Remnant cholesterol: the missing lipid

Published: 06-05-2015
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The main objective of this study is to assess the effect of elevated remnant cholesterol levels on arterial wall inflammation.

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

Summary

ID

NL-OMON41840

Source
ToetsingOnline

Brief title
The missing lipid

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
arterial wall thickening, atherosclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: CVON Genius beurs

Intervention

Keyword: Arterial wall inflammation, Atherosclerosis, Remnant cholesterol

Outcome measures

Primary outcome

The main study parameters are arterial wall inflammation (target-to-background

ratio) measured by 18F-FDG PET/CT and vessel wall dimensions measured by MRI.

Secondary outcome

- Trans endothelial migration (TEM) of monocytes

- Monocyte subtyping by FACS analysis using a CD14, CD16 and HLA-DR backbone.

- In vitro cytokine production by using isolated monocytes of subjects.

- Epigenetic changes in genes identified with FACS or in vitro stimulation

assays.

Study description

Background summary

Recent data show that elevated levels of remnant cholesterol are causally associated with ischemic heart disease. Remnant cholesterol is the cholesterol content of triglyceride rich lipoproteins, derived from chylomicrons and very-low-density-lipoproteins (VLDL). A pathophysiological explanation for the relationship with ischemic heart disease is that remnants, only slightly bigger in size than LDL, yet with a higher cholesterol load, can get trapped in the arterial wall and give rise to foam cell formation and local inflammation. Importantly, remnants, in contrast to LDL, do not require to be oxidized prior to macrophage engulfment. Recognizing the key role of systemic inflammation in atherosclerosis, these particles are also associated with elevated C-reactive protein (CRP) levels.

18F-FDG PET/CT is a nucleair imaging technique which measures metabolic activity by labelling glucose with a PET tracer (18-fluor), and is used at a read-out for the atherosclerotic plaque inflammation.

Study objective

The main objective of this study is to assess the effect of elevated remnant

cholesterol levels on arterial wall inflammation.

Study design

This study is designed as a single centre, observational, case-control study. After screening for eligibility, all subjects will undergo cardiovascular risk assessment and laboratory testing. Thereafter, all subjects will undergo subsequently an 18F-FDG PET/CT scan and MRI scan. Furthermore, trans endothelial migration (TEM) and monocyte activation will be assessed.

Study burden and risks

The results of this study contribute to better understanding of the mechanism by which elevated remnant cholesterol causes IHD. This helps us to comprehend the role of this lipid fraction in cardiovascular disease and the effects of current treatments in this state as well as design new treatments in the future. Individual subjects will gain no direct benefit from this study. The risk of participating in this study is estimated to be low. MRI is a safe imaging technique without radiation exposure. The exposure to radiation related to 18F-FDG PET/CT scan is 4.1 mSv.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Subjects with diagnosis of Familial dysbetalipoproteinemia (type III hyperlipoproteinemia)
- Aged 50 years or older
- No treatment with lipid lowering drugs or willing to stop lipid lowering therapy for 6 weeks prior to baseline measurements

Exclusion criteria

1 . Malignant diseases or any other clinically significant medical condition that could interfere with the conduct of the study in the opinion of the investigator
2 . Standard contra-indications to MRI and 18F-FDG PET/CT based on physicians experience and current practices: Claustrophobia, metal in the body, as a result of e.g. osteosynthetic material, pacemaker implantation of artificial cardiac valves.
3. Clinical signs of acute infection and/or CRP > 10
4 . Participation in a scientific study with radiation exposure in the year prior to inclusion or planned radiation exposure in the next year due to participation in a research project with radiation exposure or for clinical reasons
5. Recent (< 1 month prior to screening) or current treatment with medications that may have a significant effect on plaque inflammation, including: oral, rectal, or injectable corticosteroids or immunosuppressive medications
6. Use of lipid lowering drugs in the last 6 weeks prior to baseline measurements
7. Cardiovascular event in the last 3 months prior to baseline measurements

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-07-2015
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	06-05-2015
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	NL52205.018.15