

# Vitamin Supplementation in ESKD: Too Little or Too Much of a Good Thing?



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It is standard practice, although highly variable, that patients on chronic maintenance hemodialysis are prescribed a daily multivitamin supplement that, most importantly, includes the water-soluble vitamins because of both the dietary restrictions imposed on these patients and the clearance of small water-soluble molecules on dialysis.<sup>1</sup> A retrospective observational study of the Dialysis Outcomes and Practice Patterns Study data showed improved survival in dialysis facilities in which there was greater widespread use of water-soluble vitamin supplementation in their patients.<sup>2</sup> Those vitamin supplements formulated for patients with end-stage kidney disease have much higher levels than multivitamins formulated for the general population.

With the results of the Hemodialysis (HEMO) trial demonstrating no benefit in terms of a higher spKt/V on thrice-weekly hemodialysis, researchers have sought other ways to improve outcomes in patients on

maintenance hemodialysis. These attempts have included more frequent hemodialysis (the Frequent Hemodialysis Network [FHN] Trial) and the use of additional convective clearance by hemodiafiltration (HDF) for improved small and, potentially more importantly, middle molecule (“uremic toxins”) clearance. Both the FHN (Daily) arm and the ESHOL (Estudio de Supervivencia de Hemodiafiltración Online) study using online post-dilution HDF have shown overall improved survival.<sup>3,4</sup> But *post hoc* analysis of the FHN Trial did not show a benefit in nutritional parameters, such as serum albumin (which may be both a nutritional marker and a marker of chronic inflammation from putative proinflammatory uremic toxins) and muscle mass (although there was a gain of body fat in the study in the FHN study group on 6 times per week dialysis).<sup>5</sup>

The issue that these newer modalities raise is the clearance and loss of important small molecule nutrients, such as the water-soluble vitamins. Significant clearance of vitamin C, for example, has been demonstrated in both conventional high-flux hemodialysis (30%) and HDF (45%).<sup>6</sup> But, a

study in patients in the FHN Trial measuring vitamin C levels did not find a significant deficiency of vitamin C levels in these patients owing to the use of oral water-soluble vitamin supplementation in patients with end-stage kidney disease.<sup>7</sup> The authors thus assumed and concluded that this would reflect a similar effect on all water-soluble vitamins, although no others were measured in the study.

But we don't know if the same holds true for HDF in terms of the clearance of water-soluble vitamins and whether patients treated with this modality need additional vitamin supplementation. In this issue of *KI Reports*, we now have a more detailed analysis of water-soluble vitamin levels in these patients in the article by Schwotzer *et al.*<sup>8</sup> This was a single-center study in 40 subjects on thrice-weekly HDF receiving a standard formulation of the vitamin B-complex and C designed for patients on maintenance hemodialysis. It is important to point out that patients received their vitamin supplementation at the end of each dialysis session, which both ensures compliance and minimizes losses during dialysis. Also important to note is that the patients received an average ultrafiltration volume of 22 liters per session, which is what the ESHOL trial (and *post hoc* analysis of other HDF trials, such as CONTRAST [Convective Transport Study] and the Turkish OL-HDF [Online Hemodiafiltration]) demonstrated was needed to observe a beneficial outcome.<sup>4,9,10</sup> Of note, these researchers found that 1 session of high-volume HDF cleared from 12% to 60% of the B-complex vitamins; however, they found that deficiencies of the B-complex vitamins varied from only 0% to 2.5% and only vitamin

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C showed a greater percentage of deficiency in this cohort (5%). Potentially equally important was that anywhere from 30% to 40% of patients had high levels of the B-complex vitamins. Reducing the dose of vitamin supplementation by half reduced the frequency of high levels of the B-complex vitamins in these patients down to 12% to 24% and only increased the percentage of patients with deficiencies to 0% to 4.2% of the B-complex vitamins and only 12.5% of vitamin C.

Thus, although it is appropriate to be concerned about vitamin deficiencies in patients on maintenance hemodialysis, it is reassuring that as we search to find ways to improve dialytic clearance and outcomes, we are not harming patients by exacerbating poor nutritional status. If anything, we may need to be more concerned about iatrogenic overdosing our patients, particularly with regard to vitamins B3 (niacin) and B6 (pyridoxine).<sup>11</sup>

## DISCLOSURE

The author declared no competing interests.

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