Variation of non-cholesterol sterol levels in a population of mildly hypercholesterolaemic subjects

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Primary Objective: What is the variation in non-cholesterol sterol levels in a large population of mildly hypercholesterolaemic, but otherwise healthy subjects?Secondary Objective: Can genetic variation in proteins involved in cholesterol…

Ethical review	Approved WMO
Status	Pending
Health condition type	Lipid metabolism disorders
Study type	Observational invasive

Summary

ID

NL-OMON32378

Source
ToetsingOnline

Brief title
'DAHLIA-1

Condition

- Lipid metabolism disorders

Synonym
mild hypercholesterolaemia, slightly elevated cholesterol

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Nederlandse Hartstichting

Intervention

Keyword: cholesterol absorption, genetic polymorphisms, hypercholesterolemia, non-cholesterol sterols (plant sterols)

Outcome measures

Primary outcome

The variation in non-cholesterol sterol levels in 160 mildly

hypercholesterolaemic subjects.

Secondary outcome

The differences in genetic polymorphisms in genes coding for NPC1L1 and ABCG5

and ABCG8 proteins between subjects with high and low non-cholesterol sterol

levels.

Study description

Background summary

Intestinal cholesterol absorption varies considerably in the general population, ranging between 20-70%. Previous studies have suggested a classification of subjects with high or low cholesterol absorption. In most studies, levels of non-cholesterol sterols have been used as markers for cholesterol absorption and synthesis respectively. Based on these markers, a classification of subjects with high or low absorption, the so called high and low absorbers, has been suggested. The high absorbers are thought to have elevated cholesterol levels due to high absorption, whereas the low absorbers have elevated levels based on high synthesis. Subsequently, it has been suggested that high absorbers do not or hardly benefit from statin treatment alone, either with respect to cholesterol reduction and the recurrence of CHD. Therefore, the high absorbers may benefit from the addition of cholesterol absorption inhibitors.

This underscores the need to identify high absorbers in order to treat them accurately.
Therefore, easy accessible markers are essential in clinical practice. However, whether high and low absorbers indeed can be identified based on plasma levels of non-cholesterol sterols has never been verified by means of actual

cholesterol absorption measurement. Besides the fact that the validity of these markers may be questionable, they also do not provide any indication regarding the quantity of cholesterol that is absorbed.

In a future study, we will investigate the actual cholesterol absorption rates in mildly hypercholesterolaemic subjects, who are predefined as high and low absorbers based on their plasma levels of non-cholesterol sterols. In order to do so, we will first measure non-cholesterol sterol levels in a relatively large population of mildly hypercholesterolaemic, but otherwise healthy, subjects. This will be done in the current study.
Hereby we can determine the variation of non-cholesterol sterol levels in this population in order to evaluate whether this corresponds to the variation in cholesterol absorption markers previously found in literature. In addition, we will investigate whether genetic variation in genes coding for proteins involved in cholesterol homeostasis, such as NPC1L1 and ABCG5 and G8, can explain the variability in non-cholesterol sterol data. Combined with the data of the future cholesterol absorption studies, this genetic variation might explain variation in cholesterol homeostasis between high and low cholesterol absorbers.

Study objective

Primary Objective: What is the variation in non-cholesterol sterol levels in a large population of mildly hypercholesterolaemic, but otherwise healthy subjects?
Secondary Objective: Can genetic variation in proteins involved in cholesterol homeostasis, such as Niemann-Pick C1-like 1 (NPC1L1) and the ATP binding cassette (ABC) G5 and G8 halftransporters, explain the variation in non-cholesterol sterols?
In addition, this study will be used for selection of participants for our future studies.

Study design

A cross-sectional cohort study. The study comprises a single measurement of non-cholesterol sterol and lipoprotein levels in 160 mildy hypercholesterolemic, but otherwise healthy volunteers.

Study burden and risks

Hardly any risks are involved in this study. A single venepuncture, during which a maximum of 50ml blood will be collected, will be done. In case participants are already treated with cholesterol lowering medication, they will be asked to discontinue this medication during a 6-week period. These volunteers will undergo a second venepuncture. We do not expect any unfavorable

effects of discontinuation of this medication during 6 weeks.

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

Healthy male and female subjects, aged 18-65 years old, with an LDL-cholesterol concentration between 3.0-5.0 mmol/L.

Exclusion criteria

Excluded are persons with a genetic hyperlipoproteinemia like familial hypercholesterolemia, LPL-deficiency, familial dysbeta lipoproteinemia and familial hypertriglyceridemia. Also

people with diabetes mellitus, severe hypertriglyceridemia, uncontrolled hypertension or a history of arterial disease including unstable angina, myocardial infarction, recent transient ischaemic attacks or a cerebro-vascular accident, will be excluded.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2007
Enrollment:	160
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	NL20369.018.07