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

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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...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21336

Bron
Nationaal Trial Register

Verkorte titel
Acute K+ balance

Aandoening

Chronic Kidney Disease

Ondersteuning

Primaire sponsor: AUMC - AMC
Overige ondersteuning: Dutch Kidney Foundation

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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Contactpersonen

Publiek

AUMC
Rosa Wouda

0205666136

Wetenschappelijk

AUMC
Rosa Wouda

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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).

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	20-03-2019
Aantal proefpersonen:	50
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Toelichting
N/A

Ethische beoordeling

Positief advies

Datum:	20-03-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7618
Ander register	METC AMC : METC2018_103

Resultaten