

Dose response effect of plasma free fatty acid on insulin mediated capillary recruitment, glucose uptake and glycocalyx modulation

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Ethical review	Approved WMO
Status	Pending
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON32150

Source

ToetsingOnline

Brief title

Lipotox

Condition

- Diabetic complications
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym

diabetes mellitus

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: capillary recruitment, FMD, free fatty acids, glycocalyx

Outcome measures

Primary outcome

Increase of capillary blood volume by hyperinsulinemia

Recruitment of glycocalyx volume

Effects of FFA infusion

Secondary outcome

Glycocalyx changes (SDF)

Glucose uptake

Endothelial function

Glycocalyx degradation products

NO bioavailability

Study description

Background summary

There is strong support for the notion that free fatty acids (FFAs) are an important link between obesity, insulin resistance and type 2 diabetes. Recent findings suggest also a role for the microcirculation in the insulin mediated glucose disposal in peripheral tissues. In this study we will examine insulin mediated glucose disposal under different levels of FFAs and look at the endothelial glycocalyx, a highly hydrated mesh on the endothelium. We hypothesize that insulin mediates capillary blood volume by glycocalyx modulation and that FFA interfere with this process.

Study objective

In the current study we want to obtain fundamental insight in the role of insulin-mediated glycocalyx modulation as well as the effect of FFAs on this mechanism. We propose that increased levels of FFA degrade the glycocalyx and result in an impaired insulin mediated increase in capillary blood volume. This will concurrently result in decreased glucose disposal.

Study design

Ten lean male subjects will be studied 3 times after an overnight fast. Micro- and macrovasculature will be studied in a hyperinsulinemic euglycemic clamp combined with each visit a different level of FFAs. After a period of one week subjects will undergo the second study using the same protocol as in the first study (but with a different level of FFA).

All studies will be performed in healthy volunteers and a pilot study will be performed for power analysis. All volunteers will undergo a hyperinsulinemic euglycemic clamp. Within this clamp they will be faced with three levels of FFA: normal, postprandial and diabetic levels.

Intervention

1. Clamp with FFAs: placebo, postprandial en diabetic levels through Intralipid infusion.
2. Hyperinsulinemic clamp after 4 hours of FFA clamp
3. Capillary volume measurements: infusion of haes 6% arterially and venous sampling. Before and after hyperinsulinemic clamp.
4. Flow mediated dilation (FMD) brachial artery (non invasive). Before FFA clamp and before hyperinsulinemic clamp.
5. Veneuze plethysmografie: non-invasieve method to determine arterial flow.
6. Sidestream Darkfield (SDF) beeldvorming. During the entire protocol every hour a 5 minute recording of the sublingual microcirculation is made.

Study burden and risks

Although the protocol is extensive there is only a minimal risk involved. The arterial line will be inserted by trained personel aswell as the venous catheters. Infusio of Intralipid is by using heparin heparine minimized in dose and a hyperinsulinemic euglycemisc clamp is a low risk procedure.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

Healthy male

age between 18 and 35 years old

Exclusion criteria

diabetes

hypertension

smoking

cardiovascular disease

Study design

Design

Study type: Interventional

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Basic science

Recruitment

NL

Recruitment status: Pending

Start date (anticipated): 01-03-2008

Enrollment: 10

Type: Anticipated

Ethics review

Approved WMO

Application type: First submission

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

CCMO

ID

NL21557.018.08