AV study.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22412

Source
Nationaal Trial Register

Brief title
AV study

Health condition

Loss of muscle mass in healthy aging (sarcopenia)

Sponsors and support

Primary sponsor: Maastricht University
Source(s) of monetary or material Support: fund = initiator = sponsor

Intervention

Outcome measures

Primary outcome

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:

1. Plasma and muscle free phenylalanine concentration (expressed as µmol/L);

2. Plasma enrichment of L-[ring-2H5]phenylalanine (expressed as mole percent excess

(MPE));

3. Muscle protein bound enrichment of L-[ring-2H5]phenylalanine (expressed as MPE);

4. L-[ring-2H5]phenylalanine enrichment of the muscle free amino acid pool (expressed as MPE).

Secondary outcome

Secondary endpoints include whole body protein turnover, protein digestion and absorption kinetics and microvascular perfusion. The following parameters will be calculated:

1. Exogenous phenylalanine rate of appearance and plasma availability of phenylalanine;

2. Total rate of phenylalanine appearance and disappearance (= protein turnover);

3. Endogenous phenylalanine rate of appearance (=protein breakdown);

4. Femoral blood flow using Doppler ultrasound expressed as L/min;

5. Leg blood flow using ICG dye dilution expressed as mL/min/100mL leg;

6. Sublingual microvascular perfusion measured using the SDF camera expressed as: Proportion of perfused vessels (PPV; %), perfused vessel density (PVD; n/mm) and Microcirculatory flow index (MFI).

Study description

Background summary

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.

Study objective

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.

Study design

3 h Before ingestion of protein drink;

5 h after ingestion of protein drink.

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 (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.

Contacts

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

Eligibility criteria

Inclusion criteria

1. Healthy untrained men;

2. Age 70-85 years or age 18-30 years;

3. BMI < 30 kg•m2, with a stable body weight over the last 3 months.

Exclusion criteria

1. Cardiac abnormalities;

2. Coagulation disorders;

3. Vascular diseases;

4. Obesity (BMI > 30 kg•m2);

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.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-09-2011
Enrollment:	48
Type:	Anticipated

Ethics review

Positive opinion

Date:	24-09-2012
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	NL3492
NTR-old	NTR3638
Other	Maastricht University : 11-3-051
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A