

Prevention of skeletal muscle and myocardial free-fatty acid induced microvascular dysfunction in skeletal muscle and myocardium by exercise

Published: 16-07-2015

Last updated: 19-04-2024

We hypothesize that the amount of physical activity correlates with insulin-induced microvascular recruitment during free-fatty acid infusion in skeletal muscle as well as in the heart. In this study we aim to test this hypothesis.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Myocardial disorders
Study type	Observational invasive

Summary

ID

NL-OMON43964

Source

ToetsingOnline

Brief title

Prevention of microvascular dysfunction by exercise

Condition

- Myocardial disorders
- Glucose metabolism disorders (incl diabetes mellitus)
- Vascular disorders NEC

Synonym

ill bloodvessels, microvascular dysfunction

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: vidi-beurs

Intervention

Keyword: insulin induced microvascular recruitment, microvascular dysfunction, physical activity

Outcome measures

Primary outcome

The effect of FFA on insulin-induced changes in microvascular blood volume of skeletal muscle and myocardium will be correlated with amount of physical activity as measured with accelerometers and VO2max.

Secondary outcome

Secondary endpoints will be microvascular blood volume during basal and hyperinsulinemic state without Intralipid infusion, in myocardium and skeletal muscle. Also, whole-body insulin sensitivity as measured by the glucose infusion rate will be correlated with physical activity. Body fat percentage and blood pressure (Nexfin) will be measured to test if these parameters are equal between subjects and if not in which amount they differ. Contraction induced microvascular recruitment will be measured with the handgrip dynamometer to test if we can show an increase of MBV with Ceus during a different physiological parameter than insulin alone.

Study description

Background summary

Physical activity lowers the risk of ischemic heart disease and type 2 diabetes, but the mechanisms by which physical activity exerts these effects are incompletely understood. Excess of free fatty acids (FFA) is shown to be a key factor in the development of insulin resistance and a reduced dilatory response of arterioles and subsequent decrease of microvascular recruitment to insulin, also referred to as vascular insulin resistance, has been suggested to play a role in ischemic heart disease. Acute exposure to FFA impairs whole body insulin sensitivity and physical activity has been shown to prevent this effect. Insulin-induced microvascular recruitment in both skeletal muscle and heart are also impaired after acute FFA infusion, but the effect of physical activity has not been investigated. An improved response to FFA of the microvasculature in skeletal muscle could potentially protect against insulin resistance and a similar effect in the heart could reduce risk of developing ischemic heart disease.

Study objective

We hypothesize that the amount of physical activity correlates with insulin-induced microvascular recruitment during free-fatty acid infusion in skeletal muscle as well as in the heart. In this study we aim to test this hypothesis.

Study design

We will test healthy subjects. We will study whole-body insulin sensitivity and insulin-induced microvascular recruitment by contrast ultrasonography in skeletal muscle and myocardium before and after iv. FFA infusion and measure physical activity with accelerometers and vo2max.

Study burden and risks

After application subjects will be selected based on a short history taking by telephone.

After inclusion, the subjects will be visiting the clinical research unit once. They will undergo basic examination including measurement of length, body weight, blood pressure and plasma glucose to make sure the subject's health status is in agreement with the history provided by telephone. Next, subjects will undergo a hyperinsulinemic-euglycemic clamp, with microvascular contrast ultrasonography measurements of the skeletal muscle and the heart. Risks associated with these measurements consist of risk of hypoglycemia or hyperglycaemia during hyperinsulinemic-euglycemic clamp, headache, nausea, transient pulmonary hypertension and allergic reactions during contrast ultrasonography (rare). Bruising and local pain in the antecubital fold may be experienced during and after placement of venous catheters and/or during blood sampling. As a compensation for their time and effort subjects will receive €85 after completion of the investigation. Burden and risk of participation are

very limited.

Risk of VO2 max measurements in these healthy subjects is very small, but include myalgia because of the exercise and a very small risk of syncope.

In addition, we would like to perform a pilot in 10 participants to optimise the contrast ultrasonography protocol. This pilot protocol will take 45 minutes. Risks and burden for the participants are very limited.

Contacts

Public

Vrije Universiteit Medisch Centrum

Van der Boechorststraat 7
Amsterdam 1081 BT
NL

Scientific

Vrije Universiteit Medisch Centrum

Van der Boechorststraat 7
Amsterdam 1081 BT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

Young healthy male subjects. Age 18-30 years.

Exclusion criteria

A drastic recent change in physical activity (eg. just stopped being an athlete), conditions that can significantly influence the amount of energy that is needed for physical activity (eg. a lower-leg prosthesis), history of obesity, hypertension, diabetes mellitus, hyperlipidemia, smoking (currently, or > 1 package per month over the last 2 years), documented cardiovascular disease, use of medication that could potentially affect insulin sensitivity or microvascular function or inflammatory status.

Study design

Design

Study type: Observational invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Basic science

Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 06-08-2015

Enrollment: 38

Type: Actual

Ethics review

Approved WMO

Date: 16-07-2015

Application type: First submission

Review commission: METC Amsterdam UMC

Approved WMO

Date: 16-10-2015

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date:	04-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	01-04-2016
Application type:	Amendment
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	NL53462.029.15