

The nervous system and bone.

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

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23544

Bron

Nationaal Trial Register

Verkorte titel

Alpha2Bone

Aandoening

Osteoporosis

Ondersteuning

Primaire sponsor: Academic Medical Center (AMC), Amsterdam

Overige ondersteuning: Academic Medical Center (AMC), Amsterdam

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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 clonidine. 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).

Doel van het onderzoek

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

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Age: 18-70 years.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blinding:	Open / niet geblindeerd
Controle:	Placebo

Deelname

Nederland	
Status:	Werving gestopt
(Verwachte) startdatum:	01-02-2013
Aantal proefpersonen:	12
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies	
Datum:	19-12-2012
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 37196

Bron: ToetsingOnline

Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten

N/A