Lipid accumulation in skeletal muscle and insulin sensitivity.

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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-...

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24213

Bron
Nationaal Trial Register

Verkorte titel
Lipid infusion study

Aandoening

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

Ondersteuning

Primaire sponsor: NUTRIM - Maastricht University
Overige ondersteuning: TI Food and Nutrition (formerly WCFS: Wageningen Centre for Food Sciences)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Accumulation of lipid species in skeletal muscle;

2. Insulin sensitivity.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

Ten healthy, lean, untrained male subjects (age 18-35; BMI ≤ 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.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Male sex;

2. Age 18-35 years;

3. BMI <25 kg/m2;

4. Sedentary;

5. Stable dietary habits;

6. Healthy.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-10-2003
Aantal proefpersonen:	10
Type:	Werkelijke startdatum

Ethische beoordeling

Positief advies

Datum:	11-11-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1988
NTR-old	NTR2105
Ander register	METC Maastricht University : 03-091
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A