Insulin-induced microvascular activity in patients with essential hypertension: possible interactions with angiotensin II - Amendement 24-09-2007

Published: 19-09-2006
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The goal of this study is examining the acute effects of insulin on microcirculation in hypertensive insulinresistant subjects and investigate if angiotensine II influences these effects. Amendement: The goal of the amendement is to exame the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON30618

Source
ToetsingOnline

Brief title
Role of angII in insulin-induced vasodilation - Amendement 24-09-07

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Vascular hypertensive disorders

Synonym
high blood pressure, hypertension

Research involving
Human

Sponsors and support

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

Intervention

Keyword: angiotensin II, bloodpressure response, phenylephrine

Outcome measures

Primary outcome

Amendement:

- blood pressure

Secondary outcome

Amendement:

- plasma angiotensinII levels

Study description

Background summary

There is an 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 between these two abnormalities. In addition to its actions in mediating glucose uptake, insulin knows several vascular effects. Insulin induces a vasodilatory response by resistance 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 resis-tant phenotype, however a mechanism remains unexplained. In this study we hypothesize that angiotensin II impairs the microvascular actions of insulin (as mentioned above), resulting in a decreased level of glucose uptake and as a consequence hyperinsulinaemia and insulin resis-tance.

Study objective

The goal of this study is examining the acute effects of insulin on microcirculation in hypertensive insulinresistant subjects and investigate if angiotensine II influences these effects.

Amendement: The goal of the amendement is to exame the bloodpressure response to angiotensinII and phenylephrine, without concomittant insulin infusion.

Study design

Amendement: All subjects will bring 2 visits to the AZM after a ten hour fast. The bloodpressure response to infusion of angiotenisinII and phenylephrine will be measured during these visits (automatic blood pressure device, Accutorr). During each visit 2 catheters will be inserted in the antecubital vein of both arms. Angiotensin II (day1) of Phenylephrine (day2) (randomized) will be infused through the cathether in the non-dominant arm (dosage and time (120 min) of this infusion will be exactly the same as applied in MEC 06-2-074). Blood pressure will be measured before, after 30 minutes infusion and after 110 minutes infusion of angiotensinII of phenylefrin. At these three timepoints 2 venous bloodsamples of 5 ml will also be taken from the catheter in the dominant-arm for determination of plasma angiotensinII levels (equals 30 ml of blood in total for 1 studyday). A study day will take 3 hours. At least 24 hrs will be scheduled between each visit.

If the difference in bloodpressure respons to AngiotensinII and phenylephrine still exists without the co-infusion of insulin, we will ask the subjects to come for a third study day. The bloodpressure respons to a lower dosage (1 ng/kg/min) of angiotensin II will be measured during this visit. It is estimated that this lowered dosage will give an equal rise in blood pressure as can be seen with phenylephrine. If so, this lower dosage of ang II will be applied in MEC 06-2-074. The subjects will be imformed about the possibility of this third study day in advance.

The subjects in MEC 06-2-074 were measured during a high sodium diet. As salt intake can influence the blood pressure response we will ask the participents of this study to start with the high sodium diet again 7 days prior to the first visit. The subjects will be asked to collect there urine for 24 hours, on the day before visit 1.

Intervention

Amendement:
Angiotensin II and phenylephrine will be infused intravenously.
During the visit 6x5 ml venous blood samples will be taken, blood pressure and heart rate will be monitored.

Study burden and risks

Amendement:
Inserting the catheters can be a little bit painful and after removal sometimes bruises can appear. There are no risks involved in the infusion of angiotensin II and phenylephrine. There will be taken 30 ml of blood during one study day. No burden or risk is involved with this amount. De subject will be sober during the whole study day. Previous studies showed that this isn't a big burden for a subject.

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

Age 18-60, Caucasian, blood pressure <140/90 mmHg.

Exclusion criteria

Obesity: BMI > 27 kg/m2, 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 >4 U/day, use of medication (antihypertensive drugs, lipid lowering drugs, corticosteroids, NSAIDs), pregnancy. Having contact lenses is also an exclusion criteria.

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-02-2007
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Angiotensin II
Generic name:	Angiotensin II
Product type:	Medicine
Brand name:	Phenylephrine
Generic name:	Phenylephrine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-09-2006
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-10-2006
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-11-2006
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-10-2007
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
EudraCT	EUCTR2006-004678-29-NL
CCMO	NL13408.068.06