Multi-locus approach in pharmacogenetics. Application in the cholesterol lowering and anti-inflammatory pathways of statins

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Myocardial disorders
Study type	Observational non invasive

Summary

ID

NL-OMON29788

Source
ToetsingOnline

Brief title
Multi-locus approach in pharmacogenetics of statins

Condition

- Myocardial disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Myocardial infarction

Research involving
Human

Sponsors and support

Primary sponsor: Zorgonderzoek Nederland (ZON)
Source(s) of monetary or material Support: NWO vernieuwingsimpuls VENI

Intervention

Keyword: Anti-inflammatory, Pharmacogenetics, Statins

Outcome measures

Primary outcome

We will use different statistical methods to study the interaction between

statin use, SNPs, and MI.

Secondary outcome

na

Study description

Background summary

Multi-locus approach in pharmacogenetics. Application in the cholesterol lowering and anti-inflammatory pathways of statins

Pharmacogenetics aims to discover genetic determinants of drug response. Statins reduce the risk of coronary artery disease by approximately 30% in subjects with hypercholesterolemia and in high-risk normocholesterolemic subjects. These reductions, however, are average effects for patients included in trials; in subpopulations effects might differ. The risk reducing effect of statins is both due to their cholesterol lowering effects and to other pleiotropic effects such as anti-inflammatory effects. This project will determine if genetic variation in genes that are involved in lipid lowering and in anti-inflammatory effects of statins can predict inter-individual differences in MI reduction.

Study objective

The aim of this project is to study SNPs in genes involved in the cholesterol lowering pathway and in the anti-inflammatory pathway of statins to explain differences in the protective effect of statins against myocardial infarction

(MI). A second aim is to test and improve methods that can be used in multi-locus approaches in (pharmaco-) genetics.

Study design

A nested case-control study in a hypercholesterolemic cohort (total cholesterol >=5.0 mmol/l or use of cholesterol lowering drugs) will be performed in the population-based Pharmaco Morbidity Record Linkage System (PHARMO: www.pharmo.nl). In the PHARMO database pharmacy dispensing data (including type of drug, dose, dispensing date, dose regimen, duration of use, and prescriber) of a representable sample of all Dutch pharmacies is linked to a nationwide registration of hospital discharge records (LMR), these data include diagnostic information from ICD-9-CM and procedures during hospital stay (since 1985). At this moment drug use of 2,000,000 subjects in 25 areas in the Netherlands is monitored in PHARMO, additional clinical information is available, because there is a link with general practitioner*s practice databases and clinical laboratoria.
Potential participants will be invited to participate through their community pharmacy, they will be asked to sign informed consent and to complete a questionnaire on cardiovascular risk factors and disease history. Subjects will be asked to perform a saliva sample to collect cells for DNA extraction.

Study burden and risks

Patients will be asked to perfom a saliva sample. Furthermore the patient will be asked to fill out a questionnaire (this will take approximately 30 minutes). Patients can perform the buccal swaps and the filling out the questionnaire at home. Information obtained from DNA analyses might be a burden to the patient because of the knowledge about future risk of disease, and problems with insurance. This DNA information won't be shared with the patient.

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

age > 18 years
Hypercholesterolemia: defined as total cholesterol levels >5 mmol/l or use of cholesterol lowering medication

Exclusion criteria

controls: Myocardial infarction in medical history

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-01-2007
Enrollment:	2400
Type:	Actual

Ethics review

Approved WMO

Date:	29-08-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL11666.041.06