Diuretic testing in chronic kidney disease

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To predict the progression of CKD with diuretic testing.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON57356

Source
ToetsingOnline

Brief title
U-Tube 2

Condition

- Renal disorders (excl nephropathies)

Synonym
chronic kidney disease, reduced kidney function

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: European Research Council

Intervention

Keyword: biomarkers, chronic kidney disease, diuretic, nephrology

Outcome measures

Primary outcome

Composite outcome of CKD progression, defined as a 30% decrease in estimated glomerular filtration rate (eGFR) or the start of kidney replacement therapy with dialysis or transplantation, during a 3-year follow-up period.

Secondary outcome

To investigate tubular physiology in chronic kidney disease

• Diuretic clearance in CKD

• Fractional electrolyte excretion compared with tubular diuretic concentrations

• Uromodulin and epidermal growth factor (EGF) concentrations in urine before and after stimulation as these are both secreted by the distal tubule

• Feasibility of the tubular function test in clinical practice

• Fraction excretion of ESSs in comparison to the diuretic clearance as a marker for proximal tubular dysfunction

• eGFR slope

• Incident cardiovascular disease

• Mortality

Study description

Background summary

Chronic kidney disease (CKD) is a common and often progressive condition. CKD is currently only assessed by glomerular function and not tubular function. We hypothesize that measuring tubular function can predict the progression of CKD. To investigate this, we will test tubular function with diuretics in patients with CKD and follow them over a 3-year period to monitor CKD progression.

Study objective

To predict the progression of CKD with diuretic testing.

Study design

Single-centre, prospective diagnostic trial.

Intervention

After a 4-week washout period of interfering drugs, participants will undergo diuretic testing involving the concurrent oral administration of bumetanide (2 mg) and hydrochlorothiazide (HCTZ, 50 mg). Blood and urine will be collected to assess kidney tubular function. 24-hour urine will be collected on the day before the test. On the test day, a standardized breakfast and lunch will be served, and subjects will drink a standardized amount of water. We will recruit 81 patients with CKD, including 76 patients who will undergo the test and 5 randomly chosen patients who will not receive the diuretics and will serve as time controls (to correct for diurnal variations in urine and blood composition, age and sex matched). Additionally, 5 healthy controls will undergo the test to compare the diuretic response in patients with CKD to healthy participants (age and sex matched).

Study burden and risks

We have minimized the trial burden by organizing the test as a single-day protocol. Bumetanide and HCTZ are frequently used diuretics with a good overall safety profile. The safe use of these diuretics in a 1-day diuretic testing protocol has been reported previously. Although chronic use of these diuretics may lead to fluid and electrolyte imbalance, the risk of a single administration for diagnostic purposes is expected to be minimal. In addition, all participants are monitored for 6 hours after administration of the diuretics, including blood pressure measurement and blood gas analysis. All procedures concerning sample collection are part of routine clinical care and are generally safe. The burden of blood sample collection will be minimized by cannulating a single vein once to collect blood samples at the six necessary time points. Patients will be reimbursed for their participation.

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

Adult (>= 18 years)
CKD stage G3 (creatinine-based eGFR 30-59 mL/min/1.73m2) during the last outpatient visit

Exclusion criteria

Known intolerance or allergy to the diuretics
Current systemic chemotherapy for malignancy
Kidney transplant recipient
Use of calcineurin-inhibitors
Life expectancy < 12 months
Current immunosuppressive treatment for glomerulonephritis
Incapacitated subjects or subjects who are deemed unfit to adequately adhere to instructions from the research team
Hypokalemia or hyperkalemia (K+ < 3.0mmol/L or K+ > 5.5 mmol/L) at inclusion visit
Hypo- or hypernatremia (Na+ < 130 mmol/L or Na+ > 150mmol/L) at inclusion visit
Inherited tubulopathy as the cause of CKD

Autosomal dominant polycystic or tubulointerstitial kidney disease causing CKD
Clinically relevant heart failure (New York Heart Association class III or IV)
Therapy-resistant hypertension, defined as systolic blood pressure > 180mmHg at the inclusion visit
Current treatment with inhibitors of OATs: probenecid, pravastatin, cimetidine, cephalosporins, acetazolamide
Active hepatitis during the last outpatient visit
Liver cirrhosis in advanced stage (Child-Pugh B or C)
Active drug- or alcohol abuse
Not being able to tolerate a 28-day washout of one of the drugs interfering with diuretic testing.
Women who are pregnant, breastfeeding, or considering pregnancy in the coming 7 weeks

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-04-2025
Enrollment:	86
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	13-03-2025
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL87576.078.24