Vitamin D in addition to RAAS blockade and dietary sodium for the Treatment of Urinary Excretion of albumin.

Published: 09-10-2009
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The primary objective of this study is to determine the antialbuminuric response of vitamin D analogue in addition to ACE-inhibitor and low-sodium diet, in renal patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON40020

Source
ToetsingOnline

Brief title
Additive antialbuminuric effect of vitamine D: The ViRTUE-study.

Condition

- Other condition

Synonym
albuminuria, urinary loss of protein

Health condition

chronische nierinsufficientie (excl. diabetische nefropathie)

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Abbott,Nederlandse Nierstichting

Intervention

Keyword: albuminuria, RAAS blockade, vitamin D

Outcome measures

Primary outcome

- Albuminuria (24-hour urinary albumin excretion)

Secondary outcome

- mean arterial pressure (MAP)

- serum creatinine / creatinine clearance

- PRA (plasma renin activity)

- renal hemodynamics (measured GFR, ERPF)

Study description

Background summary

Prevention of progressive renal function loss remains the main challenge in clinical nephrology. Blockade of the renin-angiotensin-aldosterone system (RAAS), which can be potentiated by a low-sodium diet, is the therapy of choice, but still many patients develop end-stage renal disease on the long term. Recent studies underline a crucial role for the vitamin D pathway in progressive renal function loss, possibly due to interference in the RAAS. We hypothesize that treatment with a vitamin D analogue could blunt the reactive rise of renin levels seen in response to RAAS-blockade and reduce albuminuria, thus optimizing renoprotection.

Study objective

The primary objective of this study is to determine the antialbuminuric response of vitamin D analogue in addition to ACE-inhibitor and low-sodium

diet, in renal patients.

Study design

The study is designed as a multiple-center, double-blind, placebo-controlled, crossover, randomized clinical trial.

Patients will enroll in a wash-out/wash-in period in which RAAS-blocking agents and diuretics are discontinued, and 10 miligram ramipril 1dd1 is started. Bloodpressure will be titrated to a value of <140/90 mmHg with additional medication (in the fixed sequence of 100 miligram metoprolol retard 1dd1, 8 miligram doxazosin 1dd1, and 10 miligram amlodipine 1dd1), if needed. Subsequently, patients will be consecutively treated in eight week treatment periods, in randomized order, with placebo, the synthetic vitamin D receptor acivator paricalcitol (1 microgram/day). At the same time, patients will be randomly assigned to either a high-sodium diet (200 mmol Na/day) or a low-sodium diet (50 mmol Na/day) during 32 weeks (two 16-week periods).

Every 8 weeks, after an overnight fast, patients will collect 24-h urine, BP is measured, and blood is sampled to control dietary compliance and to monitor renal function and BP. Also 24-h ambulatory blood pressure will be measured in the centers that have the required devices available. In a subgroup of male patients (those recruited in the UMCG and Martini Ziekenhuis), renal hemodynamics (GFR/ERPF) will be measured. Every 4 weeks, 24-h urine is also collected to control dietary compliance. Collected data at the end of each eight week treatment period is used for analysis.

Intervention

paricalcitol 2 microgram / placebo
low-sodium diet / liberal-sodium diet

Study burden and risks

There are no direct benefits for the patients to be included. Participation in the study is on a free-will base. Patients will not receive any financial support or priority for treatment of other diseases in the clinic during this study. Patients will visit the outpatient clinic on a more regular base than standard patient care. During their visit, blood pressure, height and weight will be measured. Also 24-h ambulatory blood pressure will be measured in the centers that have the required devices available. Fasting blood samples will be drawn during the venapuncture and 24-h urine will be collected. In a subgroup of male patients (those recruited in the UMCG and Martini Ziekenhuis), renal hemodynamics (GFR/ERPF) will be measured. The amount of radioactive radiation during renal hemodynamic measurements is comparable to a single X-thorax (16% of the yearly dosage of background radiation in the Netherlands). No further

invasive measurements will be executed and therefore risks of participation in this study are minimal.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- male and female patients
- non-diabetic renal disease as established by history, serum biochemistry tests and/or renal biopsy
- age >=18 years
- residual albuminuria >300 mg/day and <10 g/day during conventional treatment of at least 8
weeks with ACE-inhibitor or ARB at the maximum recommended dose
- stable renal function (creatinine clearance of >30 ml/min/1.73m2; with <6 ml/min per year

decline)
- average of 2 consecutive PTH values of < 1.5 times the upper limit of normal (defined by the reference values of each participating center), 2 consecutive serum calcium levels between 2.0 and 2.6 mmol/l (corrected for albumin levels), 2 consecutive serum phosphorus levels of 1.5 mmol/l within 4 weeks prior to treatment
- written informed consent

Exclusion criteria

- uncontrolled hypertension, hyperkalemia (potassium >6.0 mmol/l, cardiovascular disease (myocardial infarction, unstable angina, percutanous transluminal coronary angioplasty, coronary artery bypass grafting, or stroke within last 6 months, heart failure NYHA III-IV), Diabetes Mellitus
- epilepsy
- liver disease resulting in aberrations of liver function tests
- previously treated (within 3 months of screening) with paricalcitol or vitamin D (analogue)
- contraindication to ACEi, high/low-sodium diet or paricalcitol
- medication interacting with ACEi or paricalcitol
- frequent NSAID use (>2 doses/week)
- use of immunosuppressive drugs
- use of digoxine
- active malignancy
- any bowel disorder resulting in fat malabsorption
- pregnant or nursing (lactating) women, where pregnancy is defined as a state of a female after
conception and until the termination of gestation, confirmed by a positive ß-hCG laboratory test
(>5 mIU/ml).
- incompliance with diet or study medication
- any psychiatric condition or psychofarmacon use
- drug or alcohol abuse

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-12-2012
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	tritace
Generic name:	ramipril
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	zemplar
Generic name:	paricalcitol
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	09-10-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	18-10-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	18-07-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	19-02-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2009-016159-23-NL
Other	Nederlands Trial register: 9426
CCMO	NL29900.042.09

Study results

Date completed:	10-03-2015
Actual enrolment:	45