Insulin-induced microvascular dilatation during a physiological stimulus - Studies in hypertension and obesity.

Published: 09-04-2008
Last updated: 11-05-2024

1 : Will the intake of a liquid meal lead to insulin-induced microvascular dilatation in healthy subjects? 2: Does meal composition (high fat meal vs. high carb meal) play a role in the occurence of insulin-induced microvascular dilatation in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Vascular hypertensive disorders
Study type	Interventional

Summary

ID

NL-OMON35296

Source
ToetsingOnline

Brief title
Microvascular dilatation after endogenous induced hyperinsulinemia

Condition

- Vascular hypertensive disorders

Synonym
high blood pressure, hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Hypertension, Insulin, Microcirculation, Obesity

Outcome measures

Primary outcome

- functional recruitment of capillaries in the skin.

Secondary outcome

- perfused capillary density in the nailfold.

- Endothelium- (in)dependent vasodilatation of finger skin microcirculation

- Density of arterioloes, capillaries and venules in the bulbar conjunctiva.

- Diameter of arterioles and venules in the bulbar conjunctiva.

- Insulin sensitivity

Study description

Background summary

Title: Insulin-induced microvascular activity during a physiological stimulus - Studies in hypertension and obesity.

One of mechanism involved in the insulin-mediated regulation of blood glucose levels is the vasodilatory response by resis-tance vessels and preterminal arterioles. These hemodynamic effects of insuline contribute to glucose uptake (for approx. 40%) and several studies demonstrated impaired insulin-induced hemodynamic effects in hypertension and obesity. However, in these studies the hyperinsulinemia was artificially induced by a hyperinsulinemic euglycemic clamp. Till so far it is unknown if these hemodynamic effects of insulin will also occur with a physiological stimulus. In this study we will examine if the insulin-induced microvascular effects will occur after a physiological stimulus (i.e. a liquid high carb or high fat meal (MTT)). With that the physiological importance of the insulin-induced microvascular dilatation can be elucidated.

Hypothesis:
We hypothesize that liquid meal intake and consequently the endogenous induced hyperinsulinemia will lead to insulin-induced microvascular dilatation in

healthy normotensive subjects. Moreover, we suggest that the postprandial plasma insulin concentration shows a positive correlation to insulin-induced microvascular dilatation while the postprandial free fatty acid concentration shows a negative correlation. Furthermore, we suggest that the insulin-mediated microvascular dilatation, resulting from this fysiological induced hyperinsulinemia, will be less in hypertensive and obese subjects compared to the healthy controls.

Study objective

1 : Will the intake of a liquid meal lead to insulin-induced microvascular dilatation in healthy subjects?
2: Does meal composition (high fat meal vs. high carb meal) play a role in the occurence of insulin-induced microvascular dilatation in healthy subjects?
3: Is this insulin-induced microvascular dilatation after a physiological stimulus (liquid high carb meal and liquid high fat meal) impaired in obese and hypertensive subjects compared to the healthy controls?

Study design

All subjects will bring 3 visits to the AZM. The following interventions will be applied:
- microcirculation measurement - intake liquid high carb meal - microcirculation measurement
- microcirculation measurement - intake liquid high fat meal - microcirculation measurement
- microcirculation measurement - intake placebo - microcirculation measurement

During the visits 1 catheter will be inserted in the antecubital vein of the lower dominant arm. Subsequently a set of microcirculation measurements will be performed (t=0 min.). After this set of measurements (t=90 min.) subjects will drink a liquid high carb meal, a liquid high fat meal or a placebo drink. 30 minutes after intake (t=120 min.) a second set of microcirculation measurements will be performed.

During the study days the heart rate and blood pressure will be monitored and 8 venous blood samples of 5 ml and 8 venous blood samples of 1 ml will be taken. The intake of glucose or placebo will be randomly assigned.

Intervention

The hypertensive subjects will be asked to discontinu the intake of antihypertensive medication 3 weeks prior to the study.
All subjects will be asked to collect urine during 24hrs prior to the first and second study day. Microcirculation measurements: 1) perfused capillary density and functional capillary recruitment in the nailfold, visualized by a capillary

mi-croscope, 2) endothelium- (in)dependent vasodilation of finger skin microcirculation, evaluated with laser Doppler measurements in combination with iontophoresis of acetyl-choline and sodium nitroprusside, and 3) densities and diameter of arterioles, capillaries and venules in the bulbar conjunctiva, measured with conjunctival microscopy.
The high carb meals and high fat meals will be taken orally. During the visit several blood samples will be taken, blood pressure and heart rate will be monitored.

Study burden and risks

Discontinuing the antihypertensive medication can lead to symptoms and/or unwarranted increases in blood pressure (>220/120 mmHg). When this will occur, the medication will be started again and participation to the study will be stoped. All methods used for measuring microcirculation are non-invasive. The burden of these measurements is therefore negligible. Inserting the catheters can be alittle bit painful and after removal sometimes bruises can appear. The liquid high carb and high fat meals will be taken orally, no health risks are involved. The used dose of acetylcholine and sodium nitroprusside is very low and appeared to have side effects only in very rare cases (for example during an allergic reaction). The effect is only local in the skin an whenever a side effect will occur, the study will be immediately stopped. There will be taken 48 ml of blood during one study day. No burden or risk is involved with this amount. De subject will be sober during the study day. Previous studies showed that this isn't a big burden for a subject.

Contacts

Public
Universiteit Maastricht

Postbus 5800
6202 AZ Maastricht
Nederland
Scientific
Universiteit Maastricht

Postbus 5800
6202 AZ Maastricht
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion criteria healthy normotensive subjects : 18-60 years, Caucasian, blood pressure <140/90 mmHg.
Inclusion criteria obese normotensive subjects: 18-60 years, Caucasian, blood pressure <140/90 mmHg, BMI 30-38kg/m2
Inclusion criteria hypertensive subjects: 18-60 years, Caucasian, untreated hypertension >140/90mmHg.

Exclusion criteria

Exclusion criteria for healthy normotensive and hypertensive subjects: Obesity (BMI>27kg/m2), cardiovascular disease (stroke, coronary artery disease, peripheral vascular disease, heart failure), diabetes mellitus according to the criteria of the ADA, smoking, alcohol use >4U/day, use of medication (antihypertensive drugs, lipid lowering drugs, corticosteroids, NNSAIDs), pregnancy, and wearing contact lenses.;Exclusion criteria for normotensive obese subjects: cardiovascular disease (stroke, coronary artery disease, peripheral vascular disease, heart failure), impaired glucose tolerance or diabetes mellitus according to the criteria of the ADA, smoking, alcohol use >4U/day, use of medication (antihypertensive drugs, lipid lowering drugs, corticosteroids, NNSAIDs), pregnancy, and wearing contact lenses.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-11-2008
Enrollment:	48
Type:	Actual

Ethics review

Approved WMO Date:	09-04-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	05-11-2008
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-05-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL22461.068.08