REVIEW ARTICLE

Is Routine Multivitamin Supplementation Necessary in US Chronic Adult Hemodialysis Patients? A Systematic Review

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Because of concern that United States (US) chronic hemodialysis patients are at high risk for the development of vitamin deficiencies, the great majority of such patients are routinely supplemented with a multivitamin. This policy is supported by major US dialysis providers and nonprofit organizations. Yet routine multivitamin supplementation expands hemodialysis patients' already large pill burden, probably accounts for many millions of dollars in annual costs, and in light of previous reports may even carry with it the possibility of increased risk of adverse outcomes. An analysis of the benefits of routine multivitamin supplementation in US patients is therefore in order. We performed a systematic review of the medical literature between 1970 and 2014 using the Ovid MEDLINE database to address this question. We conclude that there is insufficient evidence to support routine multivitamin use and recommend that the decision to supplement be made on an individual basis.

Introduction

VITAMINS ARE ORGANIC nutrients required in small quantities for a variety of essential biochemical functions. Vitamins are not usually synthesized by the body so must be supplied in the diet.[1] Concern has existed for some time over the possibility that chronic hemodialysis (HD) patients are at high risk for the development of vitamin deficiencies because diets prescribed for kidney disease patients tend to be low in certain vitamins,[2] the dialysis procedure may result in clearance of vitamins from blood,[2,3] metabolites that accumulate in the uremic milieu may impair the proper utilization of vitamins,[2,3] spontaneous reductions in food intake due to uremia may lead to inadequate vitamin consumption,[3] and medications and/or illnesses common to HD patients may interfere with the absorption and/or activity of vitamins.[2-4]

Because of such concerns HD patients in the United States (US) are routinely prescribed multivitamin supplements. In fact, more than 70% of US HD patients take such supplements, a far greater proportion than in other developed nations.[5] Such a policy is officially promoted by large US dialysis providers[6,7] and nonprofit institutions.[8,9] Yet, the implications of this policy must be carefully considered. Although the total cost of HD vitamin supplementation in the US is not available and probably accounts for a very small proportion of overall dialysis costs, it is likely to be in the many millions of dollars annually given the sizeable numbers of patients and available pricing.[10-12] In addition, vitamin supplementation increases the already large pill burden HD patients must contend with. Furthermore, in light of previous reports, the possibility that vitamin supplementation may actually have harmful effects should be considered.[13-16] Finally, US government–mandated fortification of foodstuffs may also have mitigated the need to supplement certain vitamins.

In light of questions about the potential benefits and drawbacks of vitamin supplementation and whether vitamin supplementation is necessary, we performed a systematic review of the medical literature to evaluate the evidence for routine vitamin supplementation in the US adult chronic intermittent HD population. In this article, we present the evidence for supplementing each individual vitamin. We chose to focus exclusively on US HD patients, the largest such population of any nationality, because their vitamin requirements may be unique in light of their food preferences and the specific influence of vitamin fortification in US foodstuffs.

Systematic Review

We limited our search to humans and the English language using the Ovid MEDLINE database between 1970 and 2014 and search terms vitamins, avitaminosis, and dietary supplements and subheadings renal dialysis, hemofiltration, and HD. From this database, we used the separate terms of vitamin A, ascorbic acid, vitamin D, vitamin E, vitamin K, thiamine, riboflavin, niacinamide,

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Financial Disclosure: The authors declare that they have no relevant financial interests.

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1051-2276/$36.00

http://dx.doi.org/10.1053/j.jrn.2014.09.003

vitamin B_6, vitamin B_{12}, biotin, folic acid, and pantothenic acid. Of the 1,076 articles that were identified, we then focused primarily on studies of adult HD patients within the United States although we did examine and occasionally include data from other HD populations, especially if the literature was sparse on the topic. We did not limit our initial search by patient age or location or study design because of concerns about the paucity of published data on this topic and our desire to capture all relevant information before excluding any studies.

What Defines Adequate Nutritional Intake?

Adequacy of body content and functional activity of vitamins have been determined traditionally by assessing dietary intake, corresponding biochemical values—usually from serum or plasma or red blood cells, although occasionally in urine, and in enzyme activities—and other biological processes or clinical manifestations of deficiency or excess. For example, the effects of certain vitamins on hemoglobin production or plasma and urinary oxalate levels may be indicators of deficiency or excess. Although not ideal, the best available objective indicator of adequate vitamin intake is blood levels because correlating vitamin intake with illness has proven more elusive. We therefore used blood vitamin content as the basis of determining the need for vitamin supplementation.

Dietary reference intakes are a set of reference values that help establish daily nutrient intake recommendations and are therefore a standard by which the adequacy of nutrient intake can be assessed.[17] Although dietary reference intakes can be used as general benchmarks, extrapolating such benchmarks to patients with chronic kidney disease or other illnesses in which they have not been carefully studied should be done with caution. Table 1 summarizes recommended daily allowances (RDA) values for vitamins in healthy adult men and women and compares them with the content of several commercially available dialysis vitamin supplements. RDA is the average daily intake level needed to meet the nutrient requirements of nearly all (97%–98%) healthy individuals. As the table demonstrates, arguably the most commonly prescribed dialysis multivitamins contain only water soluble vitamins, including several at levels higher than the RDA.

Current Recommendations on Dialysis Multivitamins

The 2005 Kidney Disease Outcome Quality Initiative guidelines state that "…it is prudent to supplement, rather than risk deficiency, especially when supplementation is safe at the recommended levels. Therefore, dialysis patients are likely to benefit from daily vitamin supplementation that provides the recommended published vitamin profile for dialysis patients, with special attention…" given to B vitamins and folic acid.[18] Similar recommendations exist for children with chronic kidney disease although this topic is not covered in this review.[19] Kidney Disease Improving Global Outcomes (KDIGO) recommends only that patients with an elevated parathyroid hormone be started on calcitriol or a vitamin D analog, and that vitamin D deficiency be excluded and treated using the strategy for the general population.[20] These recommendations are endorsed by the European Renal Best Practice guidelines.[21]

Water Soluble Vitamins

Vitamin B_1 (Thiamine)

Thiamine is a cofactor for many enzymes involved in carbohydrate metabolism and neural function.[22] Foods rich in thiamine include pork, legumes, beef, nuts, whole grains, and organ meat[23] although for decades flour has been enriched with thiamine in the United States. Thiamine deficiency can result in beriberi and subsequent heart failure and peripheral neuritis.[24]

Table 1. Comparison of Recommended Daily Allowances and the Content of Common Dialysis Multivitamin Supplements

Vitamin	Adult Male RDA	Adult Female RDA	Nephrocaps[85]	Nephrovite[86]	Dailyvite[11]
Vitamin A (mcg)	900	700	—	—	—
Vitamin C (mg)	90	75	100	60	100
Vitamin D (mcg)	15 (20 if >70 y)	15 (20 if >70 y)	—	—	—
Vitamin E (mg)	15	15	—	—	—
Vitamin K (mcg)	120	90	—	—	—
Thiamin (mg)	1.2	1.1	1.5	1.5	1.5
Riboflavin (mg)	1.3	1.1	1.7	1.7	1.7
Niacin (mg)	16	14	20	20	20
Vitamin B_6 (mg)	1.7 (≥51 y)	1.5 (≥51 y)	10	0.006	10
Folate (mcg)	400	400	1,000	1,000	1,000
Vitamin B_{12} (mcg)	2.4	2.4	6	6	6
Pantothenic acid (mg)	5	5	5	10	10
Biotin (mcg)	30	30	150	300	300
Choline (mg)	550	425	—	—	—

DRI, dietary reference intakes; RDA, recommended daily allowances.