Short term statin treatment and endothelial dysfunction due to ischemia and reperfusion injury

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To study the protective effect of pretreatment (both 3 day and 7 day) with rosuvastatin and atorvastatin on flow mediated dilation after 15 minutes ischemia and 15 minutes reperfusion.

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

Summary

ID

NL-OMON33420

Source
ToetsingOnline

Brief title
Statins-IRI-FMD

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
ischemia and 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

Intervention

Keyword: flow mediated dilation, ischemia reperfusion injury, statin

Outcome measures

Primary outcome

Difference in flow mediated dilation before and after 15 minutes ischemia.

Secondary outcome

ecto-5*-nucleotidase activity after rosuvastatin and atorvastatin treatment (3

day and 7 day)

Study description

Background summary

Apart from their cholesterol lowering effects, statins have cholesterol-independent pleiotropic actions, such as upregulation of 5*-ectonucleotidase and up-regulation of NO-synthase that may increase tolerance against ischemia-reperfusion injury (IR-injury). Several animal studies have shown reduction of IR-injury as a result of statin treatment in both the heart and the kidney. Recently we have shown, using Annexin A5 targeting after voluntary ischemic exercise to assess IR-injury, a protective effect of a 7 day oral rosuvastatin treatment. A three day treatment with atorvastatin however failed to reduce annexin targeting.
Assessment of the flow mediated dilation of the brachial artery as measure of endothelial (dys)function, is a validated model to research effects of possible protective strategies and perform mechanistic experiments on IR-injury in humans in vivo.
We hypothesize that pretreatment with statins can increase endothelial tolerance against ischemia and reperfusion injury.

Study objective

To study the protective effect of pretreatment (both 3 day and 7 day) with rosuvastatin and atorvastatin on flow mediated dilation after 15 minutes ischemia and 15 minutes reperfusion.

Study design

placebo-controlled randomised double-blind trial

Intervention

Treatment with either rosuvastatin 20 mg, atorvastatin 80mg or placebo during either 3 or 7 days

Study burden and risks

Treatment with rosuvastatin or atorvastatin is not expected to harm the volunteers. Most reported side effects of rosuvastatin and atorvastatin are gastro-intestinal complains and myalgia. 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

- Age 18-50
- Written informed consent

Exclusion criteria

- Smoking
- 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)
- Hyperlipidemia (fasting total cholesterol >5.5 mmol/L or random cholesterol >6.5 mmol/L)
- Alanine amino transferase >90 U/L
- Creatine kinase >440 U/L
- Raised rabdomyolysis risk
o GFR <60 ml/min
o Overt clinical signs of hypothyroidism
o Myopathy in family history
o Alcohol abuse
- Concomitant chronic use of medication
- Participation to any drug-investigation during the previous 60 days as checked with VIP check.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-10-2009
Enrollment:	48
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	crestor
Generic name:	rosuvastatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	lipitor
Generic name:	atorvastatin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-08-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-09-2009
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	EUCTR2009-014831-18-NL
CCMO	NL29271.091.09