ADVANCED DOSES OF VITAMIN D ARE REQUIRED TO ACHIEVE OPTIMAL VITAMIN D STATUS, PARTICULARLY DURING THE WINTER

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INTRODUCTION

Vitamin D is an essential nutrient that plays multiple roles in human health. The importance of vitamin D in calcium metabolism and bone health is well recognized but more recently, its role in cardiovascular health, immune function, glucose metabolism, and cell differentiation and proliferation have been defined (1-6). It is well established that vitamin D deficiency leads to rickets in developing children but more current research has also linked vitamin D deficiency with osteoporosis, osteomalacia, impaired muscle function, infection, autoimmune disorders, diabetes, and some cancers in adults (1-6). Thus, achieving optimal vitamin D status throughout life is essential to maintaining overall health.

Vitamin D is unique among other vitamins in that very little is obtained through a normal diet. The principal source of circulating vitamin D is endogenous production in the skin following exposure to sunlight (Figure 1). Thus, factors that limit sun exposure and/or endogenous vitamin D synthesis greatly reduce circulating vitamin D concentrations. Some of these factors include geographic latitude, season of the year, melanin content of the skin, use of sunblock, lack of outdoor activity, age, and more (1-6). Any of these factors, among others, can lead to chronic vitamin D deficiency.

Deficiencies of vitamin D are common. It is currently estimated that more than 1 billion people worldwide and 30-to-40% of the population between 15 and 49 years of age in the United States suffer from vitamin D deficiency (7-8). Consensus is building that adequate circulating vitamin D concentrations should be greater than 30 ng/mL and optimally above 50 ng/mL (7-10). Because relatively small amounts of vitamin D are obtained through the diet and so many lifestyle factors reduce endogenous vitamin D synthesis, supplementation becomes an important avenue for achieving and maintaining optimal vitamin D status. It has been shown that 100 IU of vitamin D per day increases circulating concentrations of vitamin D by ~1 ng/mL (7-10). Thus, supplementation with advanced doses of vitamin D (2000-4000 IU/day) depending on lifestyle, are required to reverse vitamin D deficiency, boost vitamin D levels into the optimal range, and maintain them thereafter.

The purpose of this evaluation was to assess the effectiveness of moderately high daily doses of vitamin D3 on increasing circulating levels of vitamin D during winter, spring, and summer seasons. Specifically, circulating vitamin D levels were measured before, during, and after a 12-week course of 4000 IU/day vitamin D3 during the winter followed by a 2000 IU/day dose of vitamin D during the spring and summer seasons.

TABLE 1. BASELINE CLINICAL CHARACTERISTICS

TREATMENT	MALE / FEMALE*	AGE	ETHNICITY**	VITAMIN D SUPPLEMENTATION AT BASELINE	BASELINE SERUM VITAMIN D
All Data (N=19)	10/9	50	16C/2A/1P	636 IU/Day	33 ng/mL
Placebo Group (N=8)	5/3	45	6C/2A	406 IU/Day	34 ng/mL
Treatment Group (N=11)	5/6	53	10C/1P	745 IU/Day	32 ng/mL

* All subjects from the greater Salt Lake City metropolitan area (~40 degrees north latitude) ** Caucasion = C; Asian = A; Pacific Islander = P

MATERIALS AND METHODS

Subjects, Study Design, and Serum Vitamin D Status

This was a two-arm, single-blind (subjects blinded only) test involving 19 healthy volunteers from the greater Salt Lake City metropolitan area, most using USANA's HealthPak™ daily dietary supplement packs, BiOmega™ and/or Active Calcium™ supplements. Subjects were randomly divided into the treatment or control (placebo) groups. The treatment group was given a daily supplement providing 4000 IU of vitamin D3 December 15th, 2008 to March 15th, 2009. The control group received a matching placebo tablet. Vitamin D3 and matching placebo tablets were both manufactured at USANA Health Sciences, Inc. (Salt Lake City, UT).

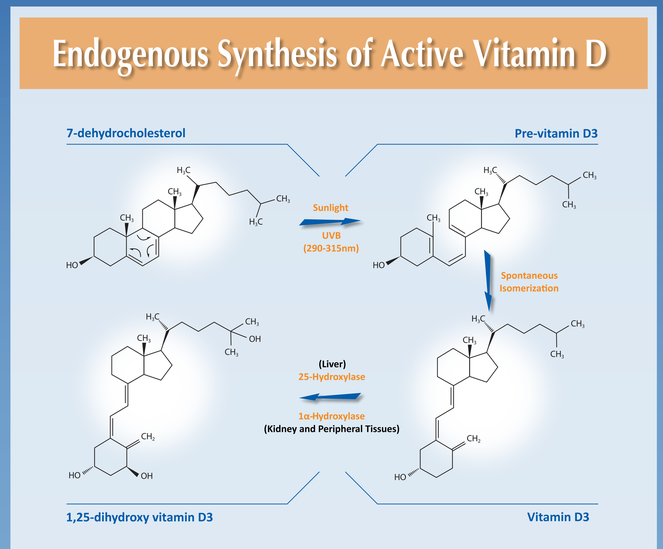
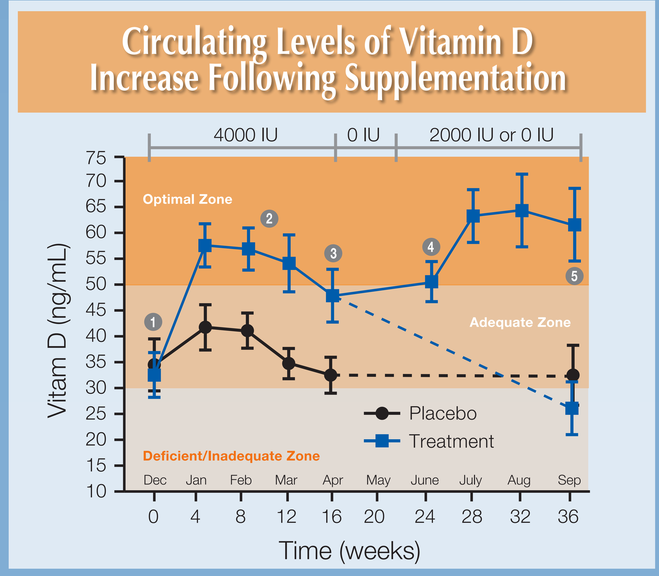


Figure 1. Endogenous synthesis of vitamin D.

Cutaneous synthesis begins from the cholesterol precursor, 7-dehydrocholesterol. 7-dehydrocholesterol accumulates in the skin and during sun exposure (specifically, ultraviolet B radiation) is converted to pre-vitamin D3 / vitamin D3 and enters circulation. In the liver, vitamin D3 is hydroxylated to 25-hydroxy vitamin D (25-OH vitamin D), the major circulating metabolite of vitamin D and the form used to clinically determine vitamin D status. 25-OH vitamin D is ultimately hydroxylated again, predominantly in the kidney but also in peripheral tissues, to form 1,25-OH vitamin D, the active form of the nutrient.

Figure 2. Supplementation with advanced doses of vitamin D3 effectively boost circulating levels of vitamin D. At time zero, subjects were randomly divided into two groups, a treatment group given 4000 IU/day of vitamin D3 and a control group given a matching placebo (1). Subjects took their supplements daily and circulating levels of vitamin D were measured every 4 weeks thereafter. After 12 weeks of supplementation (2), subjects stopped taking their respective tablets to determine the rate vitamin D levels declined (3). Following the 16 week blood draw, a subset of the treatment group went on to be supplemented with 2000 IU/day of vitamin D into the spring and summer (4). At the conclusion of the study (week 36), all subjects, regardless of the treatment group, had their vitamin D levels measured a final time (5). The blue and black dashed line indicates the trend of vitamin D levels in subjects that did not receive 2000 IU/day through the summer for both the 4000 IU/day and placebo groups, respectively. Supplementation with 4000 IU/day in the winter and 2000 IU/day vitamin D in the summer were required to maintain circulating levels of vitamin D in the optimal range. Data represents mean +/- SEM.



To analyze circulating vitamin D levels (25-hydroxy vitamin D3), blood samples were drawn at baseline and after 4, 8, and 12 weeks of supplementation. Samples were collected in Vacutainer SST tubes and centrifuged to separate serum from blood cells. Samples were sent to Quest Diagnostics for evaluation of serum vitamin D. Following the 12 week blood draw, all subjects stopped taking the assigned tablet and circulating vitamin D levels were monitored for the next 4 weeks (16 week time point). To determine the effect of vitamin D supplementation on circulating vitamin D levels during the late spring and summer, a subset of 5 individuals from the treatment group received 2000 IU/day of vitamin D beginning after the 16 week blood draw and their vitamin D status monitored for an additional 5 months (24, 28, 32, and 36 week time points). At the conclusion of the study (September 15th, 2009), all subjects initially enrolled in the study, regardless of treatment group, had their circulating vitamin D levels measured one final time to also determine the effect a lack of supplementation through the summer would have on vitamin D levels (week 36).

RESULTS

- **Treatment with 4000 IU/day significantly increased circulating vitamin D levels during the winter and maintained them in the optimal range above 50 ng/mL.**
- **Circulating vitamin D levels reached maximal levels after 4 weeks of supplementation and plateaued thereafter.**
- **Upon cessation of supplementation between weeks 12-16, vitamin D levels declined appreciably underscoring the need for continuous supplementation to maintain optimal levels throughout the winter and early spring.**
- **Supplementation of 2000 IU/day through the late spring and summer maintained vitamin D levels in the optimal range.**
- **At the conclusion of the study, vitamin D levels in all subjects that did NOT continue supplementation through the summer returned to the baseline values originally measured in December. This result emphasizes the need for continuous supplementation even through the summer when circulating vitamin D levels traditionally peak.**

CONCLUSIONS/DISCUSSION

Currently, the RDA for vitamin D is between 200-600 IU depending on age and gender. At baseline, the average intake of vitamin D (supplements and diet) for the subjects in this evaluation was between 800-1000 IU/day, well above the RDA. However, the average circulating level of vitamin D was only 33.4 ng/mL, which is in the adequate range, and significantly above the National average, but did not achieve levels considered to be optimal. Thus, vitamin D supplementation at much higher doses is necessary to achieve recently revised optimal levels.

In this evaluation, supplementation with an additional 4000 IU/day of vitamin D during the winter increased circulating levels of vitamin D by 4 weeks to within the optimal range and maintained them for the duration of the treatment. The subset of subjects who went on to receive 2000 IU/day during the late spring and summer were able to maintain their optimal vitamin D status. Interestingly, the subjects in the original supplemented group that did not go on to supplement with 2000 IU/day through the summer, reverted back to their baseline values (or even below) originally measured in December. This was surprising because vitamin D levels are at their highest in September (end of summer) when endogenous vitamin D production peaks. Thus, if individuals are not outdoors mid-day during the summer, the risk of vitamin deficiency/inadequacy remains a real threat. This study shows that continuous intakes of vitamin D—well above the RDA—are needed by many, if not most people, to obtain optimal circulating levels of vitamin D above 50 ng/mL throughout the entire year.

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