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Mini Review

To Maintain Optimum Health, Longer-Term Stable Vitamin D Levels are Necessary

Sunil J Wimalawansa*

Professor of Medicine, Endocrinology & Nutrition, USA

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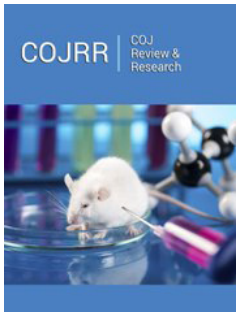

***Corresponding author:** Sunil J Wimalawansa, Professor of Medicine, Endocrinology & Nutrition, Cardiometabolic & Endocrine Institute, North Brunswick, USA

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Introduction

Vitamin D deficiency and insufficiency have become a global epidemic. This is mostly attributable to the skin cancer scare raised by the dermatology community three decades ago. Hypovitaminosis D affects people in all countries, irrespective of gender and age. Sun avoidance behavior, wearing of clothing that covers most skin, and the regular use of sunscreens and lotions markedly reduces the Ultraviolet B (UVB) rays reaching the skin. In addition, medications that increase the catabolism of vitamin D, such as anti-epileptic and anti-retroviral agents, reduce the bioavailable vitamin D concentration [1]. Vitamin D is essential for physiological maintenance of calcium.

The use of clothing that covers whole body or engaging in cultural or religious habits, and practices of reduce sun exposure, habitually using high sun protection factor containing sunscreens, increase the risks of developing hypovitaminosis. More than 80% of the required vitamin D is supposed to be generated by skin exposure to sunlight's UVB rays. Previtamin D is generated from ergosterol in the dermal tissue after exposure to UVB [2].

Vitamin D is essential for Calcium Homeostasis

Vitamin D facilitates dietary calcium and phosphorus absorption from the intestines, skeletal balance, and reabsorption from the kidney. The combination of these physiological actions maintains stable serum ionized calcium and overall homeostasis. Vitamin D is a fat-soluble vitamin, so its intestinal absorption depends on the availability of dietary fat.

Encouraging the public to get adequate sunlight exposure and efforts to fortify foods with vitamin D (and other essential nutrients), especially dairy products, have reduced the incidence of vitamin D deficiency in recent years in the United States and Europe. However, the incidence is gradually increasing again, especially in infants, children, the elderly, and in certain ethnic groups worldwide.

Vitamin D suppresses the release of parathyroid hormone (the release of which is dependent on magnesium sufficiency), a hormone that causes bone resorption [3]. Having normal serum 25(OH)D concentration keeps the parathyroid hormone under physiologic control and thus prevents excessive bone resorption and future fractures. To achieve the mentioned physiological functions, it is necessary to have a longer-term stable blood and tissue concentrations of vitamin D [1].

Physiological Serum 25(OH)D Concentration

Recent data from epidemiological, cross-sectional and longitudinal studies support the need for maintaining physiological serum concentrations of 25(OH)D greater than 30ng/mL (the minimum serum concentration) over a long period [4,5]. The data also indicate that to achieve and maintain the physiological benefits, serum 25(OH)D concentrations should be maintained between 30 and 60ng/mL (75 and 150nmol/L) throughout life.

Most people in industrialized countries do not get enough sun expose to generate adequate levels of vitamin D from the skin. Thus, most adults need a daily maintenance dose of between 1,000 and 2,000 IU [6]. However, people who are at risk for the development of hypovitaminosis D or have comorbidities, including certain vulnerable groups such as the obese, those with diabetes or an autoimmune disease or prone to infection, and pregnant women, may need between 4,000 and 6,000IU/day to achieve the optimal physiological effects [7,8]. Doses as great as 10,000IU/day have been reported to be safe [9]. Different modes of safe regimens and adequate replenishment of vitamin D were presented previously in a tabulated format [10,11].

Activated Vitamin D has no place in Vitamin D Supplementation

Except in those with liver or kidney failure, there is no scientific reason to prescribe any form of activated vitamin D. Activated forms of vitamin D, such as derivatives of one-alpha or 25-hydroxylase activated forms, are not only expensive but also have major adverse effects. Therefore, they should never be prescribed for vitamin D supplementation.

Taking cod liver oil (and some fish oils) is not a good option for vitamin D supplementation because these oils contain too much vitamin A. Excessive vitamin A intake over a period can cause liver damage and skeletal fractures. Individuals with some conditions, especially diseases affecting the intestinal tract (such as celiac disease, Crohn's disease, and ulcerative colitis), and gastric bypass surgery or cystic fibrosis, have significant problems with intestinal absorption of vitamin D and thus are unable to maintain serum 25(OH)D levels. Such patients require much higher doses of daily, oral vitamin D supplementation.

Patients with Renal Failure

Compared with those with normal renal function, patients with chronic kidney disease (CKD) have lower both, serum 25(OH)D and $1,25(OH)_2D$ concentrations. For the majority of them thus, needs supplementation of both parental vitamin D and 1α-partially or fully activated vitamin D supplements. In addition, in those with CKD, vitamin D supplements also reduce proteinuria [12] but may not prevent gradual deterioration of renal functions. In fact, patients with CKD not only need one-α activated forms of vitamin D but also normal vitamin D to reduce mortality [13]. Higher levels of serum 25(OH)D were associated with a lower risk of all-cause mortality in patients with CKD, but no conclusive evidence exists regarding serum levels of greater than 35ng/mL.

Low concentration of serum 25(OH)D, increase the serum parathyroid hormone, enhancing secondary hyperparathyroidism and bone turnover [14]. When patients with CKD are treated with both vitamin D and its one-α activated form, such as alfacalcidol (rocaltrol, paricalcitol; doxercalciferol, etc.) [15], mortality is significantly reduced [13]. Such synthetic vitamin D analogs are also indicated in hypophosphatemia and hypoparathyroidism [16]. Let's briefly look at pregnancy as one example to illustrate the importance of vitamin D sufficiency.

Vitamin D in Pregnancy

Maintaining appropriate physiological serum 25(OH)D levels during pregnancy would reduce the incidences and severity of several pregnancy-associated issues, including preeclampsia, cesarean deliveries, premature deliveries, hypertension during pregnancy, as well as premature delivery, small-for-gestation neonates, infant mortality, and minimize several common illnesses during early childhood. Having 25(OH)D concentrations above 40ng/mL before and during pregnancy would substantially reduce these maternal and fetal complications [17]. In addition, maintaining serum 25(OH)D concentrations is essential in the post-pregnancy period and during lactation. Moreover, maternal and neonatal vitamin D deficiency increase the risk of autism spectrum disorders and enhance the severity of neurodevelopmental disorders [18].

Vitamin D adequacy can be assessed only through the measurement of serum 25(OH)D. Recent data from epidemiological, cross-sectional, and longitudinal studies support that having physiological serum concentrations of 25(OH)D (i.e., >30ng/mL) leads to a reduced incidence of many extra-musculoskeletal disorders, including diabetes [19-21], osteoporosis [22,23], multiple sclerosis [24], rheumatoid arthritis [25], and certain types of cancer [26-28].

Conclusion

To maintenance of adequate serum 25(OH)D concentrations is necessary to generate its active hormone, $1,25(OH)_2D$ (calcitriol). In addition to renal tubular cells, activation of 25(OH)D is also occur in target tissue cells. The latter is an integral part of physiology to facilitate intended beneficial modulatory effects. These include enzymatic reactions, mitochondrial function, subduing inflammation and oxidative stress, immune protection, secretion of hormones, such as insulin and PTH, and modulating the renin–angiotensin–aldosterone and FGF23-Klotho hormone systems [29]. In addition, metabolomics and transcriptomics advances will enable generation of improved longer-term extra-skeletal outcomes with targeted vitamin D therapy.

Vitamin D metabolism and actions are influenced by many medications, environmental pollutants, and physical activities/lifestyles, ratio of body muscle mass to fat mass; collectively, these modulate the balance between energy intake and expenditure [30]. Thus, chronic insufficiency of vitamin D tend to increase body fat mass leading to obesity, further reducing the serum 25(OH)D concentration.

Cumulative evidence supports biological associations of vitamin D adequacy with a significant risk reduction of a variety of illnesses and improved physical and mental well-being [31], and reduce all-cause mortality [32,33]. In this regard, CYP27B1-mediated target tissue production of 1,25(OH)D was neglected till recently but physiologically, is critically important. The latter function is essential for the defense against invading pathogens [34], subduing autoimmunity [35], and paracrine and autocrine functions of calcitriol are essential for full biological activity of vitamin D and optimum health.

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