Potassium supplementation in patients with chronic kidney disease and healthy subjects: effects on potassium and sodium balance

Published: 28-08-2018
Last updated: 11-04-2024

To investigate how acute potassium administration affects potassium and sodium balance in healthy subjects as compared to patients at different CKD stages, i.e., normal kidney function and stage 3b/4 CKD.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON48661

Source
ToetsingOnline

Brief title
Acute K+ balance

Condition

- Nephropathies

Synonym
Chronic Kidney Disease

Research involving
Human

Sponsors and support

Primary sponsor: Inwendige geneeskunde/Nefrologie

Source(s) of monetary or material Support: Nierstichting

Intervention

Keyword: Chronic Kidney Disease, Potassium, RAAS inhibition, Sodium

Outcome measures

Primary outcome

Serum potassium (in mmol/L).

Secondary outcome

Red Blood Cell (RBC) potassium (in mmol/L), renal potassium excretion, serum

sodium, renal sodium excretion, total body water, and systolic blood pressure,

as well as changes in serum bicarbonate, insulin, and plasma aldosterone.

Study description

Background summary

Potassium is the most abundant cation in the intracellular fluid and its gradient across the cell membrane is pivotal for normal cell function. Under normal conditions, the kidney is primarily responsible for maintaining total body K+ (TBK) by matching potassium intake with potassium excretion. Yet, in kidney patients our understanding of potassium handling after a potassium load is incomplete. It is known, that as kidney function declines, the risk of hyperkalemia increases. At the same time, advanced chronic kidney disease (CKD) is often characterized by depleted TBK. Changes of the internal potassium balance might become the most important regulator of the serum potassium concentration in progressive CKD, but data to support this are lacking. Also, many kidney patients are treated with RAAS inhibitors, because of the renoprotective effects. However, RAAS inhibitor treatment is also associated with elevated risk of hyperkalemia and might affect the acute potassium balance. Of further interest is that potassium and sodium balance are closely related. Under normal conditions, potassium supplementation increases sodium excretion, but it is unknown whether this potassium-induced natriuresis remains intact in CKD. In summary, better understanding of potassium homeostasis in response to potassium loading in CKD is highly relevant, specifically in the context of exploring the potentially beneficial effects of potassium

supplementation in patients with CKD

Study objective

To investigate how acute potassium administration affects potassium and sodium balance in healthy subjects as compared to patients at different CKD stages, i.e., normal kidney function and stage 3b/4 CKD.

Study design

Double blind and placebo-controlled cross-over study.

Intervention

Patients and healthy subjects will be randomized to a 8-week period with RAAS inhibitor treatment (Lisinopril 10 mg once daily) followed by a 8-week period without RAAS inhibitor treatment (or vice versa). After 6, 7 and 8 weeks an acute oral dose of potassium chloride (40 mmol), potassium citrate (40 mmol) or matching placebo will be administered in random order.

Study burden and risks

Participating in this research project will not lead to personal benefit. However, little to no burden is expected when participating in this study. The subjects will be asked to visit our research department seven times which will take approximately 29 hours in total. The study visits comprise venous blood drawings, spot urine samples, collection of 24-hour urine, faeces sample, measurements of volume status (using weight and bioimpedance measurements) and central and peripheral hemodynamics (by using continuous finger arterial pressure [FinAp] waveform registration, Nexfin®, Sphygmocor® and an automated device for peripheral BP measurement (Omron®)). In addition, RAAS inhibition may affect blood pressure and withdrawal of RAAS inhibition in patients might result in hypertension. In healthy subjects RAAS inhibition might cause hypotension. Therefore, blood pressure will be measured once in two weeks.

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

Patients:
• Adult patients (>= 18 years) with CKD 3b or 4 (45 - 15 ml/min/1.73 m2).
• Hypertension (defined as office blood pressure > 140/90 mmHg and using single RAAS inhibitor treatment)., Healthy subjects:
• Healthy adults (>= 18 years), as determined by a responsible and experienced physician, based on a medical evaluation including medical history, physical examination (PE) and laboratory tests carried out in the screening visit (V0).
• Using no medication (excluding contraceptives).

Exclusion criteria

Patients:
• Hyperkalemia (serum potassium > 5.5 mmol/l).
• Medical reasons to continue dual RAAS-blockade, mineralocorticoid receptor blockers, potassium-sparing diuretics, or oral potassium binders.
• Patients with previous history of ventricular cardiac arrhythmia.
• Patients with diabetes mellitus.
• Patients with a life expectancy < 6 months.
• Expected initiation of renal replacement therapy < 6 months.
• Incapacitated subjects.
• Women who are pregnant, breastfeeding or consider pregnancy in the coming 6

months., Healthy subjects:
• Hyperkalemia (serum potassium > 5.5 mmol/l).
• Women who are pregnant, breastfeeding or consider pregnancy in the coming 6 months.
• An office blood pressure >= 140/90 mmHg.
• A body mass index >= 30 kg/m2.
• A major illness in the past 3 months or any significant chronic medical illness that the investigator would deem unfavourable for enrolment, including diabetes mellitus.
• A history of any type of malignancy within the past 5 years with the exception of successfully treated basal cell carcinoma of the skin.
• A history of any renal disease.
• A history of any blood clotting disorders.
• A history of any auto-immune disease.
• A history of cardiovascular disease (in the past 6 months) defined as documented coronary artery disease including myocardial infarction (MI), (un-)stable angina pectoris or acute coronary syndrome (ACS), percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG), cerebrovascular disease, including ischaemic and haemorrhagic stroke or a subarachnoid bleeding (SAB), or peripheral artery disease, including aortic aneurysmata (AA).
• A history of ventricular cardiac arrhythmia.
• Any significant sign or symptom of hypotension.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-04-2019
Enrollment:	50

Type:	Actual

Ethics review

Approved WMO Date:	28-08-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL65498.018.18