Acylcarnitines and Insulin Resistance

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Primary: To investigate plasma AC profiles of lean and obese subjects in relation to body composition, BMI, insulin sensitivity and energy expenditure.Secondary: To determine if plasma ACs reflect adipose (subcutaneous/visceral) tissue, liver or...

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

Summary

ID

NL-OMON35271

Source
ToetsingOnline

Brief title
AIR Study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Lifestyle issues

Synonym
Insulin insensitivity, Insulin resistance

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Acylcarnitines, Insulin Resistance, Obesity

Outcome measures

Primary outcome

- Acylcarnitine profiles in human plasma and muscle, liver and fatty tissue

- The correlation between these acylcarnitine profiles and insulin sensitivity

and resting energy expenditure in each individual patient

Secondary outcome

Not applicable

Study description

Background summary

The Western lifestyle and prevalent obesity are the main causes of the strongly increasing incidence of type 2 Diabetes Mellitus, a condition characterized mainly by decreased insulin sensitivity of liver and skeletal muscle. It is suggested that insulin sensitivity is caused by incomplete fatty acid oxidation (FAO) due to high lipid burden in obese humans. The increased lipid level enhances beta-oxidation, but is not accurately followed by tricarboxylic acid (TCA) cycle and electron transport chain (ETC) velocity. In order to be oxidized, fatty acids need carnitine to pass the mitochondrial membrane. Together they form acylcarnitine, which is transported by the membrane transporter CACT from cytosol into the mitochondrium.
Several relations between insulin resistance and acylcarnitines are studied and described, as acylcarnitines correlate negatively with insulin sensitivity. In obese insulin resistant subjects the activity of CPT1 and CACT are decreased, resulting in decreased carnitine transport over the mitochondrial membrane. Additionally, an accumulation of long chain ACs is found in obese insulin resistant subjects. We hypothesize that long chain ACs might be a keyplayer in the induction of insulin resistance.

Study objective

Primary: To investigate plasma AC profiles of lean and obese subjects in relation to body composition, BMI, insulin sensitivity and energy expenditure.
Secondary: To determine if plasma ACs reflect adipose (subcutaneous/visceral) tissue, liver or muscle ACs.

Study design

Subjects who will undergo elective abdominal surgery will be recruited on the surgical outpatient clinic. All subjects will undergo a short physical examination and laboratory investigation.

Prior to surgery the patients will be characterized metabolically and insulin sensitivity will be determined. These data will be correlated with acylcarnitine profiles in plasma, muscle, liver and adipose tissue from biopsies taken during surgery.
There is no study intervention: patients are studied once.

Study burden and risks

- Prior to surgery a full medical history, physical examination, blood withdrawal, a 7 point Oral Glucose Tolerance Test and Resting Energy Expenditure test will take place. There are no risks to these actions.
- During surgery biopsies will be taken from abdominal muscle, abdominal fat, liver tissue and optionally femoral muscle tissue. These biopsies can potentially cause haematomas, which will be managed by the surgeon during surgery.
- Subjects will experience no benefits from this study.

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- Lean and obese (body mass index > 20 kg/m2) subjects undergoing elective surgery
2- Age 18 - 60 years
3- Normal liver and renal function tests
4- Informed consent

Exclusion criteria

1- Surgery for malignant or active inflammatory conditions
2- Treated diabetes
3- Any medication interfering with insulin sensitivity (steroids, beta-blockers)
4- HbA1c >8%
5- Intensive sports (> three times weekly)
6- Malignant disease
7- Infectious disease (raised erythrocyte sedimentation rate or C-reactive protein)
8- Any medical disorder of significant relevance
9- DM II in first degree family members
10- Hypertriglyceridemia or any other lipid metabolism disorder

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-02-2013
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	18-11-2011
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	NL38148.018.11