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Original Article

Changes in urinary potassium excretion in patients with chronic kidney disease

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Abstract

Background: Hyperkalemia is one of the more serious complications of chronic kidney disease (CKD), and the cause of potassium retention is a reduction in urinary potassium excretion. However, few studies have examined the extent of the decrease of urinary potassium excretion in detail with respect to decreased renal function.
Methods: Nine hundred eighty-nine patients with CKD (CKD stages G1 and G2 combined: 135; G3a: 107; G3b: 170; G4: 289; and G5: 288) were evaluated retrospectively. Values for urinary potassium excretion were compared between CKD stages, and the associations between urinary potassium excretion and clinical parameters, including diabetes mellitus status and use of renin–angiotensin–aldosterone system inhibitors, were analyzed using a multivariable linear regression analysis.
Results: Urinary potassium excretion gradually decreased with worsening of CKD (G5: 24.8 ± 0.8 mEq/d, $P < 0.001$ vs. earlier CKD stages). In contrast, the value of fractional excretion of potassium at CKD G5 was significantly higher than that at the other stages (30.63 ± 0.93%, $P < 0.001$). Multivariable linear regression analysis revealed that urinary potassium excretion was independently associated with urinary sodium excretion (standardized coefficient, 0.499), the estimated glomerular filtration rate (0.281), and serum chloride concentration (−0.086).
Conclusion: This study demonstrated that urinary potassium excretion decreased with reductions in renal function. Furthermore, urinary potassium excretion was mainly affected by urinary sodium excretion and estimated glomerular filtration rate in patients with CKD, whereas the presence of diabetes mellitus and use of renin–angiotensin–aldosterone system inhibitors were not associated with urinary potassium excretion in this study.

Introduction

Higher urinary potassium excretion was recently associated with a lower risk of death and cardiovascular events and the potential to reduce the incidence of hypertension in prospective cohort studies involving general populations [1,2]. Therefore, urinary potassium excretion has been a concern in clinical settings.

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Patients with chronic kidney disease (CKD) frequently experience potassium metabolism disorders, and the management of which, particularly hyperkalemia, is one of the most important aspects of CKD treatment. Urinary potassium excretion is diminished in these patients [3,4], and several mechanisms, including a reduction in functioning nephron mass [5], use of a renin–angiotensin–aldosterone system (RAAS) inhibitors [6], and the presence of diabetes mellitus (DM) [7–10], are associated with this decrease. In contrast, to avoid an increase in serum potassium concentrations associated with CKD, amplification of the normal aldosterone-induced signal for potassium excretion and an increase in potassium excretion per nephron in accordance with the increase in serum potassium concentrations have previously been reported as part of the adaptation of renal potassium secretion in patients with CKD [5,11]. However, few studies have examined the extent of urinary potassium excretion in detail according to CKD progression or the relationship between urinary potassium excretion and clinical parameters in patients with CKD.

This study aimed to (1) compare the extent of urinary potassium excretion between CKD stages [12] and (2) clarify the relationship between urinary potassium excretion and clinical parameters in patients with CKD.

Methods

Patients and study design

This retrospective study included 989 patients (634 men and 355 women; mean age, 62.3 ± 0.5 years) who met the following criteria: (1) the presence of CKD categorized into stages G1–G5 according to the CKD guidelines edited by the Japanese Society of Nephrology [9] at the Division of Nephrology at Saitama Medical Center in Jichi Medical University between January 2006 and December 2010; (2) completion of urinary electrolyte measurements including potassium and sodium concentrations via 24-hour urine collection; and (3) the absence of dialysis treatment. This study was approved by the Institutional Review Board of the Saitama Medical Center, Jichi Medical University (RIN-13-30), Japan, and it conforms to the provisions of the Declaration of Helsinki (as revised in Tokyo, 2004).

We collected and retrospectively analyzed sociodemographic patient data regarding age, sex, the presence of DM, antihypertensive treatment with RAAS inhibitors including angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, and diuretic treatment with loop and thiazide diuretics. Biochemical variables including blood urea nitrogen, serum creatinine, sodium, potassium, chloride, albumin, and hemoglobin levels were measured. We calculated the estimated glomerular filtration rate (eGFR) using the following equation [12]:

$$\mathrm{eGFR}(\mathrm{mL/min/1.73\ m^2}) = 194 \times \mathrm{S{-}Cr}^{-1.094} \times \mathrm{age}^{-0.287}\ (\text{for men})$$

$$= 194 \times \mathrm{S{-}Cr}^{-1.094} \times \mathrm{age}^{-0.287} \times 0.739\ (\text{for women})$$

where S-Cr indicates the serum creatinine concentration (mg/dL).

Furthermore, 24-hour urine collection was performed for each patient to evaluate urinary sodium, potassium, and protein excretion. The 24-hour urine collection was initiated after the first morning urine was discarded in the patient's toilet. Thereafter, the entire volume of urine was collected in a disposable 3-L container. To avoid the possibility of inadequate urine collection, we trained all patients to properly collect their urine samples and reinforced that 24-hour urine collection must be initiated at a specific time and then completed at the same time the next day.

On the basis of the results of these examinations, the fractional excretion of potassium (FEK) was calculated using the following equation:

$$\mathrm{FEK}\ (\%) = 100 \times (\mathrm{U{-}K/S{-}K})/(\mathrm{U{-}Cr/S{-}Cr})$$

where the U-K, S-K, U-Cr, and S-Cr indicates the urinary potassium concentration (mEq/L), the serum potassium concentration (mEq/L), the urinary creatinine concentration (mg/dL), and the serum creatinine concentration (mg/dL), respectively.

Statistical analysis

Data are expressed as means ± standard error. A chi-square test was used to assess associations between categorical variables, including the utilization and distribution of RAAS inhibitors and diuretics, complemented by adjusted residual analysis. Correlations between the 2 groups were evaluated using the Pearson correlation coefficient and linear regression analysis, and differences between the 2 groups were evaluated using the unpaired *t* test. The differences between CKD stages were evaluated using a 1-way analysis of variance and the Scheffe test. Variables that were significantly correlated with urinary potassium excretion in a simple linear regression analysis, including the DM status and use of RAAS inhibitors, were included in the multivariable linear regression analysis to identify factors affecting urinary potassium excretion in patients with CKD. A P value < 0.05 was considered significant.

Results

Patient demographics and clinical characteristics are shown in Table 1. The numbers of patients at each CKD stage were as follows: G1 and G2 combined (G1 + G2): 135; G3a: 107; G3b: 170; G4: 289; and G5: 288. The proportion of patients with DM for CKD stages G4 and G5 significantly increased compared to CKD stages G1 + G2, G3a, and G3b ($P < 0.05$). The proportions of patients using angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers increased significantly with worsening of the CKD ($P < 0.05$, G3b vs. other stages). However, there were no significant differences between G4 and G5. The proportion of patients using loop and/or thiazide diuretics and polystyrene sulfonates also increased significantly with CKD progression (loop and/or thiazide diuretics: $P < 0.05$, G4 vs. other stages; polystyrene sulfonates: $P < 0.01$, G1 + G2 vs. G5). Serum potassium concentrations at stage G5 were significantly higher than those at the earlier stages. Furthermore, the values of urinary sodium excretion at stages G4 and G5 were significantly lower than those at CKD stages G1 + G2, G3a, and G3b.

As shown in Fig. 1A, urinary potassium excretion did not differ significantly among stages G1 + G2, G3a, and G3b; however, the values were significantly lower at G4 relative to the earlier stages, and a further significant decrease was observed at G5 (G4: 33.9 ± 0.9 mEq/d, G5: 24.8 ± 0.8 mEq/d; both $P < 0.001$ vs. earlier stages). In contrast, as shown in Fig. 1B, there was a significant decrease in urinary potassium