Undercarboxylated osteocalcin, the hypothalamic-pituitary-gonadal axis and glucose metabolism in male patients with osteoporosis.

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON36967

Source
ToetsingOnline

Brief title
HPG-axis, glucose metabolism and bone

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Bone disorders (excl congenital and fractures)
- Gonadotrophin and sex hormone changes

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, Glucose metabolism, Osteoporosis, Testosterone

Outcome measures

Primary outcome

* undercarboxylated osteocalcin

* testosterone concentrations

* glucose tolerance determined by an oral glucose tolerance test

* insulin sensitivity determined by a hyperinsulinemic euglycemic clamp

* changes in body composition by a whole-body DXA scan

All patients will be studied at baseline and after 6 and 12 weeks of

intervention. Patients will serve as their own controls.

Secondary outcome

NA

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. Normally, bone quality is maintained by a dynamic process, known as bone remodeling.
Animal research shows that osteocalcin, secreted by osteoblasts, acts as a hormone and influences the male gonal axis, insuline sensitivity and measures of adiposity. However no study in humans to evaluate the relationship between

undercarboxylated osteocalcin, the gonadal axis and insulin sensitivity and changes in body composition has been performed to date. Osteocalcin is not available for administration in humans, but endogenous osteocalcin increases by approximately 250% during daily administration of Teriparatide (rhPTH 1-34), an anabolic agent used to treat osteporosis. Since PTH has no known effects on insulin signalling and glucose homeostasis, we will administer Teriparatide to study the effect of osteocalcin on insulin sensitivity, insulin secretion and the HPG-axis in men with primary osteoporosis.

Study objective

The objective of the study is to study the effect of Teripratide (rhPTH 1-34) on undercarboxylated osteocalcin levels, testosterone concentrations, glucose tolerance and insulin sensitivity and changes in body composition in male subjects with primary osteoporosis.

Study design

Observational cohort study.

Intervention

The participants will be randomized to two treatment groups, in a cross-over design, with an one week wash-out period:
Group 1 will first receive subcutaneous Teriparatide 20*g daily (12 weeks) and then no treatment
Group 2 will first receive no treatment (12 weeks) and then subcutaneous Teriparatide 20*g daily (12 weeks)

Study burden and risks

During the intervention, participants will receive a subcutaneous injection daily. This injection will only cause minor discomfort. The most common side effect of Teriparatide treatment is leg cramps and pain (>10%). Other less common side effects (1-10%) are dizziness, nausea, vomiting, gastroesophageal reflux, chest pain, hypotension, headache, muscle weakness and depression. Teriparatide is registered for the treatment of osteoporosis for a maximal duration of 24 months, whereas our subjects will only use it for 12 weeks. When the study ends all patients will continue with bisphosponate treatment. Both anabolic and antiresorptive agents are approved for the treatment of osteoporosis. But since it is only reimbursed in certain cases, Teriparatide is not used as standard therapy for the treatment or prevention of osteoporosis. After inclusion and subsequently every 6 weeks, fasting venous blood samples will be drawn. At baseline and after 12 weeks of intervention (t=0 and t=12 weeks) patients will be admitted to the clinical research unit for two separate days, for an oral glucose tolerance test (OGTT, 75 g oral glucose load) and a

hyperinsulinemic euglycemic clamp. The hyperinsulinemic euglycemic clamp will be performed using stable isotopes. For the administration of the stable isotope, glucose and insulin and for blood sampling, intravenous canules will be inserted in an antecubital vein of each arm. Stable isotopes are not harmful and hypoglycaemia will not occur because glucose is monitored every 5 minutes. Total atmitting time on one day will not exceed 7 hours. The total volume of blood samples from the entire protocol over 3 months will not exceed 475 ml (blood samples 150 ml, OGTT 12 ml, hyperinsulinemic euglycemic clamp 320 ml). At baseline and after 12 weeks of intervention patients will also have a whole-body dual-energy X-ray absorptiometry (DXA scan) to measure body composition. DXA radiation exposure poses a negligible risk.

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

Male sex
50-80 years
Recently diagnosed primary osteoporosis
Testosterone within reference range

Exclusion criteria

Contraindication to parathyroid hormone therapy: hypersensitivity to the active substrate or to any of the excipients, pre-existing hypercalcaemia, hepatic- or renal insufficiency, metabolic bone diseases other than primary osteoporosis or glucocorticoid-induced osteoporosis, unexplained elevations of alkaline phosphatase, prior external beam or implant radiation therapy to the skeleton, patients with skeletal malignancies or bone metastases ;Any medication or disease influencing bone turnover
Diabetes mellitus
Hypogonadism
Inability to give informed consent

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-11-2012
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO Date:	17-10-2012
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

No registrations found.

In other registers

Register	ID
CCMO	NL41243.018.12