The effects of sex hormone administration on marrow and visceral adiposity

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Primary Objective: To determine the effect of sex hormones on bone marrow fat. and visceral fatSecondary Objective(s): * To determine the effect of sex hormones on visceral and liver fat.* To test whether DXA can be used to calculate the amount of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55733

Source
ToetsingOnline

Brief title
SHAMVA

Condition

- Other condition
- Endocrine disorders of gonadal function
- Bone disorders (excl congenital and fractures)

Synonym
the amount of bone marrow fat / bone vet

Health condition

Trombocytenfunctie en inflammatie

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,De Hartstichting - Dekkerbeurs

Intervention

Keyword: Marrow adipose tissue, Sex hormones, Thrombocytes, Visceral adipose tissue

Outcome measures

Primary outcome

The main study parameter is the change in vertebral bone marrow fat fraction,

measured by MRI quantitative chemical shift imaging (QCSI).

Secondary outcome

Secondary parameters are changes in visceral fat in cm2, measured by MRI and

DXA; bone mineral density in g/cm2, measured by DXA, bone turnover markers

(Ctx, P1NP, osteocalcin) and leptin. Furthermore, we will asses changes in

inflammation markers, measured by * amongst others- HsCRP, IL-6, G-CSF. And,

lastly, the assesment of changes in platelet activation, measured by PFA

Closure Time, PFA Total Volume, PFA Initial Flow Rate, Plasma Thromboxane B2,

Flow-cytometry among which p-selectin

Study description

Background summary

Marrow adipose tissue (MAT) is a unique fat depot, different from white and brown fat. The inverse relationship between MAT and bone mass, has led to the paradigm that MAT is a negative regulator of bone mass. MAT increases with ageing and men have more MAT than women below the age of 50 years. After

menopause MAT becomes higher in women than in men. Together these data suggest that sex hormones are important regulators of MAT. Another fat depot with a comparable association with sex hormones is visceral adipose tissue (VAT). Men are more susceptible to VAT accumulation than premenopausal women, however VAT also increases in postmenopausal women. Understanding the regulation of VAT is important since it is associated with cardiometabolic risks.

Study objective

Primary Objective: To determine the effect of sex hormones on bone marrow fat. and visceral fat

Secondary Objective(s):
* To determine the effect of sex hormones on visceral and liver fat.
* To test whether DXA can be used to calculate the amount of visceral fat in transgender patients and if so, what algorithm to use.
* To assess the influence of sex steroids on blood platelets, as measured by different methods;
* To assess the influence of high dose sex steroids on the general cardiovascular laboratory risk assessment;

Study design

This study is a partly randomized open-label intervention study.

Intervention

MtFs who participate in the SHAMVA and TRANS study will receive a GnRH analogue every 4 weeks from week -6 until week 12 (last injection at week 8) and cyproterone acetate from week 12 until the end of the study (week 52) and estradiol from week 0 until the end of the study (week 52).

MtFs who participate in the TRANS study will receive a GnRH analogue every 4 weeks from week 0 untill week 12 (last injection at week 8) and cyproterone acetate from week 12 untill the end of the study (week 52) and estradiol from week 0 until the end of the study (week 52).

FtMs will receive GnRH analogue every 4 weeks from week 0 until week 12, FtMs will be randomized to receive either testosterone from week 0 until week 52 or receive testosterone and an aromatase inhibitor from week 0 until week 12.

Study burden and risks

MtF subjects who participate in the SHAMVA and TRANS study need to visit the AMC and/or VUmc five times for MRI QCSI in 58 weeks. MtF subjects who participate in the TRANS study need to visit the VUmc three times in 52 weeks.

The FtMs not receiving an aromatase inhibitor will need to visit the AMC and/or VUmc four times in 52 weeks, FtMs receiving an aromatase inhibitor will have three visits in 12 weeks. The appointment at baseline, 12 and 52 weeks can be made on the same day as the regular appointments at the VUmc. Venous blood sampling will be performed at all visits and the total amount of blood will not exceed 300ml. Finally, two whole-body and lateral DXA-scans will be performed, one at baseline and one at 52 weeks. The visits will take approximately one hour each visit.

The MRI QCSI procedure is a non-invasive, non-ionizing imaging technique without contrast administration. The radiation dose of a DXA-scan is negligible. MtF subjects and half of the FtM subjects receive standard cross-sex hormone treatment, and are therefore not exposed to additional risks. FtM subjects who will receive additional anastrozole are exposed to additional risks. The most common side effects include hot flushes, headache, mood swings, nausea, rash, joint pain, asthenia and osteoporosis. In a 12 week period, anastrozole will not lead to osteoporosis.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Diagnosed with gender dysphoria according to DSM V (transmen or transwomen)
- Age between 18 and 50 years
- Transmen need to be premenopausal
- Starting cross-sex hormone treatment

Exclusion criteria

- Previous use of cross-sex hormones
- Use of hormonal contraceptives (exception for Mirena sipral)
- Contraindications to MRI scanning as determined by the standard AMC checklist
- Use of bone-modifying or adipose tissue-modifying drugs, current or in history
- Bisphosphonates (alendronic acid, clodronic acid, ibandronic acid, pamidronic acid, risedronic acid, zoledronic acid, etidronate)
- Estrogen receptor modulators (raloxifene, bazedoxifene)
- Calcium regulating agents (e.g. denosumab, calcitonin, teriparatide, strontium ranelate, cinacalcet, etelcalcetine)
- Corticosteroids
- Bone or bone marrow diseases, current or in history
- Metabolic (osteroporosis, osteomalacia, dystosis, osteodystrophia, Pagets disease, osteogenesis imperfecta)
- Malignancy (primary, metastatic)
- Infectious (osteomyelitis, periostitis), Mechanic (lumbal vertebral fracture), Bone marrow diseases (leukemia, myelodysplastic syndrome, myeloproliferative disorders)
- Platelet count <120*10^9/l
- History of non-traumatic major bleeding
- Known bleeding diathesis
- Conditions which require antiplatelet therapy
- Usage of antiplatelet therapy
- Chronic usage of medication known to influence platelet function (e.g. DOAC*s, NSAIDs, warfarin)

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-05-2019
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Anastrozole
Generic name:	Anastrozole
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Decapeptyl
Generic name:	Triptorelin
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	12-03-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	15-05-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	21-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-12-2021
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-003072-31-NL
CCMO	NL63784.029.18
Other	NTR: NL7513