ISRCTN50137410 https://doi.org/10.1186/ISRCTN50137410

Dual renin-angiotensin system-blockade by angiotension-converting enzyme-inhibition and angiotension receptor type 1 receptor blockade, role of the angiotension-converting enzyme inhibitor or D genotype and low sodium diet in non-diabetic proteinuric patients

Submission date
29/06/2006

Recruitment status
No longer recruiting

Registration date
29/06/2006

Overall study status
Completed

Last Edited
08/01/2021

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number

NL616, NTR675

Study information

Scientific Title
Dual renin-angiotensin system-blockade by angiotension-converting enzyme-inhibition and angiotension receptor type 1 receptor blockade, role of the angiotension-converting enzyme inhibitor or D genotype and low sodium diet in non-diabetic proteinuric patients

Acronym
DUAAAL

Study objectives
The recently found gene-environment interaction between dietary sodium intake and the angiotensin-converting enzyme (ACE) genotype with sodium-induced therapy resistance to ACE inhibition in DD homozygotes (that was absent in II and ID subjects) is present in renal patients as well. With regards 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 angiotensin-converting enzyme-inhibitors (ACEi). The alleged sodium-induced therapy resistance of the DD homozygotes may therefore be overcome by addition of angiotensin receptor type 1 (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 renin-angiotensin system (RAS) blockade in patients with non-diabetic proteinuria

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomized, crossover, placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Proteinuria

Interventions
Lisinopril 40 mg, with the addition of valsartan 320 mg (160 mg; twice a day) or placebo, both during low dietary sodium intake and high dietary sodium intake in randomised order

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Lisinopril, valsartan

Primary outcome(s)
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

Key secondary outcome(s))
1. Serum creatinine
2. Circulating RAS parameters
3. Lipid profile
4. Adiponectin

Completion date
01/09/2008

Eligibility

Key inclusion criteria
1. Older than 18 years of age
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 per 24 hours

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
52

Key exclusion criteria
1. Failure to meet the above inclusion criteria
2. Diabetes mellitus
3. Any contra-indication to the use of ACE inhibitors or AT1 receptor blockers

4. A history of myocardial infarction, unstable angina, coronary bypass or cardiovascular accident (CVA) during the past six months
5. Heart failure New York Heath Association (NYHA) class III-IV
6. High rate of renal function loss (decline in creatinine clearance >6 ml/min/1.73 m^2 during the past year)
7. Need for treatment with corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) or immunosuppressive drugs
8. Proteinuria >10 g per 24 hours and hypoalbuminaemia <28 g/l
9. Renovascular hypertension, malignant hypertension (diastolic blood pressure >100 mmHg)
10. Serum potassium >6 mmol/l

Date of first enrolment
28/04/2006

Date of final enrolment
01/09/2008

Locations

Countries of recruitment
Netherlands

Study participating centre
University Medical Center Groningen (UMCG)
Groningen
Netherlands
9700 RB

Sponsor information

Organisation
University Medical Center Groningen (UMCG) (The Netherlands)

ROR
https://ror.org/03cv38k47

Funder(s)

Funder type
Industry

Funder Name

Novartis Pharma B.V.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	26/07/2011	08/01/2021	Yes	No