The nervous system and bone.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23544

Source
NTR

Brief title
Alpha2Bone

Health condition

Osteoporosis

Sponsors and support

Primary sponsor: Academic Medical Center (AMC), Amsterdam
Source(s) of monetary or material Support: Academic Medical Center (AMC), Amsterdam

Intervention

Outcome measures

Primary outcome

The primary objective is to study the effect of clonidine, an alpha2-adrenergic receptor agonist, on bone resorption. We will do this by comparing the change in the bone resorption marker collagen type 1 cross-linked C-telopeptide (CTX) in healthy male and female subjects who receive a single dose of clonidine and no intervention. The changes in CTX levels on the intervention day (clonidine 0.3mg) and on the control day (no intervention) will be compared.

Secondary outcome

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

Study description

Background summary

Rationale:

Osteoporosis is a common disease that is characterized by low bone mass with microarchitectural disruption and skeletal fragility, resulting in increased risk of fracture. Normally, bone quality is maintained by a dynamic process, known as bone remodeling. Evidence demonstrates that the sympathetic nervous system negatively regulates bone formation and positively regulates bone resorption via beta2-adrenoceptor signaling. Regardless of the evidence that beta2-adrenoceptor signaling is a key element in the regulation of bone remodeling, both pharmacologic and genetic experiments have produced inconclusive results. 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. It was also found that clonidine induced osteoclast formation and activity in vitro. These findings are in contrast with evidence that activation of the sympathetic nervous system decreases bone formation and increases bone resorption exclusively via beta2-adrenoceptor signaling. 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 sympathetic nervous system in the skeleton, which certainly will contribute to novel strategies for the treatment of osteoporosis.

Objective:

The objective of the study is to investigate the effect of alpha2-adrenoceptors on bone turnover in humans.

Study design:

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

Study population:

Healthy female and male human volunteers, 18-70 years old.

Intervention:

All participants will visit the AMC on two different occasions to 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 intervention will be followed by a wash out period of 1 week.

Main study parameters/endpoints:

The main study parameter is the change in serum concentrations of collagen type 1 cross-linked C-telopeptide (CTX) on the intervention day (clonidine 0.3mg) and on the control day (no intervention). A secondary study parameter is the change in serum concentrations of procollagen type I N propeptide (P1NP) and catecholamines on the intervention day (clonidine 0.3mg) and on the control day (no intervention).

Study objective

The hypothesis is that alpha2-adrenergic receptors play an important role in bone remodeling.

Study design

Clonidine 0.3mg or no intervention (at T=9:00):

1. T=9:00;

2. T=9:15;

3. T=10:15;

4. T=11:15;

5. T=13:15;

6. T=15:15.

Intervention

After an overnight fast at bloodsamples will be drawn at 09.00 and 09.15, to determine bone turnover markers (CTX, P1NP) and catecholamine levels. After that participants will receive either a single dose of oral clonidine 0.3mg or no intervention. One, two, four and six hours later (at 10.15, 11.15, 13.15, 15.15) blood samples are drawn again to determine bone turnover markers (CTX, P1NP) and catecholamine levels.

This is a crossover design. Participants will be randomized to either clonidine followed by no intervention or no intervention followed by clonidine.

Contacts

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Eligibility criteria

Inclusion criteria

Age: 18-70 years.

Exclusion criteria

1. Hypersensitivity to the active substrate or to any of the excipients;

2. Severe bradycardia, like sick sinus syndrome and a second or third degree atrioventricular block;

3. Use of antihypertensive drugs (including diuretics);

4. Use of drugs with negative effects on heart rhythm;

5. Any medication or disease influencing bone turnover;

6. Pregnancy;

7. Inability to give informed consent;

8. RR < 110/70 mmHg on the day of the experiments.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-02-2013
Enrollment:	12
Type:	Actual

Ethics review

Positive opinion

Date:	19-12-2012
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 37196
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL3603
NTR-old	NTR3762
CCMO	NL42339.018.12
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON37196

Study results

Summary results
N/A