Lipid accumulation in skeletal muscle and insulin sensitivity.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24213

Source NTR

Brief title Lipid infusion study

Health condition

Type 2 Diabetes Mellitus, Insulin Resistance, Skeletal muscle, Lipid accumulation

Sponsors and support

Primary sponsor: NUTRIM - Maastricht University **Source(s) of monetary or material Support:** TI Food and Nutrition (formerly WCFS: Wageningen Centre for Food Sciences)

Intervention

Outcome measures

Primary outcome

1. Accumulation of lipid species in skeletal muscle;

2. Insulin sensitivity.

Secondary outcome

- 1. Substrate oxidation;
- 2. Energy expenditure;
- 3. Gene expression.

Study description

Background summary

Plasma free fatty acid (FFA) levels, which are generally elevated in obese subjects, appear to be an important link between obesity and insulin resistance. Several studies have shown that acute raising of plasma free fatty acid levels, via infusion of lipid emulsions, causes profound insulin resistance in skeletal muscle of animals and human subjects. Remarkably, the insulin resistance that occurs during lipid infusion becomes apparent only after a delay of 3-4 hours, making a direct effect of FFA on insulin action unlikely. To this issue, FFA may need to accumulate first as triglycerides inside the muscle fibres to cause disturbances in the insulin signalling cascade. The metabolic characteristics of MCFA make them an interesting tool to study the involvement of long-chain fatty acids (and derived metabolites) in the development of insulin resistance. Since medium chain fatty acids cannot be converted to diacylglycerol and subsequently stored as triglycerides and are preferentially oxidised they may not interfere with insulin signalling. Therefore, by comparing the effect of medium-chain and long-chain fatty acids on insulin signalling, it can be directly tested that the accumulation of diacylglycerol is responsible for the impaired insulin signalling.

Study objective

Administration of a lipid emulsion consisting of long-chain triglycerides will induce insulin resistance due to increased DAG mass and subsequent activation of the PKC pathway in skeletal muscle. Infusion of a lipid emulsion consisting of medium-chain triglycerides will not increase DAG mass and the PKC pathway will not be activated. Therefore, the induction of insulin resistance will be absent.

Study design

Before and after the 6h hyperinsulinemic-euglycemic clamps with simultaneous lipid/glycerol infusion, a muscle biopsiy will be obtained. Throughout each clamp, blood samples will be drawn every hour.

Intervention

Ten healthy, lean, untrained male subjects (age 18-35; BMI \leq 25 kg/m2) will undergo, in a randomized crossover design, a 6h-hyperinsulinemic euglycemic clamp (to assess insulin sensitivity) with simultaneous lipid infusion. In the first condition, the lipid infusion will consist of triglycerides containing long-chain fatty acids while in the second condition, fatty acids in the lipid emulsion will be mainly of medium-chain length. As a control condition, glycerol will be infused (to match the glycerol content of the other lipid emulsions). Before and after each glucose clamp, muscle biopsies will be obtained.

Contacts

Public

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Eligibility criteria

Inclusion criteria

- 1. Male sex;
- 2. Age 18-35 years;
- 3. BMI <25 kg/m2;

- 4. Sedentary;
- 5. Stable dietary habits;
- 6. Healthy.

Exclusion criteria

1. Female sex;

2. First or second-degree family member with diagnosed type 2 diabetes or any other endocrine disorder;

3. Participation in a regular exercise training program during the last year before the start of the study;

- 4. The use of any plasma glucose lowering medication;
- 5. Participation in another biomedical study within 1 month before the first screening visit.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

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Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2003
Enrollment:	10
Туре:	Actual

Ethics review

Positive opinion 11-11-2009 Date: Application type:

First submission

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
NTR-new	NL1988
NTR-old	NTR2105
Other	METC Maastricht University : 03-091
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results N/A