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Renal Outcomes and Dietary Potassium: The Overshadowed Electrolyte?

Kristen L. Jablonski, Ph.D.[1] and **Jessica Kendrick, M.D. M.P.H**[1,2]

[1]Division of Renal Diseases and Hypertension, University of Colorado School of Medicine Aurora, CO

[2]Denver Health and Hospital, Denver, CO

Abstract

Smyth *et al.* examined the association between urinary sodium and potassium excretion and adverse renal outcomes in adults at high cardiovascular risk. They found no association between urinary sodium excretion and adverse renal outcomes, but a reduced odds of adverse renal outcomes with higher urinary potassium excretion. This finding is quite interesting and a major advancement from this study. It will be important to ascertain whether this finding holds true in individuals free from vascular disease and diabetes, as well as in patients with chronic kidney disease.

While numerous studies have examined the relationship between sodium and to a lesser extent potassium intake with blood pressure, not much is known regarding the association of these electrolytes with renal outcomes. In this issue, Smyth *et al.*[1] examined the association between urinary sodium and potassium excretion and adverse renal outcomes, using data from the ONTARGET and TRANSCEND trials of 28,879 adults ≥55 years of age at high cardiovascular risk. During a median follow-up period of 56 months, there was no association between urinary sodium excretion and the odds of the primary (eGFR decline ≥30% or chronic dialysis) or secondary renal outcomes (eGFR decline ≥40% or chronic dialysis, doubling of serum creatinine or chronic dialysis, >5% per year loss of estimated glomerular filtration rate (eGFR), progression of albuminuria). However, higher urinary potassium excretion was associated with reduced odds of adverse renal outcomes. Compared with the lowest potassium excretion (median 1.7 g/day), both moderate (median 2.1 g/day) and high (median 2.7 g/day) potassium excretion were associated with a reduction in the odds of the primary outcome (OR 0.88, 95% CI 0.84–0.92 and OR 0.74, 95% CI 0.67–0.82, respectively). Although the study is observational, it is the first study to prospectively examine the association of potassium excretion with renal outcomes.

Corresponding Author: Jessica Kendrick MD, MPH, Division of Renal Diseases and Hypertension, University of Colorado School of Medicine, Denver Health Medical Center, 660 Bannock St, Mail Code 4000, Denver, CO 80204, Phone: (303) 602-5045, Fax: (303 602-5055, Jessica.Kendrick@ucdenver.edu.

Disclosure

The authors declared no competing interests.

Supporting the current findings is a study published earlier this year examining the association between 24-hour urinary sodium excretion and renal outcomes in patients with chronic kidney disease (CKD). In 800 nondiabetic patients with CKD who participated in the Modification of Diet in Renal Disease Study (MDRD) study, there was no independent association of sodium excretion with either kidney failure or a composite of kidney failure and mortality.[2] However, contrary data have also been reported. In the Nurse's Health study of 3296 women with preserved kidney function, higher sodium intake as assessed by a food frequency questionnaire was associated with a greater decline in eGFR over a median follow-up of 11 years.[3] In a post-hoc analysis of 500 patients with chronic kidney disease (CKD) who participated in the Ramipril Efficacy in Nephropathy trials, there was a stepwise increase in risk of end-stage renal disease (ESRD) with higher 24-hour urinary sodium excretion; however, this association was attenuated after adjusting for proteinuria.[4]

When interpreting the results of the study by Smyth *et al.*[1], it is important to consider several limitations, some of which the authors highlighted in their discussion. A single spot urine sample was used to estimate 24-hour urinary sodium and potassium excretion, thus these values must be interpreted cautiously, as highlighted in a recent commentary[5]. A single spot urine may not be an appropriate reflection of an individual's usual sodium and potassium intake. In addition, the number of subjects in the category of lowest sodium excretion (<2 g/d), consistent with recommendations by organizations including Kidney Disease: Improving Global Outcomes (KDIGO), was very small (n=818 or 2.8% of the population). For the tertile analysis, the low sodium group had a median intake (3.3 g/day) that is well above the recommended level for individuals with and without kidney disease, according to KDIGO, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI), the American Heart Association, and U.S. Department of Agriculture (USDA). The authors concluded that the results do not support recommendations for low sodium diets for the prevention of renal outcomes in this population. However, this conclusion should be interpreted cautiously, as there were few subjects actually consuming a low sodium diet upon which to draw this conclusion. In addition, it is important to consider the breadth of evidence supporting that a low sodium diet reduces blood pressure, thus recommendations for a low sodium diet should consider potential benefits beyond the renal outcomes examined in this analysis.

The finding by Smyth *et al* that higher potassium excretion was associated with reduced odds of adverse renal outcomes is quite interesting and a major advancement from this study. Potassium is often the "forgotten electrolyte" overshadowed by sodium in most studies. Unlike sodium, the only other evidence available on the association between potassium and renal outcomes is from a recent cross-sectional analysis of 13,917 participants from the National Health and Nutrition Examination Survey (NHANES). Similar to the results found by Smyth *et al*, the participants in the lowest quartile of potassium intake, as assessed by 24-hour dietary recall, had a 44% increased odds of CKD.[6] Hence, results from these studies suggest that a diet high in potassium intake may benefit the kidney. A meta-analysis of randomized controlled trials of potassium supplementation suggests that higher dietary potassium lowers blood pressure.[7] The association between

higher potassium intake and improved renal outcomes may be mediated by changes in blood pressure, other physiological mechanisms, or likely some combination of each.

Figure 1 provides a schematic of the potential physiological mechanisms by which increased dietary potassium may reduce adverse renal outcomes. Note, this is somewhat speculative and certainly incomplete, drawing from a limited number of animal and epidemiological studies. High dietary potassium may be protective via blood pressure lowering, either due to increased serum potassium concentration and a subsequent reduction in vascular resistance,[8] or via increased renal kallikrein expression,[9] as the kallikrein-kinin sytem promotes vasodilation. Reduced vascular resistance may also increase eGFR,[8] and kallikrein may reduce glomerulosclerotic lesions and tubular injury.[9] Alternatively, the benefits of a diet high in potassium may not be due directly to potassium, but instead to the anti-oxidant and anti-inflammatory properties of a diet high in fruits and vegetables, which may also lower blood pressure. In addition, the ratio of potassium and sodium may be important, as the blood pressure lowering effect of potassium is greater in the presence of high dietary sodium intake.[10] The previous study done in the NHANES population found that regardless of the sodium intake, a high potassium intake was protective for CKD. The current study by Smyth *et al.* did not examine combinations of urinary sodium and potassium excretion. Finally, the association between potassium and renal outcomes may be explained by confounding, such that individuals who have more severe renal disease may consume less potassium.

Independent of mechanism, it will be important to ascertain whether this finding holds true in individuals free from vascular disease and diabetes, as well as in a population comprised entirely of patients with CKD (approximately 30–40% of participants in this study had a baseline eGFR <60 ml/min/1.73 m^2). Future research, including well conducted randomized controlled trials, will be required to determine if higher potassium intake is indeed protective against adverse renal outcomes. In addition, the relation between sodium and potassium intake needs to be more rigorously evaluated, as not only the intake of each electrolyte alone, but rather the ratio of the two, may be important in mediating outcomes.

Acknowledgments

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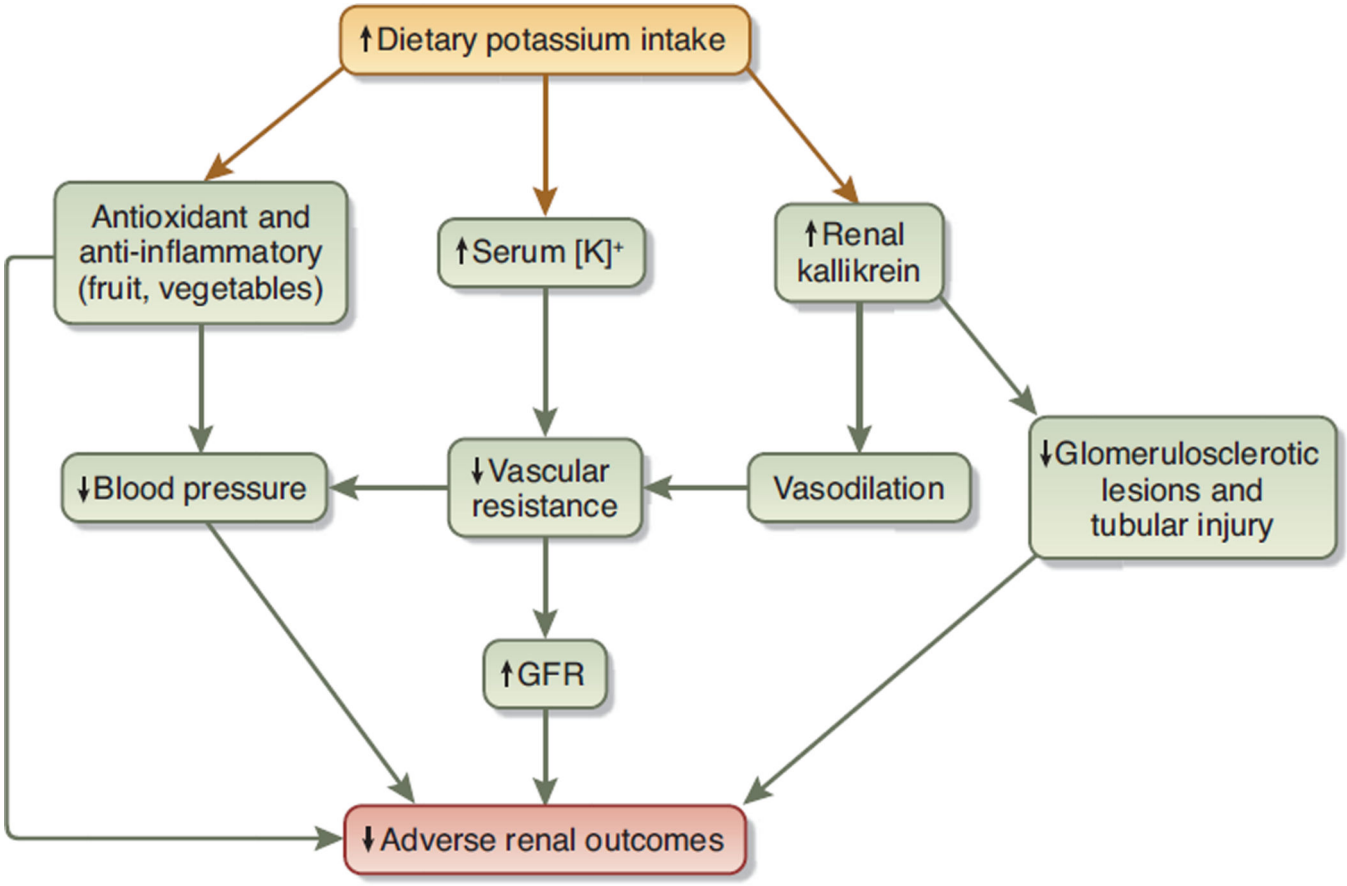

Figure 1.

Potential physiological mechanisms by which higher dietary potassium may be protective against adverse renal outcomes.