Bromocriptine and Insulin Sensitivity (the BIS study)

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Primairy objective: To determine whether there is a beneficial effect on insulin sensitivity when bromocriptine is given in the morning, as compared to bromocriptine in the evening in Caucasian, lean and obese males.Secondary Objectives: 1. To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON42270

Source
ToetsingOnline

Brief title
BIS study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Insulin Sensitivity, Sensitivity for insulin

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Eigen Stichting

Intervention

Keyword: Dopamine, Insulin sensitivitiy, Lean and obese

Outcome measures

Primary outcome

Difference in insulin sensitivity when bromocriptine is used in the morning or

in the evening in lean and obese males.

Secondary outcome

- Difference in effect of bromocriptine treatment on insulin sensitivity

between lean and obese males.

- Difference in energy expenditure due to bromocriptine usage at different time

points in lean and obese males.

Study description

Background summary

Obesity and diabetes mellitus type 2 (DM2) are health problems with a tremendous impact. Many attempts have been made to combat obesity and DM2, however, a breakthrough therapy is still lacking.
Bromocriptine, a dopamine 2 receptor agonist, has recently been approved in the treatment of DM2. Bromocriptine causes a significant improvement of fasting plasma glucose and Hba1C values. The exact mechanism of action of bromocriptine is still unknown.
Earlier, we performed a study to show the effects of bromocriptine on brown adipose tissue (BAT) activity (the DEBAT study METC nr 2013_107). Namely, BAT, known for its capacity to dissipate excess energy, might have been involved in this process as stimulation by the sympathetic nervous system is the principal driving force in controlling BAT activity. However, we have shown that bromocriptine did not influence BAT activity or energy expenditure in healthy, lean subjects.
We did found an effect of bromocriptine on insulin sensitivity unexpectedly, subjects became significantly less insulin sensitive after bromocriptine use.
Circadian neuroendocrine rhythms, especially the dopaminergic and serotonergic neurotransmitter activity, play a pivotal role in the development of seasonal

and non-seasonal changes in body fat stores and insulin sensitivity.
Therefore, the timing of bromocriptine administration might be of great importance in changes in insulin sensitivity. Indeed, in the treatment for DM2, a bromocriptine quick release variant is given in the morning. In the former study we instructed the subjects to use the bromocriptine in the evening in combination with the evening meal. We decided to do so because bromocriptine had to be taken in combination with food. We wanted a high level of dopamine just before the 18F-FDG-PET-CT scan to get a maximum effect of dopamine on BAT. But the subjects had to be fasted for the OGTT and 18F-FDG-PET-CT scan. Therefore, we decided to give the (long-acting) bromocriptine in the evening.
Also, the effect of bromocriptine might be different in lean or obese subjects. Obesity is associated with an increased sympathetic tonus. Therefore, the baseline condition is different in lean or obese subjects which may cause different effects of bromocriptine treatment.

Study objective

Primairy objective: To determine whether there is a beneficial effect on insulin sensitivity when bromocriptine is given in the morning, as compared to bromocriptine in the evening in Caucasian, lean and obese males.
Secondary Objectives:
1. To determine whether there are differential effects of bromocriptine treatment on insulin sensitivity in obese or lean healthy, Caucasian males.
2. To determine whether the difference in timing of bromocriptine influences energy expenditure during thermoneutral conditions in Caucasian, lean and obese males.

Study design

Randomized physiology study.

Study burden and risks

Study Design: Observational design with invasive measurements, randomized study physiology.
Volunteers will come to the AMC four times, each visit will take about 3.5-4 hours:
At each visit a canlua will be placed, energy consumption will be measured by indirect calorimetry and an OGTT will be performed.
The insertion of the canulacan be experienced as unpleasant and there is a small chance of developing a phlebitis at the location of the canula.
Also, the subjects could experience side effects of the bromocriptine. There is no direct benefit to the volunteers.

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
- Caucasian origin
- Subjects should be able and willing to give informed consent
- 18-35 years old
- BMI range of 19-23 kg/m2 or BMI> 27 kg/2

Exclusion criteria

- Renal failure (creatinine>135mmol/l)
- Liver failure (AST/ALT > 3 times higher than the normal upper value)
- Daily use of prescription medication and/or drugs

- Known hypersensitivity to bromocriptine.
- Uncontrolled hypertension
- Known history of coronary artery disease or valvulopathy
- History of severe psychiatric disorders.
- Prolactin-releasing pituitary tumor (prolactinoma).

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-10-2014
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO

Date:	15-07-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	25-06-2015
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
CCMO	NL49417.018.14