The role of alpha2-adrenergic receptors in bone remodeling.

Published: 01-11-2012
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The objective of the study is to investigate the effect of alfa2-adrenoceptors on bone turnover.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bone, calcium, magnesium and phosphorus metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON37196

Source
ToetsingOnline

Brief title
Alpha2-adrenoceptors and bone turnover.

Condition

- Bone, calcium, magnesium and phosphorus metabolism disorders
- Bone disorders (excl congenital and fractures)

Synonym
Osteoporosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Bone, Osteoporosis, Sympathetic nervous system

Outcome measures

Primary outcome

The main study parameter is the change in serum concentrations of collagen type 1 cross-linked C-telopeptide (CTX) on the intervention and on the control day.

Secondary outcome

The secondary objective is the change in catecholamine levels and serum concentration of another bone turnover marker, procollagen type I N propeptide (P1NP) on the intervention day (clonidine 0.3mg) and on the control day (no intervention).

We will also investigate whether osteoclasts are responsive to the alpha2-adrenoceptor agonist clonidine in vitro, by measuring osteoclast activity and formation.

Study description

Background summary

Osteoporosis is a common disease that is characterized by low bone mass with microarchitectural disruption and skeletal fragility, resulting in increased risk of fracture.
Recent research suggests that beta2-adrenoceptor is not the single receptor involved in bone turnover regulation. In a mouse model of chronic elevated sympathetic tone owing to double knockout of alpha2A/2C-adrenoceptors, mice present a phenotype of high bone mass, with an increased formation and decreased bone resorption. Further investigation of the specific functions of the alpha2-adrenoceptors and their interaction in bone metabolism in humans will be needed to enhance our understanding of the role of the SNS in the skeleton, which certainly will contribute to novel strategies for the treatment

of osteoporosis.

Study objective

The objective of the study is to investigate the effect of alfa2-adrenoceptors on bone turnover.

Study design

Open label randomized controlled cross-over trial and observational study.

Intervention

All participants will visit the AMC on three different occasions. On the first two days subjects will receive either a single oral dose of clonidine 0.3mg or no intervention. Participants will be randomized to either clonidine followed by no intervention or no intervention followed by clondine. The first day will be followed by a wash out period of 1 week. Two weeks after the second day subjects will visit the AMC a third day for a single blood sample without intervention.

Study burden and risks

During the intervention, participants will have to take a single dose of oral clondine. Clonidine, an alpha2-adrenergic agonist, is widely prescribed in patients with hypertension, menopausal flushing, as migraine prophylaxis and during withdrawal from opiates. The most common side effects of clonidine treatment are sedation, dry mouth, hypotension, fatigue and dizziness. Other less common side effects are headache, diarrhea, obstipation, nausea, vomiting, nervousness, bradycardia, insomnia, nightmares, confusion and hallucinations. The latest being less likely considering patients will only receive a single dose. Fasting blood samples will be drawn on the three days that patients visit the AMC. The total volume of blood samples during the entire protocol will not exceed 286 ml. Risks associated with venous blood sampling is also negligible.

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: 18-70 years

Exclusion criteria

- Hypersensitivity to the active substrate or to any of the excipients
- Severe bradycardia, like sick sinus syndrome and a second or third degree atrioventricular block
- Use of antihypertensive drugs (including diuretics)
- Use of drugs with negative effects on heart rhythm
- Any medication or disease influencing bone turnover
- Inability to give informed consent
- RR < 110/70 mmHg at the start of the experiment

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-01-2013
Enrollment:	12
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	01-11-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-12-2012
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

ID: 23544
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2012-004634-41-NL
CCMO	NL42339.018.12
OMON	NL-OMON23544