The difference in fractional cholesterol absorption between subjects with high versus low plasma campesterol levels

Published: 14-01-2009
Last updated: 05-05-2024

What is the difference in fractional cholesterol absorption, measured by means of the dual isotope method, between mildly hypercholesterolemic subjects with high plasma campesterol levels compared to subjects with low plasma campesterol levels?

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

Summary

ID

NL-OMON32507

Source
ToetsingOnline

Brief title
DAHLIA-2

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, hypercholesterolemia, non-cholesterol sterols (plant sterols)

Outcome measures

Primary outcome

The difference in fractional cholesterol absorption, as measured by means of

the dual isotope method, between subjects with high and low plasma campesterol

levels respectively.

Secondary outcome

not applicable

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 cholesterol 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-choelsterol 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 the current study we will measure actual cholesterol absorption rates in mildly hypercholesterolemic subjects, who have been identified as high and low cholesterol absorbers, based on their plasma plant sterol levels (campesterol levels). For this purpose, we have measured plant sterol concentrations in a relatively large population of 160 individuals (Dahlia-1 study). In the present study, cholesterol absorption will be measured in the 6 subjects with the highest and the 6 subjects with the lowest campesterol concentrations respectively. This will enable us to investigate whether plasma plant sterols can be used as a marker of cholesterol absorption. If this is indeed the case, in a series of future studies, we will evaluate whether high and low absorbers also differ in other aspects of cholesterol metabolism and whether they respond differently to cholesterol lowering therapies.

Study objective

What is the difference in fractional cholesterol absorption, measured by means of the dual isotope method, between mildly hypercholesterolemic subjects with high plasma campesterol levels compared to subjects with low plasma campesterol levels?

Study design

This is a cross-sectional study, which comprises a single cholesterol absorption measurement by means of the dual isotope method. First, subjects will attend a screening visit, consisting of a medical history, physical examination and blood sampling to determine lipid profile. At the second study visit the actual cholesterol absorption measurement will start, consisting of a bloodsample with an ensuing single intravenuous administration of 13C cholesterol and an oral administration of 2H7 cholesterol via a standardized breakfast. Subjects will return to their homes and will attend the AMC in the subsequent three mornings for additional blood sampling. Percent of intestinal cholesterol absorption will be calculated by dividing the plasma ratio of 13C and 2H7 enrichment by the ratio of 13C and 2H7 cholesterol species administered to the subjects.

Study burden and risks

Hardly any risks are involved in this study. At screening, a single blood sample will be obtained. At the second visit, an intravenous catheter will be inserted, followed by four blood drawings, during the following three days. This may lead to a hematoma at the site of venepuncture. Furthermore, two kinds of cholesterol markers will be administered to the study subjects, both orally and intravenously. These so-called stable isotopes are not harmful, as they behave as their natural substrates. Finally, we do not expect any unfavorable effects of discontinuation of any possible cholesterol lowering

medication, neither from a possible 8-week cessation of fish oil or fibrates.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1015 AZ Amsterdam
Nederland
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1015 AZ Amsterdam
Nederland

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 and 5.0 mmol/l, who participated in the Dahlia-1 study and belong to the 6 subjects with the highest or to the 6 subjects with the lowest plasma campesterol levels respectively. One subject with the subsequently highest campesterol levels will be asked to undergo a cholesterolabsorption measurement as well, in order for us to test the quantification of cholesterol isotopes by our laboratory.

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 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):	01-12-2008
Enrollment:	13
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	NL25657.018.08