Insulin-induced microvascular activity in patients with essential hypertension: a possible role for angiotensin II AT1-receptor blockers.

No registrations found.

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

Summary

ID

NL-OMON24297

Source
Nationaal Trial Register

Brief title
Role of AT1-receptor blockers in insulin-induced vasodilation.

Health condition

Hypertension
Hypertensie

Sponsors and support

Primary sponsor: Prof. CDA Stehouwer
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Source(s) of monetary or material Support: CARIM, Cardiovascular Research Institute Maastricht

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

Study description

Background summary

Background: There is a relation between hypertension and insulin resistance, both associated with increased cardiovascular risk. Hypertension and insulin resistance are characterized by dysfunctions in microcirculation, however it is unclear if microcirculation is the link be-tween these two abnormalities. In addition to its actions in mediating glucose uptake, insulin knows several vascular effects. Insulin induces a vasodilatory response by resis-tance vessels and preterminal arterioles leading to an overall increase in blood flow (glucose) to the muscles. The local activity of the vasoconstrictor angiotensin II is elevated in patients with hypertension. Previous studies show a possible role for angiotensin II in the hypertensive, insulin resistant phenotype, however a mechanism remains unexplained. In this study we hypothesize that blocking the angiotensin II AT1-receptor improves the insulin-induced microvascular dilatation.

Objectives:
1. Does blockade of the angiotensin II AT1-receptor improve the insulin-induced mi-crovascular effects in hypertensive patients.
2. Does blockade of the angiotensin II AT1-receptor impair the insulin-induced mi-crovascular effects in normotensive control subjects?

Study design:
All subjects will bring 3 visits to the AZM. The following interventions will be applied:
- hyperinsulinemic euglycemic clamp (HEC) + placebo
- HEC + irbesartan (600 mg)
- HEC + felodipine ER (20 mg)

Study objective

1: Blockade of the angiotensin II AT1-receptor improves the insulin-induced microvascular effects in hypertensive patients.
2: Blockade of the angiotensin II AT1-receptor impairs the insulin-induced microvascular effects in normotensive control subjects.

Study design

Each visit takes approx. 7,5 hr. During all visits 2 catheters will be inserted in the antecubital vein of the lower arms. On one study day (randomly assigned)
a set of microcirculation measurements will be performed on t=-90 minutes. On all three study days insulin and glucose will be infused on t=0 min. After 90 minutes of HEC a set microcirculation measurements will be done, and after these measurements placebo, irbesartan or felodipine will be taken in a single oral dose. 210 minutes after intake (t=300 min.) another set of microcirculation measurements will be done.
During the study days the heart rate and blood pressure will be monitored and blood samples will be taken. The interventions will be randomly assigned. One week is scheduled between each visit.

Intervention

Hypertensive subjects will be asked to discontinue the intake of antihypertensive medication three weeks before the start of the study. All subjects will be asked to start a low salt diet (100mmol/day) 7 days prior to the first study day and to collect urine during 24hrs prior to the first study day.
Three study days will be performed (each day lasts 7,5hr). The following measurements will be done:
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, and 3) densities and diameter of arterioles, capillaries and venules in the bulbar conjunctiva, measured with conjunctival microscopy.
Placebo, irbesartan (600mg) and felodipine (20mg) will be ingested orally in a single dose.
Insulin is infused in a primed continuous manner at a rate of 50mU·kg-1·hr-1. Euglycemia will be maintained by adjusting the rate of a 20% D-glucose infusion based on plasma glucose measurements performed at 5 min intervals. During the visit several blood samples will be taken, blood pressure and heart rate will be monitored.

Contacts

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Eligibility criteria

Inclusion criteria

Inclusion criteria hypertensive subjects:

1. 18-60 years
2. Caucasian
3. untreated hypertension >140/90mmHg.

Inclusion criteria normotensive subjects:

1. 18-60 years
2. Caucasian
3. Blood pressure <140/90 mmHg.

Exclusion criteria

1. Obesity (BMI>27kg/m2)
2. Cardiovascular disease (stroke, coronary artery disease, peripheral vascular disease, heart failure)
3. Impaired glucose tolerance or 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

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2008
Enrollment:	32
Type:	Anticipated

Ethics review

Positive opinion

Date:	04-03-2008
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	NL1158
NTR-old	NTR1202
Other	MEC : MEC 07-2-115
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A