# Local microvascular reactivity to Acetylcholine in patients with essential hypertension: possible interactions with the local renin-angiotensin system.

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

## Summary

### ID

NL-OMON31352

**Source**
ToetsingOnline

**Brief title**
Local microvascular reactivity to Ach in hypertensive patients

### Condition

- 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:** Stichting Ondersteuning Hypertensie Onderzoek (SOHO)

## Intervention

**Keyword:** Acetylcholine, Angiotensin II, hypertension, microvascular reactivity

## Outcome measures

### Primary outcome

Changes in vascular diameters of bulbar conjunctiva, and changes in skin

laser-Doppler flux.

### Secondary outcome

/

# Study description

### Background summary

In a pilot study (MEC 02-188) we investigated the effect of topically administrated Angiotensin II (0,01 %) on the microcirculation of the bulbar conjunctiva in hypertensive patients. We found that the average decrease in arteriolar diameter after Angiotensin II (Ang II) eye drops in normotensive (control) group was larger as compared to the hypertensive group. These results are in contrast with animal studies, where Ang II administration in hypertensive animals, leads to a larger blood pressure response and an increased vasoconstriction.
A possible explanation for the diminished vasoconstrictor effect of Ang II in hypertension, is the simultaneous stimulation of endogenic nitric oxide (NO) production, to counteract the effect of Ang II. Several studies have shown that the vasoconstrictor effect of Ang II is partially counterbalanced by the simultaneously stimulation of endogenous NO production, possible via activation of the AT2-receptor. Such an effect may vary between different vascular beds, due to different expression levels of the AT2-receptor.

### Study objective

We aim to study the vasoactive effects of Acetylcholine (NO dependent) in hypertensive patients and normotensive participants. Second, the correlation between the vasoreactivity of Acetylcholine and Angiotensin II will be studied.

Third, the magnitude of vasoreactivity between the microvascular beds of the bulbar conjunctiva and the finger skin will be compared.

## Study design

After a high sodium diet of 7 days (in order to suppress the activity of the endogenous renin-angiotensin system).
Participants will visit the University Hospital Maastricht, on two occasions, in the morning following an overnight fast. At the start, height, weight and blood pressure (triple) will be measured, and a venflon will be introduced into the antecubital vein for blood sampling (to determine Ang II levels).
Participants will be studied in a quiet temperature-controlled room. The following aspects will take place:
The microvascular effect of Acetylcholine, Sodium Nitroprusside (control), and placebo (NaCl, 0.9%) will be studied on the morning of day 1 in the vascular bed of the bulbar conjunctiva (using a custom build intravital microscope) and the finger skin (using laser Doppler fluxmetry combined with iontophoresis).

At the morning of day 2, the microvascular effect of Angiotensin II and placebo (NaCl, 0.9%) will be studied in the vascular bed of the bulbar conjunctiva and the finger skin.

## Intervention

Local application of Acetylcholine, Sodium Nitroprusside, Angiotensin II and placebo in the bulbar conjunctiva (eye drops) and the finger skin (iontophoresis).

## Study burden and risks

-Withdrawal of blood pressure lowering medication can lead to complaints and/or unacceptable blood pressure rise (180/120 mmHg). When withdrawal of medication leads to complaints and/or unacceptable blood pressure rise, medication will be started again and participation in the study will be stopped. This in consultation with the patient and the physician.
-The used dose of Acetylcholine, Sodium nitroprusside and Angiotensine II is very low, but in very rare cases there can be an allergic reaction.
-The Microcirculation measurements used are non-invasive, the risks for the patients are therefore very small.
- The placement of a venflon can be painful and removing it can cause bruises.

# 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

Inclusion criteria hypertensive patients:
- Age:18-65 year
- Caucasian
- Untreated blood pressure > 140/90 mmHg
- In consultation with the internist, anti-hypertensive medication will be stopped 3 weeks prior to the start of the experiment. ;Inclusion criteria normotensive volunteers:
- Age:18-65 year
- Caucasian
- Blood pressure <140/90 mmHg

### Exclusion criteria

- Secondary hypertension
- Diabetes mellitus according to the criteria of the ADA
- Kidney failure: serum creatinine > 150 µmol/l
- Unable to stop blood pressure lowering medication during a period of 3 weeks
- Use of blood cholesterol lowering medication
- (Hypertensive) retinopathy, glaucoma or conjunctival disease
- Connective tissue disease
- Contact lenses

## Study design

### Design

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

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-06-2007 |
| Enrollment: | 32 |
| Type: | Anticipated |

### Medical products/devices used

| | |
|---|---|
| Registration: | No |
| Product type: | Medicine |
| Brand name: | / |
| Generic name: | Angiotensin II |
| Product type: | Medicine |

| | |
|---|---|
| Brand name: | / |
| Generic name: | Sodium Nitroprusside |
| Registration: | Yes - NL outside intended use |
| Product type: | Medicine |
| Brand name: | Miochol-E |
| Generic name: | Acetylcholine |
| Registration: | Yes - NL outside intended use |

## Ethics review

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|---|---|
| Approved WMO Date: | 26-04-2007 |
| Application type: | First submission |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 13-06-2007 |
| Application type: | First submission |
| 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 | EUCTR2007-001917-40-NL |

| Register | ID |
| --- | --- |
| CCMO | NL17405.068.07 |