Eplerenone, Sodium restriction, hydroChlorothiazide, and ACE-inhibition in Proteinuria Evaluated.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27384

Source
NTR

Brief title
ESCAPE

Health condition

kidney disease
diabetes mellitus
albuminuria
proteinuria
hypertension
aldosterone blockade
ACE inhibition
diuretic therapy
dietary sodium restriction

Sponsors and support

Primary sponsor: Prof Dr GJ Navis, internist-nephrologist
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Intervention

Outcome measures

Primary outcome

1. Albuminuria;

2. Blood pressure.

Secondary outcome

1. Tubular injury markers;

2. Extracellular fluid volume.

Study description

Background summary

In many diabetic nephropathy patients loss of renal function occurs despite treatment with angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB), which is therapy of choice. Aldosterone, that besides sodium and water retention promotes renal inflammation and fibrosis, increases during ACEi and ARB ("aldosterone escape") which may explain the incomplete renoprotection during these therapies. Aldosterone levels can further increase when the antihypertensive and antiproteinuric effects of ACEi or ARB are potentiated by volume depletion with dietary sodium restriction and/or diuretic treatment.
Mineralocorticoid receptor blockers (MRB; i.e. spironolactone and eplerenone) inhibit the harmful effects of aldosterone, and MRB added to ACEi or ARB effectively reduce proteinuria, hypertension, and renal function decline.
Whether the added benefits of MRB on top of ACEi or ARB result from either the diuretic or the antifibrotic properties of MRB, is unknown.

Furthermore, very few studies in renal patients investigated the protective effects of eplerenone, which is a relatively new but promising agent since it acts selectively and therefore has the benefit over spironolactone (a non-selective MRB) of less/no antiandrogenic and progestational side effects.
Therefore we aim to study: 1. whether the renoprotective effects of ACEi, with and without volume depletion measures, can be improved by the addition of eplerenone, 2. whether the renoprotective effects of eplerenone added to ACEi outweigh the renoprotective effects of the diuretic hydrochlorothiazide added to ACEi; in patients with diabetic nephropathy.

Study objective

Objectives:

1. To investigate the added effects of eplerenone on top of ACEi, with and without dietary sodium restriction, on residual albuminuria, hypertension, and tubular injury markers, in patients with diabetic nephropathy;

2. To investigate whether the renoprotective effects of eplerenone added to ACEi outweigh the renoprotective effects of the diuretic hydrochlorothiazide added to ACEi, in patients with diabetic nephropathy;

3. To investigate whether the benefits of eplerenone on top of ACEi are the result of the diuretic actions (potentiating the efficacy of ACEi) or secondary to the direct antifibrotic properties of eplerenone.

Study design

Patients visit the outpatient clinic at the 42th day of each study period for assessment of the endpoints (blood pressure, proteinuria) and safety parameters (potassium). At the 14th day of each period potassium levels are checked, as well as dietary compliance (urinary sodium excretion).

Intervention

Combinations of:

1. Lisinopril 40 mg/d;

2. Hydrochlorothiazide 50 mg/d;

3. Eplerenone 25-50 mg/d;

4. Normal diet;

5. Sodium restricted diet.

Patients will be randomised into 4 groups, alike the DiNaMo study (the ESCAPE study is an addendum to the DiNaMo study). The ESCAPE study consists of 2 study periods of 6 weeks each, in which patients are treated with lisinopril 40 mg once daily and eplerenone 25-50 mg once daily. This is combined with a low sodium diet during 1 period, and a normal diet during the other period. The antiproteinuric effect of these regimens will be compared with the regimens of the DiNaMo study (which contains placebo, and hydrochlorothiazide, on top of lisinopril 40 mg/d and diet intervention).

Contacts

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Eligibility criteria

Inclusion criteria

1. Diabetic nephropathy;

2. Diabetes mellitus type II;

3. Proteinuria <3.0 g/24h;

4. Stable creatinine clearance > 30 mL/min;

5. Age ≥ 18 years.

Exclusion criteria

1. Diabetes mellitus type I;

2. Myocardial infarction or other cardiovascular event within the last 3 months prior to entry into the study;

3. Kidney disease other than caused by diabetes mellitus or hypertension;

4. Uncontrollable hypertension after the run-in period (>180/100 mmHg);

5. Serum potassium > 6.0 mmol/L;

6. Incompliance with regard to study medication or diet;

7. Unable to give informed consent;

8. Contraindication for the use of lisinopril or eplerenone.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2010
Enrollment:	27
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	04-12-2009
Application type:	First submission

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
NTR-new	NL2016
NTR-old	NTR2133
CCMO	NL30907.042.09
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A