Dietary Potassium in Chronic Kidney Disease: Do Not Restrict the Evidence

Dear Editors,

With interest we read the systematic review and meta-analysis by Morris et al., which concluded that dietary potassium (K⁺) restriction in patients with chronic kidney disease (CKD) is associated with a 0.22 mEq/L decrease in serum K⁺ and 40% lower mortality hazard, but not with progression of CKD. However, we would like to raise 2 points of concern, including (1) a discrepancy between the results of the meta-analyses and the original studies and (2) an overestimation of the effect of dietary K⁺ restriction on serum K⁺.

The meta-analysis in which Morris et al. analyzed the association between urinary K⁺ excretion (Uₖ, as proxy for dietary K⁺ intake) and mortality included 4 studies. The hazard ratios calculated from the studies by He et al., Leonberg-Yoo et al., and Eisenga et al. were all <1 and therefore favored dietary K⁺ restriction. All 3 original studies, however, reported the opposite association. Leonberg-Yoo et al. and Eisenga et al. showed that Uₖ < reference was significantly associated with a greater risk of all-cause mortality (hazard ratios 1.5-1.7 and >2, respectively). He et al. used the lowest UK quartile as reference and showed in the fully adjusted model that all-cause mortality was lower in all higher quartiles, although this was not statistically significant.

The meta-analysis by Morris et al. on urinary K⁺ and CKD progression showed a hazard ratio >1 for He et al. (favors no restriction) and <1 for Eisenga et al. (favors restriction). Again, the original studies showed the opposite association: He et al. showed that Uₖ > reference increased the risk of CKD progression (hazard ratios 1.0-1.6), whereas Eisenga et al. showed that Uₖ < reference increased the risk of CKD progression (hazard ratios >3.4). It is also unclear why some studies were excluded from this meta-analysis. The inclusion criteria reported “any stage CKD,” but the analysis of the ONTARGET and TRANSCEND trials was not included, while this study also included a subgroup with eGFR <60 mL/min/1.73m². Participants with CKD were also present in other cohorts with baseline eGFR 60-90 mL/min/1.73m² and albuminuria, which would classify as CKD Stage G2 A1-A3. Another question is why studies using a spot urine K⁺ to creatinine ratio or food frequency questionnaires to assess dietary K⁺ intake were excluded. These considerations are relevant, because at present the majority of available studies shows that higher dietary K⁺ is associated with better kidney outcomes. A placebo-controlled, double-blind randomized clinical trial is currently investigating whether K⁺ supplementation slows CKD progression.

Our second concern is the time points that were selected to analyze the association between dietary K⁺ and serum K⁺. Morris et al. included 2 randomized controlled trials and found that restricted dietary K⁺ intake (33 mEq/day) reduced serum K⁺ by 0.22 mEq/L in comparison to “liberal” dietary K⁺ intake (40 mEq/day). In both studies serum K⁺ was measured at multiple time points, but only the time points with the greatest differences in serum K⁺ were included in the meta-analysis. In the study by Arnold et al., the difference at 6 months was used (0.5 mEq/L), whereas at 24 months this difference was less prominent (0.2 mEq/L). In the study by Cockram et al., the difference in serum K⁺ at day 22 was selected (−0.3 vs. −0.5 mEq/L), whereas no differences at days 8 and 15 were observed (0 vs. 0.1 and −0.4 vs. −0.3 mEq/L). A related question is how representative the 2 studies are for dietary K⁺ intake, because one study used extremely low K⁺ liquid diets, whereas in the other study ~50% of subjects combined a low K⁺ diet with K⁺ binders, which also lower serum K⁺. Finally, the K⁺ content of the diet that was classified as liberal intake was still 2-3 times lower than current recommendations. According to a cross-sectional analysis of 3,893 patients with CKD Stage G3b or G4, lowering dietary K⁺ intake from 40 to 33 mEq/day would lower serum K⁺ by only 0.02 mEq/L. Similarly, Noori et al. showed that in 224 hemodialysis patients, predialysis serum K⁺ was only 0.1 mEq/L higher when comparing the lowest to the highest quartile of K⁺ intake (23 vs. 88 mEq/day).

In conclusion, we challenge the conclusion by Morris et al. that dietary K⁺ restriction is associated with a reduced risk of death in patients with CKD and conclude that the relationship between dietary K⁺ and serum K⁺ was overestimated.

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