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

No registrations found.

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

Summary

ID

NL-OMON21336

Source
Nationaal Trial Register

Brief title
Acute K+ balance

Health condition

Chronic Kidney Disease

Sponsors and support

Primary sponsor: AUMC - AMC
Source(s) of monetary or material Support: Dutch Kidney Foundation

Intervention

Outcome measures

Primary outcome

The primary study endpoint will be serum potassium (in mmol/L).

Secondary outcome

Secondary endpoints will include 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

Rationale:
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. 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.

Objectives:
1. To analyze how potassium handling, volume and sodium status will change in healthy and CKD stage 3b/4 subjects after an acute oral potassium load.
2. To analyze how the response to an acute oral potassium load changes during renin-angiotensin-aldosterone (RAAS) blockade in healthy and CKD stage 3b/4 subjects.
3. To analyze how supplementation with two different potassium salts (potassium chloride vs. potassium citrate) influences potassium balance in CKD 3b/4.

Study design: Double blind and placebo-controlled cross-over study.

Study population: Outpatients (age ≥ 18 years) with CKD 3b/4 and hypertension (using single RAAS inhibitor treatment) and sex-matched healthy subjects, serving as controls.

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.

Main study parameters/endpoints:
The primary study endpoint will be serum potassium (in mmol/L). Secondary endpoints will include 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 objective

Overall: when kidney function deteriorates, regulation of the potassium balance in response to potassium loading switches from renal to non-renal mechanisms.
1. Serum potassium in CKD is mainly influenced by alterations in the internal potassium balance.
2. Potassium supplementation in CKD restores TBK.
3. The increase in TBK by potassium supplementation reduces total body sodium stores in CKD.

Study design

3 study visits without Lisinopril (one week apart) and 2 study visits with Lisinopril (one week apart).

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.

Contacts

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Eligibility criteria

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 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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-03-2019
Enrollment:	50
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Positive opinion

Date:	20-03-2019
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	NL7618
Other	METC AMC : METC2018_103

Study results