Does atorvastatin reduce ischemia-reperfusion injury in humans in-vivo?

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To study the impact of 3 day exposure to atorvastatin 80mg on Annexin A5 targeting after ischemic exercise in the non-dominant forearm.

Ethical review	Approved WMO
Status	Pending
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON30203

Source
ToetsingOnline

Brief title
Ator01

Condition

- Coronary artery disorders

Synonym
ischemia reperfusion injury, myocardial infarction

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW,Pfizer

Intervention

Keyword: atorvastatin, ischemia reperfusion injury, myocardial infarction, preconditioning

Outcome measures

Primary outcome

Annexin A 5 targeting in the non dominant thenar muscle after ischemic

exercise, as a indicator for ischemia reperfusion injury

Secondary outcome

Fasting lipid profile before and after three day therapy with atorvastatin

80mg. Workload performed during ischemic exercise.

Study description

Background summary

3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (also known as statins) have been found to reduce cardiovascular events. This protective effect has been traditionally explained by lowering plasma cholesterol and subsequent reduced progression of atherosclerosis. However in animal experiments statins have also shown the ability to induce pharmacologic preconditioning and thereby reduce infarct size. This effect contributes to the beneficial effect of statins on reducing of cardiovascular events. In order to differentiate between these two mechanisms of protection we will study the effect of atorvastatin on ischemia reperfusion damage after a short exposure to atorvastatin, before the lipid lowering effect of atorvastatin becomes apparent.

Study objective

To study the impact of 3 day exposure to atorvastatin 80mg on Annexin A5 targeting after ischemic exercise in the non-dominant forearm.

Study design

Double blind-placebo controlled intervention study, cross-over design, single centre.

Intervention

in a cross-over design all volunteers receive 3 day treatment with atorvastatin

80mg daily or placebo. Between the active treatment period and the placebo period, a wash-out period of at least 4 weeks will be respected

Study burden and risks

Treatment with atorvastatin or placebo is not expected to harm the volunteers. Most reported side effects of atorvastatin are gastro-intestinal complains and myalgia. Ischemic hand gripping will temporarily result in pain in the forearm. This is completely reversible upon reperfusion. Administration of radiolabeled Annexin A5 results in an effective dose of less than 5 mSv, well within the range of accepted exposure to radioactivity for human research. Occurrence of an allergic reaction is theoretically possible upon administration of Annexin A5, however there have been no allergic reaction reported in all volunteers exposed to Annexin A5. The volunteers will not benefit directly from participating in this study.

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

-Male
-Age 18-50 years
-Informed consent
-Physical able to perform ischemic exercise

Exclusion criteria

-History of any cardiovascular disease
-Hypertension (in supine position: systole > 140 mmHg, diastole > 90 mmHg)
-Diabetes mellitus (fasting glucose > 7.0 mmol/L or random glucose > 11.0 mmol/L)
-Hyperlipidaemia (random total cholesterol > 6 mmol/l)
-Alanine-Amino-Transferase (ALAT) >90 U/L (more than twice the upper level of the normal range)
-Creatinine Kinase (CK) >340 U/L (more than twice the upper level of the normal range)
-Drug abuse
-Concomitant chronic use of medication
-Administration of radioactivity in research setting during the last 5 years
-Participation to any drug-investigation during the previous 60 days as checked with VIP check according to CRCN standard procedures

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-01-2007
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lipitor
Generic name:	Atorvastatin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	29-12-2006
Application type:	First submission
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
EudraCT	EUCTR2006-006706-29-NL
CCMO	NL15624.091.06