A double blind, randomized, cross-over placebo controlled study to investigate the efficacy of sublingual testosterone solution on physiological and subjective arousal in healthy, sexually dysfunctional premenopausal women.

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Primary objectives:To confirm the lack of effect of 0.5 mg sublingual testosterone on physiological and subjective measures of sexual arousal in women with HSDD. Secondary objective:To confirm the lack of effect of 0.5 mg sublingual testosterone on...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Sexual function and fertility disorders
Study type	Observational invasive

Summary

ID

NL-OMON34740

Source
ToetsingOnline

Brief title
PD-Testosterone

Condition

- Sexual function and fertility disorders

Synonym
Female Sexual Dysfunction; Hypoactive Sexual Desire Disorder; decreased libido

Research involving

Human

Sponsors and support

Primary sponsor: Emotional Brain
Source(s) of monetary or material Support: Emotional Brain BV (sponsor)

Intervention

Keyword: Pharmacodynamics, Physiological sexual arousal, Subjective sexual arousal, Testosterone

Outcome measures

Primary outcome

Primary endpoints

• Vaginal Pulse Amplitude (VPA): difference between pre- and post dose relative increases to erotic stimuli (as compared to neutral stimuli) between treatments (placebo vs. 0.5 mg testosterone).

• SARSAQ questionnaire: difference between pre- and post dose increases to erotic stimuli (as compared to neutral stimuli) between treatments (placebo vs. 0.5 mg).

Secondary outcome

Secondary endpoints

• VPA: difference between different post dose measurement times (150 min vs. 240 min. vs. 330 min) in primary endpoints.

• SARSAQ questionnaire: difference between different post dose measurement times (150 min vs. 240 min. vs. 330 min) in primary endpoints.

• Clitoral Blood Volume (CBV): as VPA described in primary & secondary endpoints.

Study description

Background summary

An important aspect of sexual motivation is physiological sexual responding. Measured as an increase in vaginal vasocongestion and clitoral blood volume (Gerritsen et al.,2009) elicited by sexual stimuli, this responding is considered to be preparatory for copulatory behavior (Tuiten et al., 1996). In hypogonadotropic, hypogonadal females we found that substitution with testosterone undecanoate 40 mg orally per day during an 8-week period enhanced vaginal responsiveness (Tuiten et al., 1996). This effect was not found in another group of hypogonadotropic hypogonadal patients (unpublished data). In both studies subjects received testosterone each morning, but patients in the first experiment were tested in the afternoon and patients in the second experiment in the morning. The different outcomes on physiological responding between these experiments may be caused by a time dependent effect of testosterone on vaginal arousal. Further, we examined whether administration of a single dose of 0.5 mg testosterone sublingually, as compared with placebo, increases vasocongestion during presentation of visual erotic stimuli (Tuiten et al., 2000). On treatment days we exposed eight sexually functional women with intervals of an hour and a half, to six erotic films depicting intercourse. After 0.5 mg testosterone administration, plasma levels of testosterone peaked in the first post dose plasma sample 15 minutes and then fell, reaching baseline levels after 2-3 hours. About three to four and a half hours after this testosterone peak, we found a striking increase in vaginal responsiveness when the subjects were exposed to the visual sexual stimuli. These findings demonstrate a time lag in the effect of sublingually administered testosterone on genital arousal in sexually functional women. This study was replicated 2 years later with the same results (Tuiten et al., 2002). In these previous two studies only sexually functional women participated. For women with Female Sexual Dysfunction, sublingual testosterone alone is not sufficient (van der Made et al, 2009a). This study showed a slightly increase in VPA for testosterone alone, although not significant. But the condition sublingual testosterone combined with vardenafil (a PDE-5 inhibitor) showed a strong, significant, increase in VPA, as compared to placebo, vardenafil and testosterone alone. The same results, a slight increase with testosterone alone and a high increase with testosterone combined with vardenafil, were found in a second study with sexually dysfunctional women (van der Made et al, 2009b).

The results of the above mentioned studies demonstrate that testosterone is involved in female sexual motivation in a time dependent fashion, and that this pharmacodynamic effect on sexual functioning is higher when combined with a PDE-5 inhibitor.

This research proposal describes a pharmacodynamic study of which the main goal

is to confirm the lack of effect of testosterone sublingual alone in premenopausal sexually dysfunctional healthy women using physiological and subjective measures of sexual arousal at four different time points.

Study objective

Primary objectives:
To confirm the lack of effect of 0.5 mg sublingual testosterone on physiological and subjective measures of sexual arousal in women with HSDD.

Secondary objective:
To confirm the lack of effect of 0.5 mg sublingual testosterone on physiological and subjective measures of sexual arousal at three post dose time points.

Study design

This is a single-center, double-blind, randomized, cross-over placebo controlled study with one (1) dose of testosterone administered sublingually and placebo.
A total of 16 subjects receive each medication condition once in random order, so that 8 subjects will start at the 0.5 mg dose and 8 on placebo. Wash-out between treatments will be at least 48 hours. Baseline pharmacodynamic assessments will be performed each experimental day before each dosing. Pharmacodynamic (physiological and subjective measures of sexual arousal) assessments will be performed at pre-determined time points. Subjects visit the site a total of four times: one day screening (V0), two experimental days (V1 & V2) and one follow up visit (V3). During all visits the subject*s health will be monitored.

Study burden and risks

HIV, hepatitis and pregnancy are determined during screening (pregnancy at eacht visit). A positive result on each of these 3 may have a negative impact on the subjects. Subjects are warned of this risk beforehand. Blood drawing may give rise to hematomas. Testosterone administration as used in the present study may give rise to mild decreases in blood pressure.

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

1. Provision of written informed consent;
2. Female 21-40 years of age with Hypoactive Sexual Desire Disorder (comorbidity with other sexual dysfunctions e.g Female Sexual Arousal Disorder (FSAD) is allowed).
3. Healthy according to normal results of medical history, physical examination, laboratory values and vital signs, unless the investigator considers an abnormality to be clinically relevant;
4. Subject must be heterosexually oriented;
5. BMI >= 18 and <= 30 kg/m2.

Exclusion criteria

1. A history of Childhood Sexual Abuse;
2. Subjects who had used testosterone therapy within 6 months before study entry;
3. Use of oral contraception containing anti-androgens (e.g. Diane 35; Minerva);
4. Use of oral contraception containing 50 µg estrogen or more;
5. Pregnancy, or intention to become pregnant during this study (Note: a serum or urine pregnancy test will be performed in all women prior to the administration of study medications);

6. Lactating, or subjects who have given birth in the previous 6 months;
7. Subjects who are taking CYP3A4-inhibitors: ritonavir (HIV-proteaseremmer), ketoconazol en itraconazol claritromycine, erytromycine and saquinavir;
8. Subjects who are taking CYP3A4-inducers: carbamazepine, fenytoïne, fenobarbital, st Johns Wort, rifampicine;
9. A substance abuse disorder that in the opinion of the investigator is likely to affect the subject's ability to complete the study or precludes the subject*s participation in the study; mild or moderately alcohol drinking behavior is allowed, only 24 hours before the experimental days is alcohol drinking not allowed. Three weeks before the start of the experimental day is the taking of any recreational drug not allowed. Smoking is allowed.
10. Subjects with a peri menopausal hormonal status (FSH > 30).

Study design

Design

Study phase:	2
Study type:	Observational invasive
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-05-2010
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	testosterone
Generic name:	testosterone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-03-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-05-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2010-019540-39-NL
CCMO	NL31982.040.10