DD-study: diet or diuretics for salt-sensitivity in chronic kidney disease

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Primary objective: To compare the anti-hypertensive response to dietary salt restriction with the anti-hypertensive response to the diuretics hydrochlorothiazide/amiloride in patients with CKD stages 3 or 4. Secondary objectives: * To analyze the...

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

Summary

ID

NL-OMON43616

Source
ToetsingOnline

Brief title
DD-Study

Condition

- Nephropathies
- Vascular hypertensive disorders

Synonym
High blood pressure in chronic kidney disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Nierstichting (Dutch Kidney Foundation)

Intervention

Keyword: Chronic kidney disease (CKD), Hypertension, Salt sensitivity, Therapy

Outcome measures

Primary outcome

Ambulatory (24-hour) blood pressure measurement (ABPM).

Secondary outcome

- Number of AEs and SAEs.

- Effects of the interventions on blood and urinary parameters (routine measurements, systemic RAS, intrarenal RAS, kidney injury markers, urinary exosomes)

Study description

Background summary

Patients with chronic kidney disease (CKD) are exquisitely salt-sensitive. Salt-sensitivity in CKD is linked to hypertension and cardiovascular outcomes. Dietary salt restriction is an accepted intervention for salt-sensitivity in CKD. Another strategy, however, could be to block sodium uptake by the kidney pharmacologically by diuretics. Especially diuretics acting on the distal tubule may be effective, because this appears to be the site of increased sodium reabsorption in CKD. It is currently unknown how these two strategies, diet or diuretics, relate. We hypothesize that diuretics are non-inferior to diet.

Study objective

Primary objective:
To compare the anti-hypertensive response to dietary salt restriction with the anti-hypertensive response to the diuretics hydrochlorothiazide/amiloride in patients with CKD stages 3 or 4.

Secondary objectives:
* To analyze the response in kidney parameters, the systemic and intra-renal renin-angiotensin system to the two interventions.

* To compare the side-effects of the two interventions.

Study design

Randomized open crossover trial.

Intervention

Patients will be randomized to receive amiloride/hydrochlorothiazide (tablet 5/50mg, once daily) or a dietary sodium restriction (60 mmol/day). Patients with a low dietary sodium intake prior to start of the study (24-hour urinary sodium excretion < 80 mmol/l) will receive 4000 mg sodium chloride daily (4 x capsule 500 mg, twice daily) during the study (except for the period of the low-sodium diet). The study will last 8 weeks (2 week run-in period, 2 x 2-week treatment period + 2-week wash-out period).

Study burden and risks

The study will require: 5 study visits, 1 dietician visit, 5 venapunctures, 4 24-hour urine collections, and 4 ABPMs.

The main risks of this study are uncontrolled blood pressure and side-effects of the diuretics. However, because of the daily home monitoring of blood pressure, availability of escape medication, and the short treatment periods (2 weeks), we believe these potential risks are well-controlled for.

The benefit for individual participants may be that, after the study, the best intervention for salt-sensitivity for this individual will be known and this treatment may be continued. Another benefit may be that, because of the frequent visits to the dietician, patients will have elaborate knowledge on sodium content of their food and ways to adhere to a low-sodium diet.

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

- Age > 18 years.
- Chronic kidney disease stage 3 or 4 (MDRD-GFR 15-60 ml/min)
- Use of any anti-hypertensive drugs
- No anti-hypertensive drugs but an average office systolic blood pressure > 140 mmHg (as measured by datascope)

Exclusion criteria

- Salt-wasting chronic kidney disease
- Nephrotic syndrome
- Pregnant or breastfeeding women
- Life expectancy < 6 months
- Severe heart failure (NYHA III or IV) or liver cirrhosis with ascites and the inability to withdraw diuretics
- Rapidly declining kidney function with high likelihood of dialysis or kidney transplantation in the coming 4 months
- Kidney transplant recipients
- Use of immunosuppressive drugs
- Use of non-steroidal anti-inflammatory drugs
- Previous intolerance or allergy to hydrochlorothiazide or amiloride
- Serum sodium < 135 mmol/l
- Serum potassium < 3.5 mmol/l or > 5.0 mmol/l
- Inability to adhere to the study protocol (due to language, incapacitated subjects, subjects with intellectual disability)

Study design

Design

Study phase:	4
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):	17-06-2016
Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amiloride/hydrochlorothiazide
Generic name:	amiloride/hydrochlorothiazide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-09-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-03-2016
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-07-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2015-003637-96-NL
CCMO	NL54748.078.15