

VITAMIN D

Sunshine in a Bottle?

by Ronald L. Myers, CNC

In this issue of eBytes we will review exciting new research regarding this essential nutrient in human nutrition. I consider this to be one of the most important issues of eBytes that I have written to date. Please understand this is a very brief summary and over view of the reams of current research. I have over 260 citations from current peer-reviewed literature, all of which could not possibly be used in this issue, however, if you want to pursue more detailed research on your own and would like a good starting point, let me know, I can provide you with as many citations as you feel you need.

The discovery of Vitamin D receptors in tissues other than bone and gut, such as the brain, breast, prostate and lymphocytes, has led to a flurry of research into increased efficacy of Vitamin D as a possible treatment (and preventative agent) for other conditions than rickets and osteomalacia.¹ Recent research is suggesting that higher Vitamin D levels (i.e., significantly higher than the current RDA) provide protection from diabetes mellitus, osteoporosis, osteoarthritis, hypertension, cardiovascular disease, metabolic syndrome (formerly known as Syndrome X), depression, **several** autoimmune diseases, multiple sclerosis, polycystic ovary syndrome, musculoskeletal pain, epilepsy, and cancers of the breast, prostate and colon. Heaney² provides a very helpful distinction regarding Vitamin D deficiency states, classifying them as “short-latency deficiency diseases” such as rickets and “long-latency deficiency diseases” such as cancer. This gives us a helpful understanding between the differences of the acute symptoms of severe nutritional deficiencies and the delayed manifestations of chronic subclinical nutritional deficiencies. Yes, I understand that the research I am going to present to you in this issue flies in the face of the current FDA position that we do not have vitamin deficiencies in new millennium America!

VITAMIN D

Humans obtain Vitamin D naturally from two exogenous sources: the sun and dietary consumption. Natural Vitamin D, known as Vitamin D3 is 1,25 cholecalciferol (also known as 1,25 dihydroxyvitamin D [calcitriol]) is the form of Vitamin D produced in the skin and consumed in the diet. Man-made vitamin D is ergocalciferol (Vitamin D2). This is produced by irradiating fungi and has been shown to be a very poor precursor to the biologically active form and has the potential to be toxic.³ Cholecalciferol has become the preferred form of Vitamin D used clinically and in research studies.

¹ Holick MF, Vitamin D: importance in the prevention of cancers, type I diabetes, heart disease and osteoporosis, *Am J. Clin Nutr*, 2004;79(3):362-71.

² Heaney RP, Long-latency deficiency disease: Insights from calcium and vitamin D, *Am. J. Clin Nutr*, 2003;78(5):919-12.

³ Vieth R, et al, Efficacy and safety of vitamin D3 intake exceeding the lowest observed adverse effect level, *Am J. Clin Nutr*, 2001;73(2):288-94.

Vitamin D has two metabolic pathways: 1) endocrine, in which Vitamin D is formed in the skin after exposure to sunlight and then travels in the blood to the liver for conversion to 25-hydroxyvitamin D (25(OH) D). 25-(OH) D is then metabolized in the kidney to 1,25-dihydroxyvitamin D (calcitriol), the most biologically active form of Vitamin D. This final step in the metabolism of Vitamin D is accomplished by the enzyme 25-hydroxyvitamin D3-1-alpha-hydroxylase (1-OHase). 2) autocrine (within the cell), 25(OH) D circulating in the blood stream is taken up by a wide variety of cells that contain 1-OHase as well as Vitamin D receptors and are able to make calcitriol internally and do not have to rely solely on what is available in the blood.

THE RESEARCH

Current research is showing that much of the past research regarding vitamin D that did not prove efficacy failed to do so because the dose used was too low and the duration of the study was not long enough. It is now known that 3 to 4 months of oral supplementation are required for serum Vitamin D levels to plateau. Much of this past research used dosages reflective of the current RDA's which current research is showing are far too low to be physiologically supportive or to provide therapy in deficiency states.

Vitamin D deficiency is becoming wide spread. In view of this, it is prudent to begin assessing patient's Vitamin D status as a routine part of our clinical evaluation and providing oral Vitamin D supplementation where indicated. Currently, Grant estimates that at least 23,000 and perhaps as many as 47,000 cancer deaths might be prevented each year in the U.S. if simple interventions like oral Vitamin D supplementation were employed to increase levels of this essential nutrient in those patients presenting deficiency.⁴

Cancer prevention and treatment As far back as 1941, an *inverse* relationship between exposure to sunlight and death from cancer was documented by Apperly.⁵ Hypovitaminosis D has been shown to be directly related to increased risk of death for several malignancies; among them are cancers of the colon, lung, breast ovary, prostate, kidney, etc.⁶

Cardiovascular disease It is interesting to note that death from cardiovascular disease is more common during the winter months, when our ability for direct sunlight exposure is limited.⁷ Vitamin D deficiency has been well documented as a cause of heart failure,⁸ and recently, patients with congestive heart failure were found to have significantly lower levels of Vitamin D than controls.⁹

Critical Illness (Autoimmune and Inflammatory conditions) Vitamin D deficiency is common among patients in this category.

⁴ Grant, WB, An estimate of premature cancer mortality in the U.S. due to inadequate doses of solar ultraviolet-B radiation, *Cancer* 2002;94(6):1867-75.

⁵ Apperly, FW, The relationship of solar radiation to cancer mortality in North America, *Cancer Res* 1941;1:191-5.

⁶ Grant, WB.

⁷ Scragg, R, Seasonality of cardiovascular disease mortality and the possible protective effect of ultra-violet radiation, *Int. J. Epidemiol*, 1981;10(4):337-41.

⁸ Brunvand, L, et al, Congestive heart failure caused by vitamin D deficiency?, *Acta Paediatr*, 1995;84(1):106-8.

⁹ Zittermann, A, et al, Low vitamin D status: a contributing factor in the pathogenesis of congestive heart failure?, *J. Am Coll Cardiol*, 2003;41:105-12.

Diabetes (Type 1) This is usually an autoimmune inflammatory condition leading to destruction of beta cells in the pancreas and Vitamin D supplementation has shown *significant* preventative and ameliorative benefits in this condition.¹⁰ Supplementation with 2,000 IU of vitamin D per day reduced the incidence of type 1 by 80%!!!

Diabetes (Type 2) Vitamin D deficiency is associated with insulin resistance and beta cell dysfunction in diabetics; and healthy adults with higher serum 25 (OH) D levels had significantly better insulin sensitivity than those who were vitamin D deficient.¹¹

Epilepsy Seizures can be the presenting manifestation of vitamin D deficiency!¹² Several anti-convulsant drugs interfere with calcitriol formation in the kidneys.

Hypertension Why is blood pressure higher in the winter months? Could this have something to do with vitamin D's ability to regulate blood pressure?¹³

Polycystic Ovary Syndrome This disease is seen only in humans and is characterized by amenorrhea, insulin resistance, hirsutism, obesity and polycystic ovaries. In a study of 13 women with vitamin D deficiency and PCO, supplementation with up to 50,000 IU of Vitamin D on a weekly basis for 3 months normalized menstruation and/or fertility in nine of the women.¹⁴

Musculoskeletal pain In 299 patients with non-traumatic, persistent musculoskeletal pain, 83% presented overt vitamin D deficiency. Supplementation with 5,000 to 10,000 IU of Vitamin D per day for 3 months lead to significant pain reduction in nearly 100% of these patients.¹⁵

Multiple sclerosis In a study of 10 MS patients, daily supplementation with 1,000mg of calcium, 600mg of magnesium and 5,000 IU of Vitamin D for 2 years found a reduction in the number of exacerbations and a complete absence of adverse effects!

Osteoarthritis Vitamin D is effective in the treatment and prevention of this condition. Adequate blood levels of Vitamin D have also been shown to slow the progression of this most common form of arthritis.¹⁶

Space limitations prevent me from covering other conditions shown to benefit from Vitamin D supplementation. For the complete list, see page 1 of this issue.

¹⁰ Hypponen, E, et al, Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study, *Lancet*, 2001;358(9292):1500-3.

¹¹ Chiu, KC, et al, Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction, *Am J. Clin Nutr*, 2004;79:820-5.

¹² Johnson, GH, Willis, F, Seizures as the presenting feature of rickets in an infant, *Med. J.Aust*, 2003;178(9):467-8.

¹³ Rostand, SG, Ultraviolet light may contribute to geographic and racial blood pressure differences, *Hypertension*, 1997;30(2 pt 1):150-6.

¹⁴ Thys-Jacob, S, et al, Vitamin D and calcium dysregulation in the polycystic ovarian syndrome, *Steroids*, 1999;64(6):430-5.

¹⁵ Al Faraj, S; Al Mutairi, K, Vitamin D deficiency and chronic low back pain in Saudi Arabia, *Spine*, 2003;28(2):177-9.

¹⁶ McAlindon, TE, et al, Relation of dietary intake and serum levels of vitamin D to progression of osteoarthritis of the knee among participants in the Framingham Study, *Ann Intern Med*, 1996;125(5):353-9.

ASSESSING PATIENT VITAMIN D STATUS

Research is showing that current laboratory reference ranges for vitamin D (25(OH) D) are inadequate to be physiologically supportive and can mislead you if you are not aware of the findings of most current research. Optimum values for Vitamin D presented in this issue of eBytes are based on proposed optimums in a recently published (Oct 2004) article by Vasquez, et al.

Vitamin D deficiency Serum 25(OH) D levels below 20 ng/mL indicate Vitamin D deficiency. Heaney and Holick both state that 25 (OH) D levels should always be greater than 30 ng/mL.

Vitamin D insufficiency Serum levels of 25 (OH) D less than 40 ng/mL has been shown by Zittermann, et al to be the point where tissue levels are depleted and PTH (parathyroid hormone) is slightly increased. To maintain physiologic suppression of PTH, serum levels of 25(OH) D should be greater than 40 ng/mL.

Optimal Vitamin D Status Based on several published recommendations, an optimal range of 40 ng/mL to 65 ng/mL appears to be adequate to provide physiologic needs and has not been shown to be toxic by any current researcher. In his authoritative monograph, Vieth concludes there is no “consistent, credible evidence of Vitamin D toxicity associated with levels below 80 – 88 ng/mL.” In fact, Zittermann states that concentrations up to 100 ng/mL are subtoxic. Persons experiencing frequent full-body exposure to sunlight are known to be able to safely exceed the above recommended levels for serum 25 (OH) D.

Vitamin D Excess Serum levels of 25 (OH) D can exceed 80 ng/mL with exposure to sunlight in the absence of oral supplementation with Vitamin D. According to Vieth, hypercalcemia due to hypervitaminosis D is always associated with serum 25 (OH) D concentrations greater than 88 ng/mL. And Holick has stated, “Vitamin D intoxication does not occur until the circulating levels of 25 (OH) D are over 125 ng/mL.” Clinical assessment for Vitamin D toxicity is performed by measurement of both serum 25 (OH) D and serum calcium.

Serum levels of 25 (OH) D greater than 90 ng/mL with increased serum calcium are positive indicators of direct Vitamin D toxicity. Patients presenting hypercalcemia should discontinue (or avoid) vitamin D supplementation until the cause of their hypercalcemia can be determined.

CONCLUSION

Current research allows us to expand our awareness to the significant benefit to patients of adequate Vitamin D supplementation in preventing and providing non-toxic treatment for a wide variety of chronic conditions; conditions we may not have previously considered Vitamin D supplementation to be of any effect.

Even though this research has yet to provide us with specifics regarding dosages for treatment of conditions such as cardiovascular disease, hypertension, MS, PCO, etc., routinely evaluating and increasing patient's Vitamin D status into the optimum range can only be a benefit to them. We now have the tools to accurately evaluate Vitamin D status in apparently healthy patients as well as those presenting conditions of dis-ease. In treating those chronic conditions that research shows are responsive to treatment with Vitamin D, increasing patients 25 (OH) D levels to between 65 ng/mL and 80 ng/mL appears to be safe as long as there is no hypercalcemia.

A draw back to Vitamin D supplementation is results take awhile to realize. We live in a culture of instant gratification. And this attitude spills over into the health care arena as well; your patients want results now. It is therefore advisable to explain to your patients requiring Vitamin D therapy that the results you and they are hoping for may not be evident for 3 to 5 months after beginning daily supplementation with Vitamin D.

Recommended daily safe preventative dosages are as follows:

Infants	<1,000 IU
Children	2,000 IU
Adults	4,000 IU to 10,000 IU

Evaluate healthy patient's Vitamin D status yearly with serum 25 (OH) D and serum total calcium levels.

Biotics Research Corporation provides only the natural form (Vitamin D₃; 1,25 cholecalciferol) of Vitamin D as a true emulsion to insure optimum absorption for your patients. Research has shown that supplementation with BRC **Bio-D-Mulsion** and **Bio-D-Mulsion Forte**, which are presented as true emulsions (meaning absorption occurs via the lymphatics instead of the portal vein), *patient serum levels of Vitamin D can plateau in as little as 30 days*. Product names, **Bio-D-Mulsion**, 400 IU per drop, 1 fl oz bottle; **Bio-D-Mulsion Forte**, 2000 IU per drop, 1 fl oz bottle.

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