The effectiveness of intensive treatment on sympathetic hyperactivity. A randomized, cross-over trial in patients with chronic kidney disease and hypertension

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Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON31295

Source
ToetsingOnline

Brief title
The effect of intensive treatment on sympathetic hyperactivity

Condition

- Other condition
- Nephropathies

Synonym
chronic kidney diseases, Chronic renal diseases

Health condition

Hypertensie

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Chronic Kidney Disease, Hypertension, Microneurography, Muscle Sympathetic Nerve Activity (MSNA)

Outcome measures

Primary outcome

Primary endpoint/outcome

- Primary endpoint: the effect of increasing dosage of valsartan on MSNA

- Primary expected outcome: further decrease in MSNA as compared to the MSNA

during standard dosage

Secondary outcome

Secondary endpoint/outcome

1. Secondary endpoint: assessment of normalization of MSNA after application of

higher than usual dosage of valsartan

- Secondary expected outcome: normalization of MSNA after application of higher

than usual dosage of valsartan

2. Effect of higher than usual dosage of valsartan on blood pressure

- Secondary outcome: higher than usual dosage of valsartan will not

have a further effect on blood pressure

Study description

Background summary

Cardiovascular (CV) morbidity and mortality are frequently occurring problems in chronic kidney disease (CKD) patients. Apart from the so called traditional risk factors, also risk factors more or less specific to CKD contribute in the pathogenesis of these problems. There is strong evidence that the sympathetic hyperactivity, which often characterizes CKD, is one such factor. Previously, we have shown that angiotensin converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARB) reduce but not normalize this sympathetic hyperactivity. We re-analysed the cohort of patients who were investigated in the past and subsequently treated according to present guidelines. The results show that, despite of treatment, the unfavourable relation between sympathetic hyperactivity and clinical outcome still exits. This might mean that treatment is insufficient and need to be improved.

Study objective

The primary objective is to investigate if there is an incremental inhibiting effect on MSNA by increasing dosage valsartan above the presently advised dosage.
We hypothesize that there will be a further decrease in MSNA as compared to the MSNA during standard dosage valsartan.

Study design

This study is designed as a randomized cross-over trial. We prospectively collect data on activity of MSNA at different stages of treatment by high dosage of valsartan. It will be done in hypertensive CKD patients irrespective

of renal function as sympathetic activity is not related to kidney function. However, patients on renal replacement therapy are excluded. Patients will be recruited from our outpatient clinics.
At the first visit, patients who met inclusion criteria will be prescribed 160mg/day valsartan for 8 weeks. Other ACEi or ARB will be discontinued. Diuretics are prescribed in order to maintain normovolumia, which is evidenced by extracellular volume measurements. Furthermore, they are on standard treatment, i.e. phosphate binders and vitamine D according to guidelines. Thus the baseline dosage is 160mg/day of valsartan and the other dosages applied in this study are 320mg/day and 640 mg/day. The first set of measurements will be done while patients are on 160mg/day. Then patients will be randomly allocated to receive either 640 mg/day valsartan or 320 mg/day valsartan for the following 8 weeks. After 8 weeks the measurements will be repeated and the groups will be switched to 320mg/day and 640mg/day respectively. At the end the final set of measurements will be done (see study protocol page 19 for the flowchart).
Other medication will not be changed during the entire study. In addition to MSNA measurement, blood pressure, heart rate, bromide distribution, PRA and other standard laboratory tests will be done on each occasion.

Intervention

Participants of this study receive 160mg/day valsartan for 8 weeks. After the first 8 weeks the first MSNA measurement will be done. Then patients will be randomized in group 320mg/day and group 640mg/day.
They will recieve 320mg/day or 640mg/day valsartan for 8 weeks. At the end of this period the second MSNA measurement will be done by participants of both groups.
Then the groups will be switched. The participants will receive 640mg/day or 320mg/day valsartan for 8 weeks. At the end the third MSNA measurement will be done.

Study burden and risks

The risks associated with participation in this study are very limited.

Microneurography: there are no risks associated with this procedure. Usually, nerve recordings cause minimal discomfort and negligible, transient after-effects, when studies are done by an experienced technician.

Application of valsartan:
It has been shown that side effects induced by valsartan is relatively same as placebo. Therefore the side effects could be considered negligible. A recent study indicated that dosages of 1.5 to 5 times higher than presently maximum licensed dosage in CKD patients are safe. See protocol "Summary of findings from non-clinical studies and clinical studies" page 11 for references.

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

Patients with stable chronic kidney disease and hypertension: i.e. using antihypertensive drugs and/or blood pressure >145/90mmHg when off medication.

Exclusion criteria

Patients with diabetes mellitus and patients on renal replacement therapy are excluded. In addition, patients with severe liver insufficiency, biliary cirrhosis and cholestasis, pregnant patients and patients in lactation are excluded as Valsartan is contra-indicated for these patients.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Diovan 320mg/day and 640 mg/day
Generic name:	Valsartan 320mg/day and 640 mg/day
Registration:	Yes - NL outside intended use

Ethics review

Not approved

Date:	30-10-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2007-003181-18-NL
CCMO	NL18192.041.07