The contribution of the sympathetic nervous system to the anabolic effect of estrogen on bone.

Published: 03-03-2011
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The objective is to study the effect of beta-agonist and beta-antagonist treatment on human bone remodeling.

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

Summary

ID

NL-OMON36023

Source
ToetsingOnline

Brief title
E2Bone

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: ZonMW

Intervention

Keyword: bone, estrogen, osteoporosis, sympathetic nervous system

Outcome measures

Primary outcome

The main study parameter is the difference in change of serum concentrations of bone turnover markers (procollagen type I N propeptide (P1NP) and C-terminal crosslinking telopeptides of collagen type I (CTX)) compared in the treatment and control groups(4).

Secondary outcome

A secondary parameter is the change in number of circulating stem cells and osteogenic cells(7).

Study description

Background summary

Osteoporosis is a common disease, characterized by low bone mass and skeletal fragility resulting in an increased risk of fracture. The most prevalent cause of osteoporosis is estrogen deficiency in postmenopausal women(1). Estrogen replacement therapy and bisphosphonates effectively reduce fracture risk, but there are concerns about the long-term safety of these treatments(2). Bone mass is controlled by the balance between bone formation and resorption. The anabolic effects of estrogen on bone are presumed to be mediated by the estrogen receptor in bone. However, a recent breakthrough in experimental animals indicates an important role for the sympathetic nervous system (SNS) in bone remodelling mediated by the beta-2-adrenergic receptor(3). Furthermore, there are reports that the SNS is involved in the mobilization of hematopoietic stem cells (4;5).

Study objective

The objective is to study the effect of beta-agonist and beta-antagonist treatment on human bone remodeling.

Study design

Randomized intervention trial.

Intervention

The participants will be randomized to receive hormonal replacement therapy (HRT) (zumenon 1dd 2 mg), HRT and beta-agonist (terbutaline 1dd 5 mg), beta-antagonist (propranolol SR 1dd 80 mg) or no treatment during twelve weeks.

Study burden and risks

During the intervention, participants will have to take medication daily. Beta-agonist and beta-antagonist treatment are widely prescribed and have an excellent safety profile(5;6). Hormonal replacement therapy is associated with an increase in hormone-sensitive cancers, cardiovascular disease (CVD) and venous thrombo-embolism (VTE). However, large meta-analyses confirm that these effects occur after prolonged treatment (>1 year), whereas this study discontinues treatment after 12 weeks(7). Therefore the risks seem insignificant. DXA radiation exposure poses a negligible risk. Every 4 weeks fasting venous blood samples will be drawn (at home or in the AMC), the total volume of blood samples will not exceed 100 ml.

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

female sex
last menstrual cycle 12-60 months ago

Exclusion criteria

Contraindications to HRT, beta-agonist or beta-antagonist treatment, such as cardiovascular disease, astma, COPD, renal or hepatic insufficiency
Any medication or disease influencing bone turnover
Prior VTE or breast cancer
Current osteoporosis defined by a DXA Z-score >-2.5

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-05-2011
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	propranolol
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	nvt
Generic name:	terbutaline
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	zumenon
Generic name:	estradiol
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-03-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-07-2011
Application type:	Amendment
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: 25589
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2011-000929-71-NL
CCMO	NL35737.018.11
OMON	NL-OMON25589