Metformin and Core Temperature in Obese and lean Males (McTOM)

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In this study we aim to investigate the influence of metformin (500 mg 1/day) on 18F-FDG uptake in the colon. We will also measure temperature in the colon and energy expenditure in healthy lean (BMI 28 kg/m2).

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

Summary

ID

NL-OMON42453

Source
ToetsingOnline

Brief title
McTOM

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Energy disposal, energy dissipating organ

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: Eigen stichting

Intervention

Keyword: colon, FDG uptake, Metformin

Outcome measures

Primary outcome

Difference in 18F-FDG uptake as registered by 18F-FDG PET-CT before and after 7 days of daily metformin use

Secondary outcome

- Difference in core body temperature before and after metformin use and the correlation with 18F-FDG uptake

- Difference in energy expenditure before and after metformin use and the correlation with 18F-FDG uptake.

- Correlation between difference in core temperature and respectively 18F-FDG uptake and energy expenditure, before, after 7 days of daily metformin use.

- Difference in lactate, before and after the use of metformin and the correlation between lactate and respectively 18F-FDG uptake, core body temperature and energy expenditure.

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.
Obesity is the result of an imbalance between energy intake and energy expenditure. 18F-fluorodeoxy-d-glucose (18F-FDG) positron emission tomography computed tomography (PET-CT) pinpoint areas with high glucose turnover. Physiological 18F-FDG accumulation is frequently observed in the colon. Therefore, the colon might play an important role in increasing energy

expenditure by consuming calories. However, the possibility of the colon as an energy dissipating tissue has not yet been explored. The colon could become an interesting new target of research to find a method to combat obesity.
Metformin is one of the few drugs in the treatment of DM2 that is associated with moderate weight loss. Interestingly, patients using metformin show an increased 18F-FDG-uptake in the colon. Whether this higher uptake of glucose also cause an increase in core temperature and/or an increase in energy expenditure is not known. The cause for this increase in glucose uptake in the colon by metformin use is unknown. Also, it is unknown whether this increase in glucose uptake results in an increased energy expenditure and/or an increase in core body temperature.

Study objective

In this study we aim to investigate the influence of metformin (500 mg 1/day) on 18F-FDG uptake in the colon. We will also measure temperature in the colon and energy expenditure in healthy lean (BMI <24 kg/m2) and obese subjects (BMI>28 kg/m2).

Study design

In this non-randomised intervention study we will study the influence of metformin (1000 mg/day (500 mg in the morning, 500 mg in the evening) during 1 week) on 18F-FDG uptake in the colon. The main outcome will be difference in 18F-FDG uptake. Furthermore, we will measure core body temperature, energy expenditure and HOMA-index.
Visit 1. (screening) : Informed consent, evaluation of eligibility, medical history, laboratory measurements.
Visit 2. : Weight, length, waist circumference, blood drawing, core body temperature, EE, 18F-FDG PET CT. Start using metformin
Visit 3. : Weight, length, waist circumference, blood drawing, core body temperature, EE, 18F-FDG PET CT.

Study burden and risks

Subjects will have to visit the AMC three times. Two times in a fasted state. Furthermore, subjects will have to use metformin. Metformin is a widely used drug with an established safety profile. The most-occurring side-effect is gastrointestinal discomfort (diarrhoea, bloating, dyspepsia). This is mostly seen at high doses and often ameliorates when using metformin for a longer period. A rare but important complication is lactic acidosis. However, this is most often seen in patients with either renal insufficiency or other underlying causes of impaired lactate metabolism. Therefore, we only include healthy subjects and kidney function will be checked before subjects start with the metformin.
Also, we will use 18F-FDG PET-CT scans to evaluate the glucose uptake in the

intestine. The resulting dose from the two radioactive tracers + scans is 7.8 mSv.
The maximal dose for a participant during one year is 10 mSv. Nonetheless, we will strongly emphasize that the participants will not participate in research involving radiation in the two years following this study. Although the change of developing cancer is minimal after participation in this study, we will only include subjects aged over 40 years to minimalize the potential effect of inducing cancer.
Last, the placing of the intravenous canulla in our study can be a unpleasant experience for the subjects and there is a low risk of flebitis at the intravenous injection sites.

Although the methods of our study are accompanied with a moderate risk for healthy subjects, we find this to be justified with adding knowledge to finding a solution for the major obesity and type 2 diabetes epidemic.

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
- > 50 years old
- BMI> 28 kg/m2 or BMI < 24 kg/m2

Exclusion criteria

- Renal failure (GFR< 60ml/min)
- Liver insufficiency (AST or ALT 3 times upper value)
- Chronic use of drugs or medication
- Diabetes mellitus
- Lactate acidosis or precoma diabeticum in medical history
- Acute or chronic diseases such as: dehydration, severe infection, shock, heartfailure, pulmonary insufficiency, recent heart attack
- Alcoholism

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):	15-10-2015
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	22-07-2015
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	NL53453.018.15