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.

No registrations found.

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

Summary

ID

NL-OMON23057

Source
Nationaal Trial Register

Brief title
DUAAAL

Health condition

non-diabetic proteinuria

Sponsors and support

Source(s) of monetary or material Support: Novartis Pharma B.V.

Intervention

Outcome measures

Primary outcome

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.

Secondary outcome

1. Serum creatinine;
2. Circulating RAS parameters;
3. Lipid profile;
4. Adiponectin.

Study description

Background summary

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 lisonopril 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.

Study objective

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.

Intervention

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.

Contacts

Public
University Medical Center Groningen (UMCG), Department of Nephrology,
Hanzeplein 1
F. Waanders
Groningen 9700 RB
The Netherlands
+31 (0)50 3611564
Scientific
University Medical Center Groningen (UMCG), Department of Nephrology,
Hanzeplein 1
F. Waanders
Groningen 9700 RB
The Netherlands
+31 (0)50 3611564

Eligibility criteria

Inclusion criteria

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 ml/min/1.73 m;
4. Residual proteinuria > 1 g/24h.

Exclusion criteria

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 ml/min/1.73m2 during the previous year);
7. Need for treatment with corticosteroids, NSAID’s or immunosuppressive drugs;
8. Proteinuria > 10 g/24h and hypoalbuminaemia < 28 g/L;
9. Renovascular hypertension, malignant hypertension (diastolic blood pressure > 100 mmHg);

10. Serum potassium > 6 mmol/L.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-04-2006
Enrollment:	56
Type:	Anticipated

Ethics review

Positive opinion

Date:	05-05-2006
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	NL616
NTR-old	NTR675
Other	: N/A
ISRCTN	ISRCTN50137410

Study results

Summary results

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 plublicatie: 21791491