Effect of Statins on Sympathetic Activity in Hypertensive Patients with Chronic Kidney Disease: a Randomized trial in Hypertensive Patients with Chronic Kidney Disease

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The central hypothesis of this project is that atorvastatin (added on standard antihypertensive treatment ARB) causes a substantial decrease in MSNA in hypertensive patients with CKD.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON33524

Source
ToetsingOnline

Brief title
Statin and MSNA in hypertensive patients with chronic kidney disease

Condition

- Other condition
- Nephropathies

Synonym
chronic kidney disease, Chronic renal diseases

Health condition

Hypertensie

Research involving
Human

Sponsors and support

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

Intervention

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

Outcome measures

Primary outcome

Primary endpoint

- the effect of atorvastatin 20mg/day added on standard antihypertensive

treamten (ARB) on MSNA

Primay outcome:

- a substantial decrease in MSNA after 6 weeks treatment with atorvastatin

added on standard antihypertensive treatment (ARB)

Secondary outcome

Effect of atorvastatin 20mg/day on plasma renin activity and kidney function.

Secondary outcome:

-We expect no or little effect on heart rate, inhibition of plasma renin

activity and no effect on kidney function.

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 (ACE) inhibitors 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. In present study, we want to study the effect of atorvastatin 20mg/day combined to standard antihypertensive treatment on sympathetic nerve activity.

Study objective

The central hypothesis of this project is that atorvastatin (added on standard antihypertensive treatment ARB) causes a substantial decrease in MSNA in hypertensive patients with CKD.

Study design

First visit:
ACE inhibitor or ARB is considered *standard* treatment in CKD patients. Therefore, all eligible patients will be on such medication. The patient will be asked to provide written informed consent form and his/her eligibility for enrolment into the trial will be checked. Physical examination will be performed. Their regular ACE inhibitor or ARB will be replaced by Losartan 100mg/day and their regular statin will be replaced by atorvastatin 20mg/day. If all inclusion criteria and no exclusion criteria are fulfilled, the patients will be randomized into two groups:

Group 1) patients will receive losartan 100mg/day for 6 weeks (and no atorvastatin), followed by the first set of MSNA measurements. Then, atorvastatin 20mg/day will be prescribed (on top of losartan 100mg/day) for 6

weeks, followed by a second set of MSNA measurements.
Or:
Group 2) patients start with atorvastatin 20mg/day and losartan 100mg/day for 6 weeks, followed by the first set of MSNA measurements. Then, atorvastatin 20mg/day will be stopped for 6 weeks (losartan 100mg/day will be continued), followed by a second set of MSNA measurements.

In both groups, blood samples will be drawn during this visit to test the kidney function and PRA. The amount of blood sample needed is 6ml.

Group 1

Second visit group 1: this visit will take place six weeks after the first visit.
During this visit the first MSNA measurement will be done. Blood pressure and heart rate will be measured and blood samples will be drawn during this visit to test the kidney function and PRA. The amount of blood sample needed is 6ml. Then atorvastatin 20mg/day will be added on ARB.

Third visit group 1: This visit will be planned six weeks after the second visit. During this visit the second MSNA measurement will be done. Blood pressure and heart rate will be measured and blood samples will be drawn during this visit to test the kidney function and PRA. The amount of blood sample needed is 6ml. In addition, the possible side effects of the drug will explicitly be asked (See CRF).

Group 2

Second visit group 2: this visit will take place six weeks after the first visit. The first MSNA measurement will be done during this visit and the possible side effects of the drug will explicitly be asked (See CRF). Blood pressure and heart rate will be measured and blood samples will be drawn during this visit to test the kidney function and PRA. The amount of blood sample needed is 6ml. Patients will be ask to stop atorvastatin and continue other medications including ARB.

Third visit group 2: this visit will take place six weeks later than the second visit. The second MSNA measurement will be done during this visit. Blood pressure and heart rate will be measured and blood samples will be drawn during this visit to test the kidney function and PRA. The amount of blood sample needed is 6ml.

In both groups: All medication, including phosphate binders, vitamin D derivatives, erythropoietin etc will be continued during the whole study. Importantly, also diuretics are continued throughout the study in order to maintain normovolemia. Patients will be weighed before each MSNA measurement in

order to test the volume status.

Intervention

Their regular ACE inhibitor or ARBs will be replaced by Losartan 100mg/day and their regular statin will be replaced by atorvastatin 20mg/day. If all inclusion criteria and no exclusion criteria are fulfilled, the patients will be randomized into two groups:

Group 1) patients will receive losartan 100mg/day for 6 weeks (and no atorvastatin), followed by the first set of MSNA measurements. Then, atorvastatin 20mg/day will be prescribed (on top of losartan 100mg/day) for 6 weeks, followed by a second set of MSNA measurements.
Or:
Group 2) patients start with atorvastatin 20mg/day and losartan 100mg/day for 6 weeks, followed by the first set of MSNA measurements. Then, atorvastatin 20mg/day will be stopped for 6 weeks (losartan 100mg/day will be continued), followed by a second set of MSNA measurements.

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.

De safety of atorvastatin 20mg/day is studied among 1035 patients. The incidence of side effects was comparable to the placebo group.

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 older than 18 years old with stable chronic kidney disease and hypertension using an ACE inhibitor or an ARB are included in this project.

Exclusion criteria

Patients with diabetes mellitus, patients on renal replacement therapy, preganant patients and patients on antihypertensive medication (which cannot be stopped) are excluded.

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:	Recruitment stopped
Start date (anticipated):	01-12-2009
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lipitor 20mg/day
Generic name:	Atorvastatin 20mg/day
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	08-09-2009
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	28-12-2009
Application type:	First submission
Review commission:	METC NedMec

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	EUCTR2009-009334-32-NL
CCMO	NL25734.041.09