Systemic effects of mild renal insufficiency: the relation between forearm blood flow and ADMA.

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The results of this study will give better insights in the role of ADMA in the development of systemic endothelial dysfunction.

Ethical review	Approved WMO
Status	Pending
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON33594

Source
ToetsingOnline

Brief title
Mild renal insufficiency and forearm blood flow.

Condition

- Renal disorders (excl nephropathies)
- Vascular hypertensive disorders

Synonym
deterioration of kidney function, renal dysfunction

Research involving
Human

Sponsors and support

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

Intervention

Keyword: asymmetric dimethylarginine, forearm blood flow, hypertension, mild renal insufficiency

Outcome measures

Primary outcome

The main study parameter is forearm blood flow.

Secondary outcome

The secundairy end point is ADMA-concentration. Other parameters include SDMA

(symmetric dymethylarginine) and L-arginine concentrations and DDAH-activity.

Study description

Background summary

According to different studies in patients with mild renal insufficiency the cardiovascular risk is elevated more than can be explained on the basis of traditional risk factors. At the same time the concentration of ADMA (asymmetric dymethylarginine) in the blood is elevated in patients with mild renal insufficiency. ADMA is an endogenous inhibitor of nitric oxide (NO) and elevated concentrations of this substance lead to diminished endothelium-dependent vasodilatation. The increased ADMA levels may originate either from the kidney or from the systemic vasculature. Nevertheless, abnormalities of the endothelium-dependent vasodilatation lay the foundation for the development of atherosclerosis. It is likely that the ADMA-induced endothelial dysfunction is a causal factor in the progression of systemic atherosclerosis found in patients with mild renal insufficiency.
In this study the relationship between the systemic NO-mediated endothelium-dependant vasodilatation, measured as forearm blood flow and venous ADMA-level is studied, in hypertensive as well as healthy subjects. In the hypertensive subjects it also will be examined to what extend the forearm blood flow (FBF) can be influenced by treatment with an angiotensin-II-receptorblocker (olmesartan) and/or a statin (rosuvastatin).
It has been documented that ADMA levels in hypertensive subjects are higher than in healthy subjects. The ADMA-level in hypertensive subjects will be reversely related to the basal blood flow and the endothelial NO-availability in the forearm. Pre-treatment with an angiotensin-II- receptorblocker and/or a statin will decrease the ADMA-levels via increased clearance of ADMA and,

consequently, will *normalise* the forearm blood flow and NO-availability.

Study objective

The results of this study will give better insights in the role of ADMA in the development of systemic endothelial dysfunction.

Study design

The study is an intervention study. A control group (n=15) will undergo a FBF measurement once and 4 patients groups (n=60) will undergo FBF measurement twice. After a baseline FBF measurement without medication the patients will be treated with placebo, olmesartan and/or rosuvastatin during a three-weeks interval. Next, FBF will be assessed again after sampling for ADMA and DDAH activity (ADMA degrading enzyme).

Intervention

The intervention will consist of a three-week treatmentperiod with placebo, eprosartan 600mg and/or rosuvastatin 20 mg.

Study burden and risks

The patients will visit the hospital twice for FBF-measurements with an interval of 3 weeks. During this interval medication will be used and home blood pressure measurements will be performed. For the FBF-measurements 80 and 85 ml of blood will be drawn. The control group will undergo one screening visit (7 ml blood will be drawn) and one FBF-measurements (60 ml blood will be drawn) 7-10 days later. The control group has to collect urine for 24 hours.
The week before the FBF-measurements a low-salt diet will be followed by all participants.
The risks associated with participation include mainly small inconveniences (tingling feeling in the arm during the FBF, small haematoma at the site of the puncture of the brachial artery and veins, and sometimes muscle aches as a side-effect of the statin use. The solutions used to determine the FBF are safe. The hypertensive subjects will be deprived of antihypertensive medication 3 weeks longer than usual.

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

hypertension (without medication BP >140/90 mmHg and <180/110 mmHg) creatinine clearance 60-90 ml/min
microalbuminuria (30-300 mg albumin/24 hour)
age 18-75
total cholesterol >4,5 mmol/l
BMI between 18 and 30 kg/m2

Exclusion criteria

diabetes mellitus
contra-indication for use of an angiotensin-II-receptorblocker or statin
statin use

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2007
Enrollment:	75
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Crestor
Generic name:	Rosuvastatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Teveten
Generic name:	Eprosartan
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-10-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-02-2008

Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-02-2008
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-06-2009
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	EUCTR2007-005546-20-NL
CCMO	NL19978.068.07