Review Article

Preventive Aspects of Vitamin D and Health: an Overview

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Abstract

Bioactive vitamin D or calcitriol is a steroid hormone that has long been known for its role in regulating body levels of calcium and phosphorus, and in mineralization of bone. Research also suggests that vitamin D is important for muscle strength and performance, stimulates the immune system, helps to treat infection and protects against autoimmune diseases and more than a dozen type of cancer, including prostate, breast and colon cancer. The relevance of the frequently low vitamin D status is not completely clear. There is growing evidence for the contribution of a circulating 25(OH)D level below 50 nmol/l to the development of various chronic diseases.

Key words: Vitamin D, Preventive Medicine, Chronic Disease

Introduction

Vitamin D was discovered by McCollum and Davis in the year 1913. The role of vitamin D is very well documented in regulation of musculoskeletal health and health-related homeostatic process. [1] Recently in the last decade role of vitamin D has in different clinical conditions has attracted many researchers. Giving its role into pathogenesis of several chronic diseases, including diabetes, hypertension, autoimmune disease's, cancer, obesity.

Vitamin D deficiency is a major public health problem across the world in every country to pandemic proportions [2]. Vitamin D deficiency is highly prevalent in India in all age group, whether school going children [3] or pregnant and postmenopausal women [4] and even in apparently healthy middle-aged healthcare professionals. [5]

Vitamin D Metabolism and Mechanism of Action

As discussed by Lin and Lane [6] vitamin D_3, (cholecalciferol) is generated in the skin of animals when light energy is absorbed by a precursor molecule 7-dehydrocholesterol after exposure to u. v. B rays. Then it is transported to the liver where it is converted to 25-hydoxyvitamin D [25(OH)D] and, rapidly released into the blood and reaches the kidney and enzymatically converted to the vitamin D hormone 1, 25-dihydroxyvitamin D (calcitriol) by the activity of 1-alpha-hydroxylase, which is tightly regulated and induced by parathyroid hormone, which is regulated by serum concentration of Ca and P. Bouillon et al pointed out that biological potency of 1, 25-dihydroxycholecalciferol is several times higher than that for 25-hydroxycholecalciferol [7]. Calcitriol can be locally produced in more than thirty tissues, which are having a cytosolic vitamin D receptors so a paracrine role has been proposed to it [8].

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Association of Low Vitamin D Status with Chronic Diseases

Osteomyopathy

Vitamin D deficiency can result in rickets and osteomalacia in childhood and adulthood, respectively, which is due to failure or delayed mineralization of newly formed osteoid at sites of bone turnover or periosteal or endosteal apposition due to the marked suppression in intestinal Ca absorption. [9] Vitamin D deficiency is associated with osteoporosis of the elderly bone.

Low vitamin D status is associated with poorer muscle function and increased hip fracture prevalence [10]. Osteomalacia patients suffer from muscular weakness skeletal as well as cardiac muscle both [11, 12].

Orthostatic Hypotension (OH)

The association between vitamin D deficiency and OH could be due to a number of factors involved in the pathogenesis of OH. There is decreased sensitivity of baroreceptor in aorta and carotid artery leading to hypotension due to age-related increase in arterial stiffness and vascular calcification leading to increase in thickness of carotid intima and media. [13] Maximum carotid plaque thickness and vascular calcification found in those patients with 25(OH) vitamin D deficiency has been demonstrated in the study [14].

Infections

Searching the English literature, very few studies are there which, are correlating infectious diseases to vitamin D status. Lawson et al demonstrated the acute respiratory infections were more common in infants with nutritional rickets as compared to the control group [15].

Recently a double blinded, randomized controlled clinical trial suggested supplementation with high doses of vitamin D accelerates radiographic improvement in all TB patients and increased host immune activation favouring a therapeutic role for vitamin D in the treatment of TB [16]. Calcitriol activates enzyme 1α-hydroxylase activated macrophages leading to a marked increase of cytotoxic activity of macrophages and thereby enhancing the rate of phagocytosis [17].

Diabetes Mellitus

A meta-analysis of prospective studies from various populations was undertaken to quantify the association between circulating 25(OH)D levels and subsequent risk of type 2 diabetes.

A total of 21 independent prospective studies (extracting from 15 articles) were included in the meta analysis and an inverse and significant relation between 25(OH)D and type 2 diabetes in a dose-response manner in diverse population was seen moreover, baseline 25(OH)D levels more than 50 nmol/l were significantly associated with a lower risk of type 2 diabetes. Study suggests a severe vitamin D deficiency probably results in low serum insulin levels indicating reduced insulin secretion. [9,18]

Inflammatory and Autoimmune Diseases

Calcitriol can inhibit the synthesis of mRNA of the leucocytes-derived cytokine's interleukin and tumour-necrosis factor, also decrease the expression of MHC-II molecules on the cell surface which are prime steps in autoimmune and inflammatory diseases [19].

Vitamin D deficiency is associated with periodontal disease, rheumatoid arthritis and psoriasis [9]. T here is growing epidemiological evidence to suggest a role for vitamin D deficiency in the development as well as severity of inflammatory bowel diseases [9,20,21].

Also experimental studies showed that diets high in Ca and calcitriol can completely suppress the induction of autoimmune encephalomyelitis, which is the main pathology of multiple sclerosis [9,22]. McAllindon et al suggested that the risk of osteoarthritis is high when a serum 25(OH)D level is below 85 nmol/l and oral intake of vitamin D is below 9·7 µg/d [23].

Pulmonary Hypertension (PHT)

Vitamin D deficiency activates the rennin-angiotensin-aldosterone system (RAAS) which affects cardiovascular system. Activation of RAAS is associated with PHT. This could suggest a possible relation between vitamin D deficiency and PHT. Pulmonary vascular alteration result in sustained elevated pulmonary vascular resistance and pulmonary remodeling by RAAS are main pathogenetic mechanism of PHT. Demir et al suggests that hyperparathyroidism secondary to vitamin D deficiency may a play role in higher pulmonary arterial presuure and there might be an association between PHT and vitamin D deficiency [24].

Cardiovascular Diseases

A meta-analysis of eighteen randomized controlled trials in which high-dose vitamin D supplementation was evaluated suggests that daily intake of more than 500IU decreases all causes of mortality in part, by decreasing cardiovascular deaths [25]. Possible mechanism includes an activity of the intracellular adenylate cyclase in the sarcoplasmic reticulum is calcitriol-dependent and improvement of the activity of this enzyme may thus reduce free cellular Ca concentrations by decreasing calcium reuptake into sarcoplasmic reticulum [9,26].

Epidemiological investigations also brought forward evidence for an inverse association between myocardial infarction and plasma 25-hydroxyvitamin D levels. Decreased mean serum calcium and phosphorus and a significant increase in alkaline phosphatase level was noted in stroke patients. 25(OH)D deficiency was more prevalent in stroke patients than controls, which was statistically significant[27].

Epidemiological studies have demonstrated a inverse association between serum 25(OH)D levels and diastolic blood pressure. A normalization of the enhanced

intracellular Ca levels seems to be an important measure in order to reduce blood pressure [9,28].

Obesity

It should be mentioned that cardiovascular diseases, hypertension, and diabetes mellitus is often associated with obesity. Obese subjects have relatively low circulating 25(OH)D levels due to the storage of vitamin D and 25(OH)D in adipose tissue so insufficient circulating level. The alterations in vitamin D metabolism of obese subjects in comparison with lean subjects are also associated with functional alterations such as elevated PTH levels [29,30].

Cancer

There is evidence that enhanced sunlight exposure is associated with lower prostate, breast and colon cancer incidence. In some studies inverse associations for vitamin D intake and colon or colorectal, breast, and prostate cancer were found [9,31,32]. Although changes leading to cancer cell generation can occur quickly, but most cancers develop over decades making it difficult to perform reliable human intervention studies on the association between vitamin D and cancer risk [34].

Assessment of Vitamin D Status

Circulating 25(OH)D levels closely reflect the amount of sunlight to which the epidermis is exposed and the dietary intake of vitamin D, so there is general agreement that the serum 25(OH)D level is the best indicator to define vitamin D status [9,33]. Adequacy of vitamin D status is based on the minimum serum 25(OH)D level to normalize 1,25(OH)D, prevent secondary hyperparathyroidism, optimize intestinal calcium absorption and avoid bone histology abnormalities. Based on these criteria most epidemiologists define vitamin D deficiency, insufficiency, sufficiency, and toxicity [9,33]. While the normal ranges vary, it is difficult to define cut-off values for each stage. Everybody agrees that 25(OH)D levels below 12.5nmol/l can result in bone disease such as rickets in infants and osteomalacia in adults. There is however, also evidence that 25(OH)D levels below 25 nmol/l leads to rickets and osteomalacia in the long run so may represent Extreme Deficiency. Concentration of 25(OH)D below 50 nmol/l reflects Vitamin D Deficiency. Serum 25(OH)D concentrations between 50nmol/l and 80 nmol/l can be regarded as Vitamin D Insufficiency, where body stores are already depleted, and PTH levels can be slightly elevated, but are still in the normal range [9]. Circulating 25(OH)D levels between 100 and 200 nmol/l can be regarded as adequate concentrations, where vitamin D dependent body functions occur smoothly [9].

Prevention of Vitamin D Insufficiency

Reasons for a low vitamin D status are: (i) high indoor activities, (ii) the seasonal variation of sunlight, (iii) the ageing decreases vitamin D synthesis, (iv) the low vitamin D content of processed foods. Available modes of prevention are twofold: increased exposure to u.v. light or increased oral vitamin D intake. By increasing u. v. light exposure increased side effects like photo-ageing, cataract, keratoconjunctivitis and skin cancer may occur [34].

Adequate daily oral vitamin D intake is a easy and cost-effective measure to maintain a physiological vitamin D status. The adequate intake values are crude estimates in order to prevent vitamin D-dependent diseases such as rickets and osteomalacia since no recommended intake level for vitamin D exists. Vitamin D intakes of 5–20 μg/d alone in the absence of u. v. irradiation or sun exposure may be inadequate to significantly improve the amount of absorbed Ca. By increasing oral Ca and vitamin D intake can increase the amount of absorbed Ca so decreasing vitamin D associated chronic diseases [34].

Conclusions

An adequate serum 25(OH) D level above 50 nmol/l is necessary to prevent the development of various chronic diseases. Treatment with a high dose of vitamin D has been recommended for the management of vitamin D deficiency.

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