Dietary Potassium in Chronic Kidney Disease: High Quality Evidence Is Still Needed

Dear Editors,

WE PUBLISHED A meta-analysis which considered the strength of the current evidence for restricting dietary potassium in chronic kidney disease (CKD).[1] We thank Visser et al.[2] for their comments and for taking the time to pay such close attention to our results. We have reviewed our analysis in light of these and have found 2 errors. The labeling of the forest plots (Figs. 3 and 4) is incorrect, "Favors no restriction" should be "Favors restriction" and vice versa. In our meta-analysis, we inserted a negative figure, when it should have been positive in Noori et al.[3] (Fig. 4). We apologize for these errors and wish to publish the corrigendum in this issue.

In response to Visser et al., further comments are detailed below:

Visser et al. questioned the exclusion of 2 observational studies[4,5] which reported higher urinary potassium was associated with reduced CKD progression.[4,5]

Araki et al.[4] and Smyth et al.[5] met our inclusion criteria but were both excluded as it was impossible to separate those with and without CKD in their cohorts. In Araki et al. study, the mean (standard deviation) estimated glomerular filtration rate (eGFR) was 89 (19) and median (interquartile range) urine albumin excretion rate (AER) was 12 μg/min (6-29). Converted to AER (mg/24 hours) this is 17.28 mg/24 hours (8.64-41.76) (by converting μg to mg per minute and then to 24 hours) meaning that there was a mixed sample of people with AER $<$30 mg/24 hours and therefore no CKD, as well as those with AER $>$30 mg/24 hours and therefore with CKD in the same cohort. Results for the CKD proportion of the cohort alone were not available. It was similar for Smyth et al. as the baseline cohort had people with CKD and no CKD based on the overall cohort of n = 28,879 who had a mean eGFR 68.4 (17.6) and a mean urinary albumin to creatinine ratio 5.33 mg/g (24.21) which is less than 30 mg/g, which is the threshold for diagnosis in those with eGFR $\geq$ 60.[6]

Visser et al. suggested that the relationship between dietary and serum potassium was overestimated from the RCTs.

They also stated dietary potassium intakes were not a realistic reflection of current recommendations and also questioned why studies using spot urine analysis and food record charts were excluded.

We searched for a direct effect of restricting dietary potassium on serum potassium which is the rationale underpinning practice. Three RCTs met our inclusion criteria. The ClinicalTrials.gov registered RCT (NCT00949585) comparing outcomes in people with CKD Stage 3 on 40 mmol/day or 100 mmol/day potassium diets was excluded as we could not obtain data from a publication or on request from the principal investigator. We therefore considered whether to combine 2 RCTs due to the differences between both interventions and timescales; however, decided to combine them as both restricted dietary potassium in CKD. In Arnold et al. study,[7] we took the baseline to the first data point (6 months) which was as close to the 3 weeks in Cockram et al.[8] for comparison. It did not seem appropriate to compare 3 weeks with 24 months. We stated that these intakes were not in any way representative of current recommendations or actual intakes in free living individuals with CKD.[1] No included studies undertook spot urine analysis. Dietary potassium intakes from food record charts were included, for example, Noori et al.[3]

We acknowledged that numerous biases existed in these RCTs.[1] We therefore downgraded Arnold et al. and Cockram et al. twice to very low GRADE quality evidence which implied that the true effect of dietary restrictions is probably markedly different from our point estimate of -0.22 mEq/L (-0.33, -0.10). This suggests that there may be less of an effect of dietary restrictions in a well-controlled trial given that the upper confidence interval was -0.10 mEq/L: the effect Visser et al. judged realistic. However, the direction of the effect also suggests that a well-controlled clinical trial, with realistic intakes of dietary potassium, may show a greater reduction of serum potassium from baseline compared to our estimated -0.22 mEq/L mean difference.

We conclude that high-quality evidence is still needed to support the dietary management of serum potassium in CKD.

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