

Vitamin D Treatment and Mortality in Chronic Kidney Disease: A Systematic Review and Meta-Analysis

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Commentary

By Professor Richard Glasscock

There is little doubt that the prevalence of vitamin D insufficiency and deficiency (based on serum 25-OH vitamin D [calcidiol] levels) is increased in patients with various forms of chronic kidney disease compared to normal health controls of similar age and sun exposure. The mechanisms underlying this finding are not completely understood but are likely to be a combination of lower endogenous synthesis (or increased catabolism) and impaired dietary intake. Observational studies, included in the systematic review by Duranton et al., rather consistently (11/15 studies) show an association between lowered vitamin D levels and attempts to restore levels to normal by supplementation with calcidiol, calcitriol, paricalcitol or doxercalciferol and the risk of all-cause mortality. Indeed, subjects with treated ESRD or late stages of CKD remaining untreated with such vitamin D compounds have a 27% increased risk of dying compared to those receiving such treatment, even after adjustment of other co-morbid factors. Similarly, treatment with vitamin D compounds is also associated with a 45% reduced risk of a cardiovascular mortal event. These effects appear to persist for many years, might be dose-related, appear in both dialysis and non-dialysis treated CKD and are associated with lowered parathyroid hormone levels. What is missing is proof of a causal association for the described effects, as provided by a suitably designed and adequately powered randomized clinical trial. Unfortunately, such randomized clinical trials are few and have not yet firmly confirmed that such vitamin D therapy is directly beneficial for cardiovascular structure, and no adequately powered study as yet established a benefit of vitamin D therapy on all-cause or

fatal cardiovascular end-points. Therefore, the common use of vitamin D compounds in CKD should be regarded as not firmly evidence-based, and the systematic review of Duranton et al. is primarily hypothesis-generating. In general, supplementation with oral calcidiol is believed to be safe in patients with non-dialysis CKD who have low levels of 25-OH D; however, one needs to be careful about the adverse effects of such supplementation, such as aggravation of hyperphosphatemia and possibly vascular calcification.

Several questions are unanswered by this study.

They include:

- 1) Is the association of vitamin D therapy with improved outcomes a casual relationship?
- 2) Will supplementation with ergocalciferol be sufficient to result in a measurable beneficial effect or are more target vitamin D analogues required?
- 3) Will augmentation of intestinal phosphate absorption by certain vitamin D compounds have deleterious effects on the cardiovascular system?

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