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

Gepubliceerd: 04-12-2009 Laatst bijgewerkt: 18-08-2022

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...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27384

Bron
Nationaal Trial Register

Verkorte titel
ESCAPE

Aandoening

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

Ondersteuning

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Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Albuminuria;
2. Blood pressure.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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).

Onderzoeksproduct en/of interventie

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).

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-02-2010
Aantal proefpersonen:	27
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	04-12-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
N/A