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

No registrations found.

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

Summary

ID

NL-OMON20799

Source
NTR

Brief title
Microvascular dilatation after endogenous induced hyperinsulinemia

Health condition

Hypertension - hypertensie
Obesity - obesitas
Microcirculation - microcirculatie

Intervention

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 arterioles, capillaries and venules in the bulbar conjunctiva.

- Diameter of arterioles and venules in the bulbar conjunctiva.

- Insulin sensitivity (HOMA-IR)

Study description

Background summary

One of mechanism involved in the insulin-mediated regulation of blood glucose levels is the vasodilatory response by resistance 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 insulininduced microvascular effects will occur after a physiological stimulus (i.e. a oral glucose tolerance test). With that the physiological importance of the insulin-induced microvascular dilatation can be elucidated.
In this study we hypothesize that oral glucose intake and consequently the endogenous induced hyperinsulinemia will lead to insulin-induced microvascular dilatation in healthy normotensive subjects. 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 healthy controls.

Objectives:

1. Will the intake of glucose lead to insulin-induced microvascular dilatation in healthy subjects?

2. Is this insulin-induced microvascular dilatation after a physiological stimulus impaired in obese and hypertensive subjects compared to healthy controls?

Study design:

All subjects will bring 2 visits to the AZM. The following interventions will be applied:

- microcirculation measurement – intake glucose sollution – microcirculation measurement
- microcirculation measurement – intake placebo sollution – microcirculation measurement

During the 2 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 glucose- or placebo sollution. 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 6 venous blood samples of 5 ml and 5 venous blood samples of 1 ml will be taken. The intake of glucose or placebo will be randomly assigned.

Study objective

We hypothesize that oral glucose intake and consequently the endogenous induced hyperinsulinemia will lead to insulin-induced
microvascular dilatation in healthy normotensive subjects. 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 healthy controls.

Study design

Each visit will take approx. 3,5 hours. During each visit 1 catheter will be inserted in the antecubital vein of the lower arm and 1 venous blood sample of 5 ml will be drawn. Next, a set of microcirculation measurements will be performed (t=0 min.)

On t=90 min. one venous blood sample of 5 ml and one venous blood sample of 1 ml will be drawn. And after this, the glucose or placebo solution will be taken orally.

On t=105 min., t=120 min., t=150 min. and t=120 min. 1 venous blood sample of 5 ml and 1 venous blood sample of 1 ml will be taken.

On t =120 min. a second set of microcirculation measurements will be performed. The catheter will be removed at t=210 min.

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 study day.
Microcirculation measurements:

1. perfused capillary density and functional capillary recruitment in the nailfold, visualized by a capillary microscope

2. endothelium- (in)
dependent vasodilation of finger skin microcirculation, evaluated with laser Doppler measurements in combination with
iontophoresis of acetyl-choline and sodium nitroprusside

3. densities and diameter of arterioles, capillaries and venules in the bulbar conjunctiva, measured with conjunctival microscopy.

The glucose sollution will be taken orally. During the visit several blood samples will be taken, blood pressure and heart rate will
be monitored.

Contacts

Public
Department of Internal Medicine
University Hospital Maastricht
P.O. Box 5800

A.J.H.M. Houben
Department of Internal Medicine

Maastricht 6202 AZ
The Netherlands
Scientific
Department of Internal Medicine
University Hospital Maastricht
P.O. Box 5800

A.J.H.M. Houben
Department of Internal Medicine

Maastricht 6202 AZ
The Netherlands

Eligibility criteria

Inclusion criteria

- Inclusion criteria healthy normotensive subjects:

1. 18-60 years

2. Caucasian

3. Blood pressure <140/90 mmHg

- Inclusion criteria obese normotensive subjects:

1. 18-60 years

2. Caucasian

3. Blood pressure <140/90 mmHg

4. BMI 30-38kg/m2

- Inclusion criteria hypertensive subjects:

1. 18-60 years

2. Caucasian

3. Untreated hypertension >140/90mmHg.

Exclusion criteria

- Exclusion criteria for healthy normotensive and hypertensive subjects:

1. Obesity (BMI>27kg/m2)

2. Cardiovascular disease (stroke, coronary artery disease, peripheral vascular disease, heart failure)

3. Diabetes mellitus according to the criteria of the ADA

4. Smoking

5. Alcohol use >4U/day

6. Use of medication (antihypertensive drugs, lipid lowering drugs, corticosteroids, NNSAIDs)

7. Pregnancy

8. Wearing contact lenses

- Exclusion criteria for normotensive obese subjects:

1. Cardiovascular disease (stroke, coronary artery disease, peripheral vascular disease, heart failure)

2. Impaired glucose tolerance or diabetes mellitus according to the criteria of the ADA

3. Smoking

4. Alcohol use >4U/day

5. Use of medication
(antihypertensive drugs, lipid lowering drugs, corticosteroids, NNSAIDs)

6. Pregnancy

7. Wearing contact lenses

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-04-2008
Enrollment:	48
Type:	Anticipated

Ethics review

Positive opinion

Date:	19-03-2008

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	NL1206
NTR-old	NTR1251
Other	MEC : 08-2-031
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A