The role of RBP4 in human lipid and glucose metabolism

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

Summary

ID

NL-OMON33098

Source
ToetsingOnline

Brief title
RBP4 and metabolism

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
glucose intolerance, Insulin resistance

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Metabole Fonds

Intervention

Keyword: Insulin sensitivity, Obesity, RBP4

Outcome measures

Primary outcome

Expression of RBP4 in liver, skeletal muscle and adipose tissue

Glucose production, glucose uptake and lipolysis

RBP-4 concentration in plasma

Secondary outcome

Correlation tissue levels of RBP4 and phosphorylation of insulin signaling

proteins

Study description

Background summary

The prevalence of obesity, insulin resistance and diabetes type 2 is increasing worldwide and threatens human health. How obesity interferes with glucose metabolism is not completely elucidated yet.
Recently, retinol binding protein-4 (RBP-4), derived from adipose tissue and liver has been described to be elevated in plasma of obese insulin resistant subjects. Also, it has been shown that insulin sensitivity is correlated negatively to levels of circulating RBP-4. In studies with rodents, RBP-4 interfered directly with glucose uptake in muscle and with glucose production in the liver. Whether this is also true for humans, is unknown.

Study objective

In this study we want to investigate whether the increased levels of RBP-4 are correlated to the expression levels in liver, skeletal muscle and adipose tissue. Also, we want to study the correlation between the levels of expression and glucose and lipid fluxes.

Study design

We will study two groups of obese subjects scheduled for bariatric surgery, one

group with obese subjects who are metabolically healthy and one group who is metabolically unhealthy. This will show whether RBP-4 is indeed important in the induction of insulin resistance. We will also study differences in expression levels of RBP-4 in subcutaneous adipose tissue, liver and skeletal muscle between lean and obese subjects.

Intervention

Glucose fluxes will be measured during a hyperinsulinemic clamp using stable isotopes. Biopsies of skeletal muscle and subcutaneous adipose tissue will be performed during the clamp. Biopsies of the liver and intra abdominal fat from subjects which will be operated will be taken during surgery.

Study burden and risks

The hyperinsulinemic clamp and the use of stable isotopes are safe. Hypoglycemia during the clamp will be avoided by measuring plasma glucose regularly. The risk of prolonged bleeding from the biopsies of muscle and subcutaneous adipose tissue will be minimized by use of a pressure bandage and manual external compression. The risk of bleeding from the liver and intra abdominal fat biopsies will be reduced by checking local hemostasis during and twice after the biopsy. If needed electrical coagulation will be performed.

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

Lean subjects:
BMI 20-25 kg/m2 (stable weight)
Age between 20 and 60 years
Obese subjects:
- BMI > 30 kg/m2 for part one or > 35 kg/m2 for part two
- Age between 20 and 60 years
- HOMA-IR > 1.95 for part one

Exclusion criteria

Lean subjects:
any medical condition (except for gallstone formation) or use of medication
family history of diabetes mellitus type 2
performance of vigorous exercise
Obese subjects:
primary lipid disorder or secondary lipid disorder treated with fibrates
diabetes mellitus type 2 (DM2) treated with thiazolidinediones, DPP4-inhibitors or GLP1-analogues
any medical condition except for glucose intolerance, DM2, hypertension and secondary dyslipidemia

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:	Pending
Start date (anticipated):	01-01-2010
Enrollment:	50
Type:	Anticipated

Ethics review

Approved WMO

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	NL29089.018.09