

Dual RAS-blockade by ACE-inhibition and AT1 receptor blockade, role of the ACE I/D genotype and low sodium diet in non-diabetic proteinuric patients.

Gepubliceerd: 05-05-2006 Laatste bijgewerkt: 18-08-2022

The recently found gene-environment interaction between dietary sodium intake and the ACE genotype with sodium-induced therapy resistance to ACE inhibition in DD homozygotes (that was absent in II and ID subjects) is present in the renal patient as...

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

Samenvatting

ID

NL-OMON23057

Bron

NTR

Verkorte titel

DUAAL

Aandoening

non-diabetic proteinuria

Ondersteuning

Overige ondersteuning: Novartis Pharma B.V.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary endpoint will be reduction of proteinuria and blood pressure expressed as percentage change from baseline and analysed with each patient as his or her own control.

Toelichting onderzoek

Achtergrond van het onderzoek

The DUAAAL study is a double blind, randomized, crossover study to study whether the gene environment interaction between the ACE genotype, dietary sodium intake and the response to ACE inhibition which is present in healthy subjects, is also present in a clinically relevant setting, in renal patients. Moreover, we study if this assumed therapy resistance in the DD genotype, could be overcome by the addition of an ARB and whether this assumed additional effect is dependent on the genotype and dietary sodium intake. 56 patients with a stable non-diabetic proteinuria will be included, who will, after a run-in period of 6 weeks where lisinopril 40 mg will be prescribed, treated with either placebo or valsartan 320 mg (160 mg 1dd2) for 6 weeks on top of their ACEi treatment in randomized order on both a low and a high sodium diet.

Doel van het onderzoek

The recently found gene-environment interaction between dietary sodium intake and the ACE genotype with sodium-induced therapy resistance to ACE inhibition in DD homozygotes (that was absent in II and ID subjects) is present in the renal patient as well. With regard to the pathophysiological mechanism, we hypothesise that a high dietary sodium intake induces an increase in tissue ACE activity, which is stronger in the DD homozygotes, resulting in a worse therapy response to ACEi. The alleged sodium-induced therapy resistance of the DD homozygotes may therefore be overcome by addition of AT1 receptor blockade, since AT1 receptor blockers act “downstream” of the ACE.

Moreover, we hypothesize that low dietary sodium intake has additional effects on proteinuria and blood pressure on top of dual RAS blockade in patients with non-diabetic proteinuria.

Onderzoeksproduct en/of interventie

Lisinopril 40 mg, with the addition of valsartan 320 mg (160 mg 1dd2) or placebo, both during low dietary sodium intake and high dietary sodium intake in randomised order.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age older than 18 year;
2. Chronic non-diabetic renal disease, as established by history, urine analysis, serum biochemistry tests and/or renal biopsy;
3. Creatinine clearance $> 30 \text{ ml/min/1.73 m}^2$;
4. Residual proteinuria $> 1 \text{ g/24h}$.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Failure to comply with the above inclusion criteria;
2. Diabetes mellitus;
3. Any contra-indication against the use of ACE inhibitors or AT1 receptor blockers;
4. A history of myocardial infarction, unstable angina, coronary by-pass or CVA during the past 6 months;
5. Heart failure NYHA class III-IV;
6. High rate of renal function loss (decline in creatinine clearance $> 6 \text{ ml/min/1.73m}^2$ during the previous year);
7. Need for treatment with corticosteroids, NSAID's or immunosuppressive drugs;
8. Proteinuria $> 10 \text{ g/24h}$ and hypoalbuminaemia $< 28 \text{ g/L}$;

9. Renovascular hypertension, malignant hypertension (diastolic blood pressure > 100 mmHg);
10. Serum potassium > 6 mmol/L.

Onderzoeksopzet

Opzet

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

Deelname

Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	28-04-2006
Aantal proefpersonen:	56
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies	
Datum:	05-05-2006
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	NL616
NTR-old	NTR675
Ander register	: N/A
ISRCTN	ISRCTN50137410

Resultaten

Samenvatting resultaten

Moderate dietary sodium restriction added to angiotensin converting enzyme inhibition compared with dual blockade in lowering proteinuria and blood pressure: randomised controlled trial.

Slagman MC, Waanders F, Hemmelder MH, Woittiez AJ, Janssen WM, Lambers Heerspink HJ, Navis G, Laverman GD; HOLLand NEphrology STudy Group.

BMJ. 2011 Jul 26;343:d4366. doi: 10.1136/bmj.d4366.

PMID nummer van de publicatie: 21791491