Characterization of functionality of HDL in patients with familial hypercholesterolemia

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1. to investigate whether the known chronic inflammatory and hyperoxidative state in patients with severely increased LDL is associated with dysfunctional HDL.2. to investigate whether CVD in FH is associated with dysfunctional HDL.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON29851

Source
ToetsingOnline

Brief title
Functionality of HDL in FH patients

Condition

- Endocrine disorders congenital
- Lipid metabolism disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: cholesterol, FH, HDL, oxidation

Outcome measures

Primary outcome

Compositional and structural properties of HDL subfractions as well as their

protective activity towards LDL oxidation will be characterised.

Secondary outcome

Not applicable

Study description

Background summary

Heterozygous familial hypercholesterolemia (FH) is characterized by high plasma concentrations of atherogenic low-density lipoprotein cholesterol (LDL) due to a mutation in the LDL-receptor gene. Clinically, FH results in tendinous xanthomas and premature coronary heart disease.
LDL plays a key role in the deposition of cholesterol in the arterial wall, leading to atherosclerotic plaque formation; this process is intimately associated with induction of oxidative stress in arterial wall cells. This oxidative stress leads to formation of oxidized LDL, which has multiple atherogenic properties.
High-density lipoprotein cholesterol (HDL) has cardioprotective properties such as: reverse cholesterol transport from the arterial wall and the capacity to protect LDL against oxidative stress. However, HDL particles are highly heterogeneous in their anti-oxidative activities. There are suggestions that the functionality of HDL in FH patients is diminished and that elevated levels of HDL-associated acute-phase proteins, such as serum amyloid protein A (SAA) are present. It is believed that these proteins displace apoA-1 from the HDL particle, which could make HDL small en dense and decrease its anti-oxidant properties.
However, data on HDL functionality in FH patients are scarce. Because of the high prevalence of cardiovascular disease in FH patients, it is important to explore the functionality of HDL in more detail in these patients. Ultimately, this could lead to better treatment strategies for this population.

Study objective

1. to investigate whether the known chronic inflammatory and hyperoxidative state in patients with severely increased LDL is associated with dysfunctional HDL.
2. to investigate whether CVD in FH is associated with dysfunctional HDL.

Study design

Observational, cross-sectional

Study burden and risks

Not applicable

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

Diagnosis of Familial Hypercholesterolemia, age between 18 en 70 years, LDL-cholesterol level>200mg/dl, triglyceride-level<150mg/dl

Exclusion criteria

Type 2 diabetes mellitus, presence of inflammatory or infectious diseases, acute myocardial infarction or stroke during last six months, smoking, use of anti-inflammatory drugs (except aspirin) or anti-oxidant vitamins during last month

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):	10-10-2006
Enrollment:	36
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	22-05-2006
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-06-2009
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL11648.078.06