High dose statins in post-coarctectomy patients.

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To reduce atherosclerotic progression in post-coarctectomy patients.

Ethical review	Approved WMO
Status	Pending
Health condition type	Congenital cardiac disorders
Study type	Interventional

Summary

ID

NL-OMON31321

Source
ToetsingOnline

Brief title
High dose statins in post-coarctectomy patients.

Condition

- Congenital cardiac disorders
- Cardiac and vascular disorders congenital

Synonym
Coarctation, narrowing of the aorta

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ICIN

Intervention

Keyword: coarctectomy, hypertension, IMT, statine

Outcome measures

Primary outcome

The main study parameter is change in carotid IMT, determined by ultrasonography.

Secondary outcome

o the quality of life

o the concentration of serum lipids

o lipid lowering and time effects on the femoral vascular conduit

o liver- and renal function

o hypertension

o disproportionate systolic hypertension with exercise (cardiovascular exercise testing)

o exaggerated rise in systolic pressure in response to exercise (cardiovascular exercise testing)

o left ventricular hypertrophy (echocardiography)

o heart failure (echocardiography)

o cerebrovascular accident

o ruptured aortic aneurysm

o aortic volume (MRI)

o LVEDV, LVESV, EF, CO (MRI)

o pulse wave velocity through the thoracic aorta (MRI)

o extent of LV fibrosis (%) (MRI)

o the number of deaths

Study description

Background summary

Coarctation of the aorta is typically a discrete narrowing of the thoracic aorta just distal to the left subclavian artery. Coarctation of the aorta is a common malformation, accounting for 6 to 8 percent of all congenital heart defects.
The major clinical manifestation in adults with coarctation of the aorta is hypertension in the upper extremities, diminished or delayed femoral pulses, and low or unobtainable arterial blood pressure in the lower extremities. Although the blood pressure typically falls after successful repair, persistent or recurrent hypertension and disproportionate systolic hypertension with exercise are not uncommon. Normotensive patients, especially those repaired at an older age, often have an exaggerated rise in systolic pressure in response to exercise. The factors responsible for the persistent risk of hypertension after coarctation repair are not well understood.
Studies have shown decreased survival rates in post-coarctectomy patients1. The most common cause of this premature death was coronary artery disease, followed by sudden death, heart failure, cerebrovascular accident and ruptured aortic aneurysm.
Intima-media thickness (IMT) is nowadays considered a validated and reproducible endpoint for atherosclerosis2. In post-coarctectomy patients IMT is significantly increased3. Statin treatment might prevent additional damage and even lead to regression of existing damage in the main arteries of these patients. In a recent study of by Shukla et al4 it was shown that low-dose statins reduced progression of atherosclerosis as observed by carotid intima thickness in patients with known coronary heart disease and normal lipid values independent of lipid lowering. The study favours use of this therapy in patients with normal cholesterol levels. A large intervention trial in post - coarctectomy patients is needed to confirm the benefit of statin treatment on the long term outcome in these patients.

Study objective

To reduce atherosclerotic progression in post-coarctectomy patients.

Study design

Multi-centre, prospective, randomised trial with double-blinded evaluation of patient outcomes. Follow-up three years.

Intervention

One group daily receives a 80 mg tablet of atorvastatine, the other group will

not get a statin or placebo.

Study burden and risks

All investigations, blood analysis excepted, are non-invasive and free of risk. The burden for the patients mainly consists of the time that is consumed by the investigations, namely: history taking + physical examination (15 min); Quality-of-Life score (15 min); laboratory tests (lipids, glucose, renal function, liver function, CPK); EKG (10 min); exercise testing; echocardiogram (30 min); IMT measurement (1/2 hour); MRI (1/2 hour); ambulatory blood pressure monitoring (24 hr), pulse wave analysis (45 min).

Possible side effects of LIPITOR:
1) Serious side effects in a small number of people:
- Rhabdomyolysis and myalgia: muscle weakness or pain, sometimes in combination with fever or tiredness. Rhabdomlyolysis may lead to increased CK serum levels and decrease renal function.
- Decreased liver function.

2) The most common side effects of LIPITOR are:
Headache, constipation, diarrhea and rash. These side effects often disappear by themselves.

The efficacy and safety of atorvastatin 80 mg daily has been shown in several studies5,6. Treatment with atorvastatin resulted in regression of carotid IMT in the ASAP study7.

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

Post-coarctectomy patients

Exclusion criteria

- Incapable of giving informed consent
- Hypersensitivity to atorvastatin or any of its help substances
- Current treatment with statins.
- Indication for treatment with statins based on the CBO-guideline for cardiovascular risk management.
- Raised plasma transaminases level > three times limiting value
- Raised CPK level > five times limiting value
- Myopathia
- Pregnant or nursing women (a pregnancy test is offered to every female patient within the fertile age) or desire to have children within the study period

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2007
Enrollment:	150
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO

Date:	28-09-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2007-003883-23-NL
CCMO	NL18596.018.07