ADMA and renal endothelial dysfunction: de effects of ARB and/or statins in hypertensive patients with mild renal insufficiency

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The results of this study will give better insights in the role of ADMA in the development of systemicendothelial dysfunction and the relation with mild renal insufficiency.

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

Summary

ID

NL-OMON32808

Source
ToetsingOnline

Brief title
ADMA and renal endothelial dysfunction

Condition

- Renal disorders (excl nephropathies)
- Vascular hypertensive disorders

Synonym
deterioration of renal 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, hypertension, mild renal insufficiency

Outcome measures

Primary outcome

Basal renal perfusion, fractional change in renal perfusion after intrarenal

L-NMMA infusion, arterial en venous ADMA, SDMA (symmetric dimethylarginine) and

L-arginine concentrations and renal elimination of systemic ADMA, SDMA and

L-arginine

Secondary outcome

Microalbuminuria, creatinin clearance, blood pressure, plasma LDL (low density

lipoproteins), HDL (high density lipoproteins), triglycerides and total

cholesterol concentrations

Study description

Background summary

ADMA (asymmetrical dimethylarginine) is an endogenous inhibitor of nitric oxide (NO), the most important determinant for endothelial dependent vasodilatation. ADMA plasma concentrations are elevated in several cardiovascular risk populations, including patients with essential hypertension and/or kidney insufficiency. Recent clinical studies demonstrated that ADMA has also a pronounced impact on (primary NO-regulated) renal perfusion. Furthermore, medication like angiotensine-II-receptorblokkers (ARB) and statines lower ADMA concentrations and improve endothelial dependent dilation.
Hypothesis: ADMA plasma concentrations are higher in persons with mild renal insufficiency compared to persons with normal kidney function. ADMA plasma concentrations are inversely proportional to renal perfusion and endothelial nitric oxide (NO) availibility in the kidney. Medical treatment with statins and/or angiotensin II receptor blockers (ARB) will reduce ADMA plasma

concentrations, improves kidney perfusion and NO availibility.

Study objective

The results of this study will give better insights in the role of ADMA in the development of systemic
endothelial dysfunction and the relation with mild renal insufficiency.

Study design

The study is a singleblind, randomized controled intervention trail. Sixty nine patients will be randomized in 3 intervention groups and treated during 3 weeks with eprosartan, rosuvastatin or both till the renal angiography.

Intervention

The intervention will consist of a three-week treatment period with eprosartan 600mg and/or rosuvastatin
20 mg. During the renal angiography, L-NMMA will be intrarenally administered after the regular 133 Xenon perfusion measurement, followed by an additional 133 Xenon perfusion measurement and blood sampling.

Study burden and risks

We expect from participants that they (besides the clinical indicated diagnostic investigations) 1) take the prescribed medication during 3 weeks before the renal angiography, 2) go through an additional 133 Xenon perfusion measurement during 20 minutes and 3) 2 blood samples (a. renalis and v. renalis) will be collected from the catheter during the renal angiography 4) a non-invasive Laser Doppler Flow measurement will be performed during 15 minutes. Besides all these measurements, 2 venous blood samples of 5 mL will be collected.

There is a risk on side effects due to the study
medication, however this risk is very small. Since the pretreatment period is only 3 weeks, participants have no direct benefit by participating in this study other than the quantification of renal flow due to treatment with a ARB and/or statin.

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

o Hypertension
(Office blood pressure >140 and/or >90 mmHg or ABPM blood pressure:
>125 and/or >80 mmHg)
o Age: 18-75 jaar
o Creatinin clearance of 60-90 mL/min
(Cockcroft-Gault formula)
o Renal angiography indicated, based on the following criteria:
- Refractory hypertension
- Accelerating or malignant hypertension
- Elevating serum creatinin after an ACE-inhibitor or ARB
- Kidney size < 8 cm measured by ultrasound
- Unexplained hypokalemia
- Abdominal or
renal souffle
- Manifestations of atherosclerosis
elsewhere
- *Flash* oedema

Exclusion criteria

o Primary kidney diseases or urological complaints
o Diabetes Mellitus
o Chronic inflammatory diseases
o Recent infections (< 3 weeks)
o Unilateral or bilateral renal artery stenosis
o Fibromuscular dysplasia (FMD)
o Contraindication for ARB or statin
o Use of > 4 units alcohol a day

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-09-2009
Enrollment:	69
Type:	Actual

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:	10-10-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-12-2008
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	EUCTR2008-004743-10-NL
CCMO	NL24152.068.08