by advertisement.

Study burden and risks

The risks involved with participating in this study are estimated to be low with blood withdrawal and imaging without radiotion exposure (MRI) being the main study methods.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Included are all healthy heterozygous carriers and non-affected family members of patients diagnosed with congenital disorder of glycosylation, aged 18 or older. Healthy individuals will be included as a control population.

Exclusion criteria

- Known systemic disorders such as hepatic, renal, hematologic, and malignant diseases or any clinically significant medical condition that could interfere with the conduct of the study in the opinion of the investigator.
- Standard contra-indications to MRI based on physicians experience and current practices
- Claustrophobia
- Metal in the body, as a result of e.g. osteosynthetic material, pacemaker implantation or artificial cardiac valves.
- Inability or unwillingness to comply with the protocol requirements.;When dyslipidemia is present, exclusion criteria are all secondary causes of dyslipidemia (nephrotic syndrome, adrenal insufficiency, renal insufficiency, hypothyroidism, heavy alcohol use, cholestasis, use of protease inhibitors).

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:	Recruitment stopped
Start date (anticipated):	07-05-2014
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	14-01-2014
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	NL46676.018.13