

# AV study.

Gepubliceerd: 24-09-2012 Laatste bijgewerkt: 18-08-2022

Increased local insulin supplementation can reverse the blunted postprandial muscle protein synthetic response in the elderly, whereas local insulin supplementation does not affect the postprandial muscle protein synthetic response in the young.

|                             |                       |
|-----------------------------|-----------------------|
| <b>Ethische beoordeling</b> | Positief advies       |
| <b>Status</b>               | Werving gestart       |
| <b>Type aandoening</b>      | -                     |
| <b>Onderzoekstype</b>       | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON22412

### Bron

Nationaal Trial Register

### Verkorte titel

AV study

### Aandoening

Loss of muscle mass in healthy aging (sarcopenia)

## Ondersteuning

**Primaire sponsor:** Maastricht University

**Overige ondersteuning:** fund = initiator = sponsor

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

The main study endpoint is the muscle protein synthesis rate, expressed as fractional synthetic rate (FSR). In order to determine the FSR, the following parameters will be measured in blood and muscle tissue:<br>

1. Plasma and muscle free phenylalanine concentration (expressed as  $\mu\text{mol/L}$ );<br>

2. Plasma enrichment of L-[ ring-2H5]phenylalanine (expressed as mole percent excess (MPE));<br>
3. Muscle protein bound enrichment of L-[ ring-2H5]phenylalanine (expressed as MPE);<br>
4. L-[ ring-2H5]phenylalanine enrichment of the muscle free amino acid pool (expressed as MPE).

## Toelichting onderzoek

### Achtergrond van het onderzoek

Rationale:

Age related muscle loss (sarcopenia) is assumed to be related to the impaired postprandial muscle protein synthetic response to protein and/or amino acid administration in the elderly vs the young. Increased insulin secretion affects skeletal muscle blood flow and may therefore affect substrate availability and postprandial muscle protein synthesis. However, it is unclear whether the anabolic resistance in the elderly can be explained by a reduced muscle perfusion due to a diminished response to insulin after protein ingestion.

Hypothesis:

Increased local insulin supplementation can reverse the blunted postprandial muscle protein synthetic response in the elderly, whereas local insulin supplementation does not affect the postprandial muscle protein synthetic response in the young.

Objective:

The primary objective of the study is to investigate whether local insulin supplementation augments the in vivo postprandial muscle protein synthetic response after protein ingestion and whether this response differs between young and elderly subjects. The secondary objective of the study is to assess the effect of local insulin supplementation on femoral leg blood flow and on microvascular perfusion in young and elderly subjects.

Study design:

Single-blind, placebo controlled, parallel, human intervention study.

### Study population:

1. 24 healthy young men (18 - 30 yr old);
2. 24 healthy elderly men (65-85 75 yr old).

### Intervention:

The intervention consist of a single test day during which the subjects will receive a drink containing 20 gram intrinsically labeled casein followed by local administration of insulin or saline (placebo). In addition, continuous intravenous tracer infusions will be applied. During the test day 54 plasma samples and 3 muscle biopsies are collected over a period of 8 h. Furthermore, femoral blood flow, leg blood and microvascular perfusion will be determined using Doppler ultrasound, dye dilution and sidestream dark field imaging (SDF) in sublingual position, respectively.

### Endpoints:

Primary endpoint: Muscle protein synthesis and breakdown rates. Secondary endpoints: Rate of protein digestion and absorption, whole body protein balance, femoral and leg blood flow and microvascular perfusion.

### Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

Insertion of the catheters in a vein is comparable to a normal blood draw and the only risk is a small local hematoma. This is the same for the muscle biopsies. Muscle biopsies will be taken through a small (5 mm) incision, following local anesthetics of the skin and muscle fascia, and will heal completely. The insertion of the arterial and venous catheter in the leg may feel uncomfortable, but once the catheter is in place, the pain lessens. To minimize the risk of infection, only sterile materials will be used and the catheter will be removed directly after completing the test. To prevent bleeding after withdrawal of the catheters, pressure will be applied to the leg for at least 10 min followed by a bed rest of another 4 hours to prevent bleeding. However, there is a risk for a small local hematoma. Finally, a small chance exists that blood clots can be formed in and around the catheter. This risk will be minimized by regularly flushing the catheter with sterile saline containing 1% heparin as an anticoagulant. Such a study with femoral arterial and venous lines has been previously conducted successfully at the University of Maastricht (METC 98-030.3). Muscle biopsies and the insertion of the arterial and venous catheters will only be obtained by experienced physicians. The test beverages contain intrinsically labeled dietary protein that is safe for human consumption and has been used in previous studies (METC 06-3-064, METC 07-3-086,

METC 09-3-078.3). The labeled amino acids tracers that will be infused intravenously are not radioactive and are completely safe, furthermore, these solutions are produced according to GMP standards.

## **Doel van het onderzoek**

Increased local insulin supplementation can reverse the blunted postprandial muscle protein synthetic response in the elderly, whereas local insulin supplementation does not affect the postprandial muscle protein synthetic response in the young.

## **Onderzoeksopzet**

3 h Before ingestion of protein drink;

5 h after ingestion of protein drink.

## **Onderzoeksproduct en/of interventie**

The intervention consist of a single test day during which the subjects will receive a drink containing 20 gram intrinsically labeled casein followed by local administration of insulin (0.3 mU/min/100mL) or saline (placebo). In addition, continuous intravenous tracer infusions will be applied. During the test day 54 plasma samples and 3 muscle biopsies are collected over a period of 8 h. Furthermore, femoral blood flow, leg blood and microvascular perfusion will be determined using Doppler ultrasound, dye dilution and sidestream dark field imaging (SDF) in sublingual position, respectively.

## **Contactpersonen**

### **Publiek**

B. Groen  
[default]  
The Netherlands  
+31 (0)6 10475964

### **Wetenschappelijk**

B. Groen  
[default]  
The Netherlands  
+31 (0)6 10475964

# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Healthy untrained men;
2. Age 70-85 years or age 18-30 years;
3. BMI < 30 kg•m<sup>2</sup>, with a stable body weight over the last 3 months.

## Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Cardiac abnormalities;
2. Coagulation disorders;
3. Vascular diseases;
4. Obesity (BMI > 30 kg•m<sup>2</sup>);
5. Diabetes mellitus type 1 and type 2;
6. Glucose intolerance;
7. HbA1c > 7.0%;
8. Diagnosed impaired renal or liver function;
9. Smoking;
10. All co-morbidities interacting with mobility and muscle metabolism of the lower limbs (e.g. arthrosis, arthritis, spasticity/rigidity, all neurological disorders and paralysis);
11. Cancer;
12. Hypertension (according to WHO criteria);
13. Acute or chronic pulmonary diseases;
14. Allergy for lidocain or iodine;

- 15. Use of NSAIDs and acetylsalicylic acid;
- 16. Patients suffering from PKU (Phenylketonuria);
- 17. Infectious disease;
- 18. Participation in any regular exercise program;
- 19. Unstable body weight over the last 3 months.

## Onderzoeksopzet

### Opzet

|                  |                       |
|------------------|-----------------------|
| Type:            | Interventie onderzoek |
| Onderzoeksmodel: | Parallel              |
| Toewijzing:      | Gerandomiseerd        |
| Blinding:        | Enkelblind            |
| Controle:        | Placebo               |

### Deelname

|                         |                      |
|-------------------------|----------------------|
| Nederland               |                      |
| Status:                 | Werving gestart      |
| (Verwachte) startdatum: | 29-09-2011           |
| Aantal proefpersonen:   | 48                   |
| Type:                   | Verwachte startdatum |

## Ethische beoordeling

|                 |                  |
|-----------------|------------------|
| Positief advies |                  |
| Datum:          | 24-09-2012       |
| 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        | NL3492                              |
| NTR-old        | NTR3638                             |
| Ander register | Maastricht University : 11-3-051    |
| ISRCTN         | ISRCTN wordt niet meer aangevraagd. |

## Resultaten

### Samenvatting resultaten

N/A