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

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ABSTRACT

Because of concern that U.S. 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 U.S. 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 U.S. 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 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 hemodialysis patients may interfere with the absorption and/or activity of vitamins[2-4].

Because of such concerns hemodialysis patients in the U.S. are routinely prescribed multivitamin supplements. In fact, over 70% of U.S. hemodialysis patients take such supplements, a far greater proportion than in other developed nations[5]. Such a policy is officially promoted by large U.S. dialysis providers[6,7] and nonprofit institutions[8,9]. Yet the implications of this policy must be carefully considered. While the total cost of hemodialysis vitamin supplementation in the U.S. 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 hemodialysis 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 mitigate the need to supplement certain vitamins.

In light of questions about the potential benefits and drawbacks of vitamin supplementation and whether vitamin supplementation is beneficial, we performed a systematic review of the medical literature to evaluate the evidence for routine vitamin supplementation in the U.S. adult chronic intermittent hemodialysis population. In this article we present the evidence for supplementing each individual vitamin. We chose to focus exclusively on U.S. hemodialysis patients, the largest such population of any nationality, because their vitamin requirements may be unique in light of their food preferences and the specific pattern of vitamin fortification in U.S. 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 hemodialysis. From this database we used the separate terms of vitamin A, ascorbic acid, vitamin D, vitamin E, vitamin K, thiamine, riboflavin, niacinamide, vitamin B_6, vitamin B_{12}, biotin, folic acid and pantothenic acid. Of the 1076 articles that were identified, we then focused primarily on studies of adult hemodialysis patients within the U.S., though we did examine and occasionally include data from other hemodialysis 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 wanted to be certain to capture all relevant information prior to excluding any studies.

What Defines Adequate Nutritional Intake?

Adequacy of body content and functional activity of vitamins has been determined traditionally by assessing dietary intake, corresponding biochemical values—usually from serum or plasma or red blood cells, though 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. Though not ideal, the best available objective indicator of adequate vitamin intake is blood levels because correlating vitamin intake with illness has been much more elusive. We will therefore use blood vitamin content as the basis of determining the need for vitamin supplementation.

Dietary reference intakes (DRI) 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]. While DRIs can be used as general benchmarks, extrapolating such benchmarks to patients with CKD 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 (KDOQI) 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, though this topic is not covered in this review[19]. Kidney Disease Improving Global Outcomes (KDIGO) recommends only that patients with an elevated PTH 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 (ERBP) 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] though for decades flour has been enriched with thiamine in the U.S.

Thiamine deficiency can result in beriberi and subsequent heart failure and peripheral neuritis [24].

Evidence for Altered Requirements in Hemodialysis Patients

Dialysis patients are theoretically at risk for thiamine deficiency because of poor nutritional intake and loss of water-soluble vitamins in the hemodialysis effluent[24]. However, studies examining thiamine blood content in hemodialysis patients report equivocal findings. In the only study of U.S. patients, Ramirez et al demonstrated in the mid-1980s that 15 hemodialysis patients who were taken off their B vitamin supplementation were able to maintain normal thiamine blood levels over a six-month period. In five of those patients they measured thiamine directly pre- and post-HD and noted no significant change[25]. A subsequent study reported normal thiamine blood levels (mean 162 ± 42 ng/ml; normal range: 92-224 mg/ml) in twenty German patients not on supplementation who had been on hemodialysis for a median of 24 months[26].

In contrast, several reports of modest size have described low thiamine blood levels in hemodialysis patients[24,27-29]. Two of them—from Taiwan and Japan—reported an association between low thiamine levels and confusion or encephalopathy[24,27], with one of them describing an unusually high prevalence (33%) of Wernicke Encephalopathy. An additional study in patients in an intensive care unit setting found that the initiation of continuous renal replacement therapy was associated with an acute but nonstatistically significant drop in plasma erythrocyte thiamine levels (382 ± 109 to 264 ± 136 nmol/L) over eight hours, though levels remained within the normal range (100-300nmol/L)[30].

The lack of long term, contemporary data makes it difficult to assess the rate or risk of thiamine deficiency in U.S. hemodialysis patients. Further complicating data interpretation is differences between nations in thiamine enrichment in flour and grains and their consumption. It is not surprising that the reports of Wernicke Encephalopathy described above originated in Asian countries, where a combination of low thiamine enrichment[31] and high carbohydrate consumption make this presentation more likely[22]. One would reasonably expect a much lower risk of thiamine deficiency--even among hemodialysis patients--in nations such as the U.S., which has very high levels of enrichment and consumption of flour products.

Vitamin B_2 (Riboflavin)

Riboflavin is a hydrophilic B vitamin that is part of the moiety of flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN) that comprise flavoenzymes. Its function involves metabolism of fats, carbohydrates and proteins[23]. Riboflavin is found in milk and dairy products, meat, fish, eggs and broccoli. In the U.S. breads and cereals have been enriched with riboflavin since the 1940s[23]. Riboflavin deficiency is not fatal due to very efficient tissue conservation[1] and is characterized by nonspecific symptoms and signs, though more advanced deficiency may involve cheilosis, desquamation and inflammation of the tongue, seborrheic dermatitis, and microcytic anemia[22].

Evidence for Altered Requirements in Hemodialysis Patients

There are currently no studies of riboflavin status in U.S. or other hemodialysis populations. We expect that deficiency is less likely to occur in U.S. hemodialysis patients because of longstanding enrichment of foodstuffs with riboflavin.

Vitamin B_3 (Niacin)

Niacin, ingested as either nicotinamide (from animal sources) or nicotinic acid (from plants), becomes active *in vivo* when converted to cofactors used for oxidative processes[22]. Rich sources of niacin include baker's yeast, animal and dairy products, cereals, legumes, and leafy green vegetables[22]. Niacin can also be synthesized from the amino acid tryptophan. Niacin deficiency leads to pellagra, characterized by the "4 Ds": dermatitis, diarrhea, dementia, and death. Pellagra is typically observed with intakes deficient in niacin and tryptophan, such as maize-based diets[22].

Evidence for Altered Requirements in Hemodialysis Patients

Fifteen American hemodialysis patients dialyzed using parallel-plate dialyzers were able to sustain normal niacin levels for 6 months after being taken off vitamin supplementation[25]. An additional study in Japanese patients on hemodialysis for a mean of 7 years found mean blood nicotinamide adenine dinucleotide (NAD) levels to be no different from controls not on hemodialysis[32]. There is inadequate data to definitively assess the risk of niacin deficiency in U.S. hemodialysis patients, but current fortification of foodstuffs with niacin makes it less likely to occur.

Vitamin B_5 (Pantothenic Acid)

Pantothenic acid is used to synthesize Coenzyme A (CoA), a critical factor in many metabolic processes including fatty acid oxidation, protein transport, and the formation of acetyl CoA, a key molecule in energy metabolism[23]. Although pantothenic acid appears to be ubiquitous in the food supply, whole grains, vegetables, liver, and egg yolks are especially rich sources[23]. Deficiency has not been clearly identified in humans except in specific depletion studies.

Evidence for Altered Requirements in Hemodialysis Patients

No data exists on this topic.

Vitamin B_6 (Pyridoxine)

Vitamin B_6 exists *in vivo* in several forms: pyridoxal, pyridoxine, pyridoxamine, and the 5' phosphates of these compounds. Pyridoxal-5-phosphate (PLP) is a cofactor for many enzymes, particularly those involving amino acid metabolism, and is necessary for heme synthesis[3]. Vitamin B_6 is generally abundant in foods but especially rich sources include meats, whole grain products, vegetables, and nuts[22]. Severe vitamin B_6 deficiency may lead to peripheral neuropathy, convulsions, dermatitis, abnormal electrocardiogram findings, depression, confusion and due to its involvement with hemoglobin synthesis, microcytic anemia[22,23]. Interestingly, sensory neuropathy has been reported in patients taking daily doses of B_6 as low as 200 mg, with residual damage remaining after stopping supplementation[1].

Evidence for Altered Requirements in Hemodialysis Patients

A systematic review of the international literature estimated that between 24 and 56% of all hemodialysis patients have vitamin B_6 deficiency[33], while a 1981 study using an older assay reported that levels were lower in dialysis patients versus healthy Americans[34]. If true, part of the explanation may lie in the plasma clearance of vitamin B_6 during dialysis, which was reported to be between 28 and 48% depending upon the dialyzer used[35], with cellulose triacetate high-flux/high-efficiency (HF/HE) dialysis membranes clearing vitamin B_6 to a much greater extent than cuprophane membranes[36]. Similarly, continuous renal replacement therapy has been noted to clear PLP by a mean of 0.02 mg/day[35]. However, the assertion that pyridoxine is cleared by hemodialysis has been challenged in a more recent study[37]. While greater clearance of vitamin B_6 heightens the risk of deficiency, an older study found that U.S. hemodialysis patients taken off B_6 vitamin supplementation were able to maintain stable levels within the normal range for the six month study period[25]. Additional and more recent studies have confirmed that U.S. hemodialysis patients have PLP levels within the normal range[38,39].

While vitamin B_6 may possibly be cleared from plasma during hemodialysis, there exists no clear evidence that stable U.S. hemodialysis patients are at appreciable risk for vitamin B_6 deficiency.

Vitamin B_7 (Biotin)

Biotin helps mediate carboxylation and cell cycle regulation by biotinylating key nuclear proteins[1]. Biotin is widely distributed in many foods as biocytin (-amino-biotinyllysine), which is released with proteolysis. It is also synthesized by intestinal flora in excess of

requirements[1]. Though deficiency is rare it can occur with prolonged total parental nutrition or massive consumption of egg white, which contains avidin, which binds biotin in the intestine. Deficiency results in mental status changes, paresthesias, and nausea[23].

Evidence for Altered Requirements in Hemodialysis Patients

There are no studies of biotin status in US hemodialysis patients. In a study by Oguma et al, 27 Japanese HD patients found that biotin levels were significantly higher than controls, but the assay used may have been measuring biotin and its metabolites[40].

Vitamin B_9 (Folic Acid)

Folic acid transports single carbons or methyl groups to help synthesize nucleotides needed for cell division and growth[22]. It is also needed for the metabolism of several amino acids[3]. Food sources rich in folic acid include leafy green vegetables, fruit, yeast, and liver[22]. Nationwide fortification of cereal grains in the United States and Canada began in 1996[41]. Deficiency results in megaloblastic anemia and neural tube defects. Of note, initial support for supplementing hemodialysis patients with folic acid, vitamin B_6, and vitamin B_{12} was partly related to their ability to lower the putative atherothrombotic risk factor plasma homocysteine. The rationale for such a strategy has dissipated now that homocysteine lowering has been demonstrated not to have cardioprotective effects[42].

Evidence for Altered Requirements in Hemodialysis Patients

While the risk of folic acid deficiency may be higher in HD patients because leafy green vegetables tend to be restricted due to high potassium content, this is likely offset by the

fortification of grains and cereals in the U.S.[43] A series of older and contemporary U.S. studies including many hundreds of patients, pre- and post-fortification, report that folate levels are well maintained in chronic hemodialysis patients[25,38,39,44-46]. Based on the available evidence, it appears that folic acid deficiency is very uncommon among U.S. chronic hemodialysis patients.

Vitamin B_{12} (Cyanocobalamin)

Vitamin B_{12} plays a major role in the methylation cycle and is a cofactor in the synthesis of the amino acid methionine[22]. Major food sources are those of animal origin like eggs, liver, beef, chicken and salmon because with rare exception it is only synthesized by bacteria found in higher predatory organisms and not plant foods[1]. Vitamin B_{12} is also found in fortified foods like breakfast cereals[3]. Vitamin B_{12} deficiency causes a functional folate and methionine deficiency leading to megaloblastic anemia and irreversible degeneration of the spinal cord (i.e. pernicious anemia)[1]. Vitamin B_{12} can be measured directly in serum or plasma, though methylmalonic acid levels is a more specific and sometimes more sensitive indicator of vitamin B_{12} deficiency[22].

Evidence for Altered Requirements in Hemodialysis Patients

In a study of fifteen U.S. hemodialysis patients, B_{12} levels remained in the normal range during a six-month study period despite not taking B vitamin supplementation[25]. Multiple additional studies have demonstrated that U.S. hemodialysis patients have normal B_{12} levels[38,39,45,46] and are not at high risk of vitamin B_{12} deficiency.

Vitamin C (Ascorbic Acid)

While the main function of Vitamin C is to maintain collagen function, it also acts as an electron donor and cofactor in the production of catecholamines, many peptide hormones, osteocalcin, C1q (part of the complement cascade), protein C, and carnitine[1,22]. Major sources include green vegetables, citrus fruits, potatoes and tomatoes[23]. Vitamin C deficiency causes scurvy which manifests as tooth loss, gum decay, fragility of capillaries, bone fractures and skin changes[1].

Evidence for Altered Requirements in Hemodialysis Patients

Achieving optimal vitamin C status is a challenge in hemodialysis patients. Renal dietary restrictions imposed on such patients make it more likely they will avoid foods with high vitamin C content. Additionally, vitamin C is cleared during standard hemodialysis sessions[47-49]. However, vitamin C supplementation contributes to a rise in oxalate[47] which can deposit in tissues and lead to bone disease, arthropathies, vascular calcification, skin deposits, and liver failure[50].

The only study in U.S. patients was performed over twenty years ago and demonstrated that white and black hemodialysis patients—most of whom took a daily vitamin C-containing multivitamin--had similar and normal mean vitamin C plasma concentrations[51]. Several other reports from Europe and Asia report a relatively high prevalence of vitamin C deficiency, though the whether this led to detrimental effects was not well described[47,48,52-54]. Oral and/or intravenous vitamin C supplementation have

been shown in hemodialysis patients to increase vitamin C blood levels with relative ease[47,48,53,54].

The available medical literature is not helpful in ascertaining the risk of vitamin C deficiency in US hemodialysis patients, though theoretical concerns cited above remain. This must be balanced by contrary concerns about oxalate deposition and end-organ damage from vitamin C supplementation and the lack of reports of vitamin C deficiency in countries that do not use vitamin supplementation.

FAT SOLUBLE VITAMINS

Vitamin A

Vitamin A plays an important role in the proper function of the visual and immune system, cell differentiation, and cell turnover[1,22]. Carotenoids, which are precursors to vitamin A, are abundant in dark green and deeply colored fruits and vegetables[23], while preformed vitamin A is present in animal source foods like liver, fish, and eggs[22]. Vitamin A deficiency results in night blindness and xerophthalmia and is the leading cause of preventable blindness in children[22]. It also decreases normal function of vitamin D and increases susceptibility to infection[1] by compromising the innate and acquired immune system [23].

Evidence for Altered Requirements in Hemodialysis Patients

While there are no studies of vitamin A in the U.S. hemodialysis population, studies from Europe and Australia[55-59] reported that vitamin A levels in chronic hemodialysis patients

were generally within the normal range and frequently at least as high, if not higher, than healthy controls.

Vitamin E

Vitamin E influences the fluidity of cell membranes and prevents oxidative damage by reacting with lipid peroxide radicals[1]. Because vitamin E is widely dispersed in foods and oils deficiency is uncommon though can occur with diseases like cystic fibrosis or other diseases associated with fat malabsorption[23]. Vitamin E deficiency is associated with nerve and muscle damage, opthalmoplegia, pigmented retinopathy and hemolytic anemia[1,23].

Evidence for Altered Requirements in Hemodialysis Patients

A recent study of eleven U.S. hemodialysis patients found that baseline levels were within the normal range and increased significantly with vitamin E supplementation[60]. These findings have been replicated in several other studies performed outside the US[55,57,61,62], though not all concur[58].

Vitamin K

Vitamin K is a critical cofactor for the clotting system and nervous system development[1]. Vitamin K is found in two forms: phylloquinone (PK) (vitamin K1), found in green leafy vegetables and animal products, and menaquinone (MK) (vitamin K2), which is synthesized by intestinal bacteria. Sources of vitamin K include kale, spinach, liver, margarine, vegetable oils, and soybean oils[23]. Vitamin K deficiency is caused by low

dietary intake, chronic liver disease, and conditions that alter intestinal flora or fat content of bile salts. Prolonged prothrombin time is the most common and earliest finding of deficiency and is associated with increased bleeding risk from inactivation of vitamin K-dependent clotting factors[23].

Evidence for Altered Requirements in Hemodialysis Patients

There are no studies of vitamin K in US hemodialysis patients. Several European studies reported that mean vitamin K levels of hemodialysis patients were normal[63-65], though a minority of subjects did have low levels[65], as did subjects in a separate study that indirectly measured vitamin K status as reflected in protein carboxylation[66]. The clinical implications of this are unknown.

Vitamin D

Vitamin D is found in several forms: D2 from plant sources (ergocalciferol) and vitamin D3 (cholecalciferol) from animal sources. Both D2 and D3 undergo hydroxylation to form 25-hydroxy (calcidiol) and 1,25-hydroxyvitamin D (calcitriol), the active forms of vitamin D. Vitamin D functions to maintain calcium homeostasis[23] though it is under investigation for additional effects. Vitamin D is abundant in fish and its oil. Risk factors for deficiency include old age, dark skin, lack of sun exposure, obesity and fat malabsorption. Deficiency is manifested by muscle soreness, weakness and bone pain[23], leading to rickets in children and osteomalacia in adults[1].

Evidence for Altered Requirements in Hemodialysis Patients

Kidney failure is known to lead to inadequate production of calcitriol and secondary hyperparathyroidism, which is why calcitriol or its analogues are routinely supplemented in hemodialysis patients. The more pertinent question is whether the earlier forms of vitamin D (i.e. D2, D3, calcidiol) are needed for supplementation. Indeed, a cross-sectional analysis of 825 U.S. hemodialysis patients demonstrated that calcidiol deficiency is widely prevalent [67]. However, the benefits of D2, D3 or calcidiol supplementation are unknown[68-70]. Of note, recommended doses used to treat vitamin deficiency are far higher than what is usually contained in standard multivitamin tablets[68].

ASSESSMENT OF THE LITERATURE AND RECOMMENDATIONS

Hemodialysis patients are prescribed multivitamins for an increased theoretical risk of (primarily water soluble) vitamin deficiencies. As our review indicates, the available information does not strongly support routine water-soluble vitamin supplementation. With regard to fat-soluble vitamins, only vitamin D has been consistently demonstrated to be low in a significant segment of U.S. hemodialysis patients, and a daily multivitamin therapy is not appropriate treatment for this deficiency because supplementation recommendations require much higher doses.

In light of our findings we advise against a blanket recommendation to supplement all hemodialysis patients and recommend instead that supplementation be individualized based on clinical judgment and necessity. Reasons include the lack of supportive evidence as well as the associated inconvenience, cost, and possibly even hazards of

consuming a daily dialysis vitamin. The latter concern is rarely cited but should not be ignored. There is epidemiologic and clinical trial data supporting an increased risk of cardiovascular events in men taking supplemental calcium[13], of advanced and fatal prostate cancers in healthy men[14] and transaminitis in HIV patients[16] with multivitamin use, and of mortality in lung cancer patients taking beta carotene and vitamin A[15]. Apart from the risks, the literature is littered with negative clinical trials studying multivitamins[71-76]. Thus, we should not automatically assume that multivitamin therapy is not without risks. Rather, *primum non nocere* should be our code of action.

Of note, a recent epidemiologic analysis from the international Dialysis Outcomes and Practice Patterns Study (DOPPS)[77] observed that greater use of water soluble vitamin supplementation was associated with lower mortality rates. We would urge caution in accepting this finding in light of the study's limitations, which include lack of face-to-face confirmation that supplements were or were not being used, lack of direct measurements of blood vitamin levels, limitations in the variables accounted for in the final statistical model, and the interesting observation that vitamin supplementation is nearly existent in countries with much lower mortality rates like Japan.

We do recognize that the medical literature on this topic is limited and that existing studies in U.S. patients are typically small or may reflect outdated dietary or societal fortification patterns or dialysis technology. We also understand that there exists a subgroup of hemodialysis patients who are clearly at risk for vitamin deficiencies. This is why we advocate for individualization of multivitamin use. Specific conditions that

would argue for vitamin supplementation include pregnancy[78], gastric bypass surgery[79], anorexia with poor food intake[80], vegetarian diet or malabsorption states[81,82], and the use of certain medications[83,84]. Finally, our findings should not automatically be extrapolated to hemodialysis populations outside the U.S., which have different dietary intake patterns and exposure to vitamin fortification in foodstuffs.

In summary, a review of the literature offers no strong evidence arguing for routine multivitamin supplementation in U.S. chronic hemodialysis patients. In light of the potential benefits and risks of dialysis vitamin use, we recommend that supplementation be individualized based on each patient's needs and risk profile. Further study of this topic using adequately powered and well-designed trials would be in order.

PRACTICAL APPLICATION

Multivitamin supplements are commonly provided to hemodialysis patients in the United States. We systematically reviewed the literature and found no strong evidence for routine supplementation. We argue that supplementation should be individualized according to each patient's needs.

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

	Adult Male DRI	Adult Female DRI	Nephrocaps[85]	Nephrovite[86]	Dailyvite[11]
Vitamin A (mcg)	900	700	--	--	--
Vitamin C (mg)	90	75	100	60	100
Vitamin D (mcg) [a,b]	15 (20 if > 70 yr)	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 yr)	1.5 (≥51 yr)	10	0.006	10
Folate (mcg)	400	400	1000	1000	1000
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	--	--	--