Inadequate Dietary Potassium and Progression of CKD

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The serious consequences of abnormal potassium concentrations in patients with advanced kidney disease (CKD) are not uncommon but have focused more attention on treatment and prevention of hyperkalemia than hypokalemia. Nevertheless, the prevalence rates in CKD of hyperkalemia (15%–20%) and hypokalemia (15%–18%) are similar, and both are associated with equally high mortality rates (1,2). Moreover, values for [K+]s in the low normal range (3.5–3.9 mEq/L) in CKD are associated with higher mortality than in patients with [K+]s between 4.0 and 4.5 mEq/L (2), implying that inadequate dietary K+ may be the explanation.

The Western diet is typically low in potassium and high in sodium content. The average K+ intake in the United States population is ≈2000 mg/d of K+ because of insufficient intake of fruits and vegetables. Although outdated, the recommendation for “adequate intake” of K+ by the institute of medicine for healthy adults is 4700 mg/d, whereas in contrast, diets of our hunter-gatherer ancestors provided an abundant source of K+ (≥9000 mg K+/d) and much less Na+ than contemporary diets (3).

Potassium and sodium intakes should be considered concurrently, because a higher intake of K+ tends to blunt the consequences of hypertension and cardiovascular disease associated with excessive dietary Na+, whereas lower dietary K+ augments the consequences of a higher dietary Na+. Approximately 60% of the daily salt load is from prepared foods purchased in the supermarket or fast food restaurants. These same food sources are low in K+ (3). To accompany a high-sodium diet, the average individual consuming a meat-based diet would need to ingest 10–12 servings of fruits and vegetables to provide sufficient K+ and alkali precursors (e.g., potassium citrate). Growing evidence suggests that higher dietary Na+ and lower K+ contribute to high rates of hypertension, diabetes, and cardiovascular disease as well as CKD. Conversely, a plant-based diet improves markers of vascular endothelial function and increases vascular relaxation in patients with hypertension (3).

Poverty is associated with poor outcomes for CKD, and food insecurity affects about 25% of low-income patients (4). Dietary potassium insufﬁciency may be an underappreciated consequence of food insecurity and carries a signiﬁcant public health risk.

The assessment of dietary K+ intake by history or food frequency questionnaires is challenging, and more reliable means of stratification of patients with CKD into those with lower or higher dietary potassium intake are needed to identify those at risk. Collection of a 24-hour urine [K+] is considered widely to be predictive of dietary K+, but it is similarly problematic in the ambulatory setting.

In this issue of the Clinical Journal of the American Society of Nephrology, Kim et al. (5) describe the association of urinary K+ excretion and progression of CKD in Korean subjects enrolled in the Korean Cohort Study for Outcome in Patients with CKD (KNOW-CKD), a large, multicenter, prospective study. This study analysis selected 1821 subjects with baseline and follow-up spot urine potassium-to-creatinine ratios (K/Crµ) who were stratified into quartiles on the basis of levels of K+ excretion from lower to higher. The primary outcome was occurrence of a kidney event defined as a ≥50% decline in eGFR from baseline. Several strengths of this study include (1) 24-hour urine K+ excretion data were available for one half of the subjects and outcomes were analogous to those having spot K/Crµ values; and (2) subjects represented stages 1–5 CKD, with relatively equal distribution for each. When divided into quartiles from the lowest to highest K/Crµ, significantly higher hazard ratios were documented in subjects in the lowest quartile. Regression analysis (figure 1 in ref. 5) revealed an inverse relationship between K/Crµ and risk of decline in eGFR (P<0.001). This relationship held when adjusted for age, sex, smoking, body mass index, comorbid disease, BP, albumin, and calcium (tables 3 and 4 in ref. 5). Conversely, higher urinary K+ excretion was associated with better kidney outcomes and longer survival (supplemental figure 2 in ref. 5). These data suggest that lower urinary K+ excretion identifies lower dietary K+ intake and is associated with a higher risk for CKD progression.

The Chronic Renal Insufﬁciency Cohort (CRIC) cohort study reported directionally opposite results—higher incidence rates of ESKD and death were seen in subjects with higher rather than lower values for K+ excretion (6). Nevertheless, both the Prevention of Renal and Vascular End-Stage Disease study (7) and a post hoc analysis of the Modiﬁcation of Diet in Renal Disease database (8) are in general agreement with the KNOW-CKD findings (5). The Renal Research Institute Chronic Kidney Disease study involving 820 patients with CKD (2) also supports these ﬁndings. Therefore, four studies to date have shown that subjects with early- to later-stage CKD with higher urinary K+ excretion and by inference, higher dietary K+ intake

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maintained better kidney function than those in groups with low K⁺ excretion. The reasons for the differences in these data and the CRIC cohort are not immediately apparent.

The KNOW-CKD was conducted exclusively in Korean subjects. The major sources of dietary K⁺ (average of 2900 mg/d) in the typical Korean diet include white rice, vegetables, kimchi, and fruit. Dietary Na⁺ sources are kimchi, salt, soy sauce, and soybean paste (average of 5202 mg/d). In addition to cultural differences, clinical features of the KNOW-CKD cohort (7) include (1) that 33% were on diuretic therapy and that 85% were on renin-angiotensin-aldosterone system blockers (table 1 in ref. 5). Both diuretics and renin-angiotensin-aldosterone system blockers clearly have an effect on urinary K⁺ excretion that may vary across the spectrum of CKD. However, these drugs were similarly represented in each quartile, suggesting that urine K⁺ excretion was not affected disproportionately by either medication. (2) Smokers were represented in the study (47%), but this risk was evenly distributed among the quartiles of K⁺ excretion. Additionally, (3) kidney disease was attributed to “GN” in 35% of subjects, which was disproportionately higher than in the CRIC study. However, none of these variations provide adequate explanation for directional differences in outcomes on the basis of K⁺ excretion (7,8). Therefore, the study by Kim et al. (5) augments a growing body of evidence that dietary K⁺ inadequacy may be a significant factor in the progression of CKD and supports measurement of a spot K/Cra in lieu of a 24-hour collection (7). This latter point requires confirmation in additional populations but could simplify clinical assessment if the range of target values for spot K/Cra could be defined more precisely.

American and Korean diets are not only typically insufficient in K⁺ but also, acid producing, because both are “meat-based” diets. High net endogenous acid production, as anticipated in individuals consuming meat-based diets with inadequate representation of fruits and vegetables, is a recognized contributor to progression of CKD. Dietary supplement with endogenous alkalai administration or liberalization of dietary fruits and vegetables slows progression of CKD, reduces net endogenous acid production, and increases the [HCO₃⁻]ᵢ (9).

Although the precise mechanisms for the association between diet and progression of kidney and vascular diseases have not been elucidated entirely, a recent scholarly and highly informative review on this topic by Sebastian et al. (3) proposes that suboptimal consumption of fruits and vegetables may activate reactive oxygen species and oxidative stress, diminish nitric oxide bioavailability, trigger vascular endothelial dysfunction, increase vascular smooth muscle resistance, and cause hypertension and vascular disease. Comprehensive studies are needed to explore this potentially highly significant proposal.

The practice of restricting dietary K⁺ in patients with CKD is not a “one size fits all” phenomenon. A diet rich in fruits and vegetables should be encouraged in patients with early-stage CKD with clinical hypokalemia (≤3.0–3.5 mEq/L) and recommended in patients with borderline hypokalemia (3.5–3.9 mEq/L). Dietary K⁺ restriction should be reserved for patients with more advanced CKD and documented hyperkalemia. Well designed multicenter, controlled trials will be necessary to accurately delineate appropriate recommendations for each stage of CKD.

There is a sense of urgency, however, in view of a recent report that the national burden of CKD is increasing, specifically in younger adults (10). These disturbing data should prompt an effort to address contributing causes more comprehensively. The growing prevalence of obesity in young adults implies that metabolic abnormalities from dietary indiscretion rather than dietary quality are a likely feature. Additional information on the relationship between dietary practices in patients with CKD is needed and could favorably affect the overall health of United States and global populations.

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Disclosures

None.

References


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