Effect of Statins on epigenetic reprogramming of monocytes in patients with elevated levels of LDL: an observational study

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

Summary

ID

NL-OMON42146

Source
ToetsingOnline

Brief title
Statins and trained immunity

Condition

- Lipid metabolism disorders

Synonym
dyslipidemia, high cholesterol, hypercholsterolemia

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: De Nederlandse Hartstichting

Intervention

Keyword: epigenetic reprogramming, inflammation, monocytes, Statins

Outcome measures

Primary outcome

Epigenetic changes in the promotor regions of pro-inflammatory cytokines in

monocytes before and after statin treatment

Secondary outcome

cytokine release upon stimulation with TLR agonists and ex vivo

characterization of monocytes

Study description

Background summary

The innate immune system plays a pivotal role in the development and progression of atherosclerosis. Recently, it was reported that monocytes can develop a long-lasting immunological memory after stimulation with various microorganisms, but also with oxidized LDL, which has been termed *trained innate immunity*. This memory is induced by epigenetic reprogramming.

We hypothesize that trained monocytes augment atherogenesis. Intensive lipid lowering with statins is capable of lowering plaque inflammation in patients at high risk for cardiovascular events. In addition to their lipid lowering effects, the pleiotropic effects of statins include lowering of inflammation. Here we hypothesize that statins lower epigenetic changes in monocytes responsible for increased inflammation.

Study objective

The main objective is to study whether patients with elevated levels of LDL show increased H3K4 trimethylation in the promoter regions of pro-inflammatory cytokines and have an augmented ex vivo TLR agonist-induced cytokine production in isolated monocytes compared to control patients without atherosclerosis.

Next we will study the effect of Statins on the increased H3K4 trimethylation.

Study design

Observational study

Study burden and risks

There is no risk associated with participation. After signing for informed consent, additional blood will be drawn for the ex vivo experiments

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

Elevated levels of LDL in the blood (LDL >4.9 mmol/l)
Age > 18 years

Exclusion criteria

- Current lipid lowering treatment
- Previous cardiovascular events
- Known malignant disorders or any clinically significant medical condition that could interfere with the conduct of the study in the opinion of the investigator.
- Inability or unwillingness to comply with the protocol requirements, or deemed by investigator to be unfit for the study.
- Clinical signs of acute infection

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:	Recruiting
Start date (anticipated):	04-06-2015
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	09-12-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-08-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL50608.091.14