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ROLE OF CHOLECALCIFEROL (VIT-D) IN LIFE STYLE DISORDER & AUTOIMMUNE DISEASE

Anoop Kumar Singh[1], J. S. Tripathi[2] and K. H. H. V. S. S. Narasimha Murthy[3]
[1]Junior Resident, [2]Professor and In-charge and [3]Mentar & Assistant Professor Stage–III, Division of Manas Chikitsa (Psychosomatic medicine & Neuropsychiatry), Department of Kayachikitsa, Institute of Medical Sciences, Banaras Hindu University, Varanasi, E-mail: anoopimsbhu07@gmail.com, Corresponding Author: Anoop Kumar Singh

Abstract: *Vitamin D deficiency is a very common problem now days. Vitamin D is mostly made in the skin by exposure to sunlight. Most foods contain very little vitamin D naturally, though some are fortified (enriched) with added vitamin D. Vitamin D is important for good health, growth and strong bones. Some people are more at risk of deficiency, in particular pregnant women, breast-fed babies and people with black or Asian skin types. There is mounting evidence for beneficial roles for vitamin D in reducing the risk of diseases bone and fractures, many types of cancer, bacterial and viral infections, autoimmune diseases, and cardiovascular diseases. Recently, several reports have also been published regarding the role of vitamin D in neuroprotection. Vitamin D supplements can be used in these groups to prevent vitamin D deficiency.*

Key words: *Vitamin D, sunlight, bone disease, dementia, autoimmune disease, cordio vascular disease, cancer.*

Introduction: Vitamin D is taken for granted and is assumed to be plentiful in a healthy diet. Unfortunately, very few foods naturally contain vitamin D, and only a few foods are fortified with vitamin D. This is the reason why vitamin D deficiency has become epidemic for all age groups in the many countries. Vitamin D deficiency not only causes metabolic bone disease among children and adults but also may increase the risk of many common chronic diseases. The aim of this review is to provide a broad perspective on the evaluation, evolution, discovery, and many biological functions of vitamin D.

What is vitamin D?: Vitamin D is actually a hormone and not technically a vitamin: a vitamin is defined as a substance that is not made naturally by the body but must be supplied in the diet to maintain life processes. Vitamin D, however, is predominantly made by the action of ultraviolet light (sunlight) on 7-dehydrolcholesterol, the vitamin D precursor that is found in the skin. We only get very small amounts from our diet in vitamin D fortified foods. Ninety per cent or more of our vitamin D comes from the sun. A major cause of deficiency is insufficient sun exposure of the skin. Vitamin D is metabolized by the liver to 25-hydroxyvitamin D, which circulates in the blood until it is needed. Enzymes in the kidneys metabolize it further to form the highly active hormone that is involved in essential biochemical processes throughout the body.[1]

Vitamins are a group of chemicals that are needed by the body for good health. Vitamin D is a fat-soluble vitamin. The fact that it dissolves in fat is important, because it means the body can store it for future use. Unlike other vitamins, we do not need to get vitamin D from the food that we eat. This is a good thing because most foods contain very little vitamin D naturally. Foods that contain vitamin D include:[2]

- Oily fish (such as sardines, pilchards, herring, trout, tuna, salmon and mackerel).
- Liver of animals.
- Egg yolk.
- Mushrooms.
- Cheese, milk and butter (small amounts).
- Fortified foods (vitamin D added) such as margarine, some cereals, infant formula milk.

- Our main source of vitamin D is made by our own bodies. 90% of our vitamin D is made in the skin with the help of sunlight. [2]

UVB (ultraviolet B) sunlight rays convert cholesterol in the skin into vitamin D. Darker skins need more sun to get the same amount of vitamin D as fair-skinned persons. The sunlight needed has to fall directly on to bare skin (through a window is not enough). 2-3 exposures of sunlight per week in the summer months (April to September) are enough to achieve healthy vitamin D levels that last through the year.[2]

Chemical processes occur in the liver, and then the kidney, to produce calcitriol which is the active form of vitamin D. Calcitriol is a chemical that helps calcium and phosphorus to be absorbed from the gut. The calcium and phosphorus are essential for the structure and strength of our bones.[2]

So, vitamin D is really important for strong bones. In addition, vitamin D seems to be important for muscles and general health. Scientists have also found that vitamin D may help prevent other diseases such as cancer, diabetes, heart disease, depression, schizophrenia and some autoimmune diseases such as multiple sclerosis, rheumatoid arthritis etc.[2]

Factor that Alter the Production of Vitamin D

People with Limited Sunlight Exposure: People living at northern latitudes or who have limited sunlight exposure because of their working environment or cultural dress rules may have low vitamin D levels.[3]

Dark-skinned People: Higher melanin levels in the skin of dark-skinned people block the action of sunlight on vitamin D precursors in the skin, requiring much longer sunlight exposure to generate adequate circulating vitamin D compared to fair skinned people.[3]

Musculoskeletal Pain Sufferers: People with symptoms of hypothyroidism, non-specific musculoskeletal pain, chronic low back pain or fibromyalgia are frequently found to have low vitamin D levels and may show clinical improvement after supplementation.[3]

Overweight or Obese People: Vitamin D can be locked up in fat stores in obese people, who have been found to have lower levels of 25-hydroxyvitamin D and are at risk of deficiency.[3]

Breast-fed Infants and Children with Limited Sunlight Exposure: All children require adequate circulating vitamin D to prevent rickets. Dark-skinned children and those who spend much of the day in indoor daycare centers are at risk of deficiency. Breast-fed children often receive inadequate amounts of vitamin D, particularly when their mothers are deficient.[3]

The Elderly: Amounts of the vitamin D precursor in the skin decrease with age, therefore elderly people are particularly prone to deficiency. And living in rest homes or becoming home-bound can limit exposure to sunshine. Muscle weakness and osteoporosis associated with vitamin D deficiency make the elderly more susceptible to falling and fracture risk, and research indicates that vitamin D supplementation may decrease the risk of fractures.[3]

Malabsorption Disease: Intestinal malabsorption of dietary fats leads to vitamin D deficiency. This is further exacerbated in the presence of terminal ileal disease, which results in impaired enterohepatic circulation of vitamin D metabolites. In addition to intestinal diseases, accelerated inactivation of vitamin D metabolites can be seen with drugs that induce hepatic cytochrome P450 mixed function oxidases, such as barbiturates, phenytoin, and rifampin. Impaired 25-hydroxylation, associated with severe liver disease, is an infrequent cause of vitamin D deficiency.[4]

Renal Dysfunction: Patients with CKD have an exceptionally high rate of severe vitamin D deficiency that is further exacerbated by the reduced ability to convert 25-(OH)vitamin D into the active form, 1,25 dihydroxy-vitamin D. In patients with CKD [5,6-8], the new non-classical role of vitamin D also encompasses regulation of the reninangiotensin system (RAS) [9].

Liver Disease: Vitamin D deficiency is extremely common in chronic liver disease patients. Up to 93% of these patients have some degree of vitamin insufficiency [10,11]. Severe liver disease decreases vitamin D hydroxylation and albumin and vitamin D-binding protein (DBP) production, all of which are linked to low levels of 25(OH)D.[12]

Effect of Vitamin D Deficiency

1. Effect of Vitamin D Deficiency on Bone Health and Calcium and Phosphorus Metabolism: In a vitamin D-deficient state, the intestine typically absorbs 10-15% of dietary calcium. In a vitamin D-sufficient state, 30% typically is absorbed from the diet; as much as 60-80% can be absorbed during periods of growth and pregnancy or lactation, with increased demand for calcium [13]. Vitamin D deficiency, which causes secondary hyperparathyroidism, results in PTH-induced

loss of phosphorus into the urine and decreased intestinal phosphorus absorption. This results in low or low-normal fasting serum phosphorus concentrations. The lownormal serum phosphorus concentrations with low-normal serum calcium concentrations often result in an inadequate calcium-phosphate product, which is important for the mineralization process. This is what causes the mineralization defects that result in rickets among children and osteomalacia among adults.[14-15]

2. Vitamin D Deficiency Related Dementia: Dementia includes Alzheimer's disease (AD), vascular dementia (VaD), Lewy Body disease, and frontotemporal dementia [16]. Dementia is a significant disease among older residents of Western developed countries.[17] Dementia may involve several mechanisms, including oxidative stress [18], inflammation [19], small infarcts [20], transition metal and aluminum ions from diet leading to oxidative stress [21,22], nitric oxide production [23], reduced neurogenesis in the adult brain [24] and embolism [25]. Following Mechanisms whereby vitamin D metabolites protect the brain: (1) Ca2+ regulation, stimulation of neurotrophin release, interaction with reactive oxygen and nitrogen species, and neuroimmunomodulatory effects of calcitriol [26,27].Facilitates detoxification through inhibiting synthesis of inducible nitric oxide synthesis and increased glutathione levels[28-30]. (2) Reduces risk of thrombosis. [31] (3) 3-By increasing calcium absorption, may decrease transition metal (copper, iron, zinc) ion levels.[32] (4) 4-Enhances antioxidant pathways.[28]

3. Vitamin D deficiency related Cardiovascular Disease: Several mechanisms have been proposed on how vitamin D could be involved in blood pressure regulation and the pathophysiology of arterial hypertension, which is a major risk factor for stroke. Following Mechanisms whereby vitamin D metabolites protect the cordiovascular system: (1) Vitamin D supress the Renin angiotensin aldosteron system (RAAS)[33]. Vitamin D receptors (VDR) activation down-regulates renin expression.[33-34] (2) High PTH levels, which are a hallmark of vitamin D deficiency, may also increase blood pressure.[35,36] (3) Vitamin D have antiatherosclerotic properties and improvement of endothelial function [37]. (4) Renoprotective action including antiproteinuric and anti-inflamatory effect [38,39].

4. Vitamin D Deficiency Related Risk of Cancer: Both colon and breast cancer risks were higher for those living at higher latitudes in the United States [40,41]. A prospective study revealed that, if 25(OH)D concentrations were 50 nmol/L (20 ng/mL), then there was a 2-fold increased risk of developing colon cancer [40]. Men and women with more sun exposure were less likely to die prematurely as a result of cancer [42,43].

5. Vitamin D Deficiency Related Autoimmune Disease: There is also a latitudinal association with increased risk of developing multiple sclerosis [44,45]. People who were born below 35° N latitude and lived at or below that latitude for the first 10 years of their lives had decreased lifetime risks of developing multiple sclerosis, compared with those who were born above 35° N latitude [44,46]. There is compelling evidence that this is attributable to a decrease in UVB light exposure. One study suggested that the seasonal variation in multiple sclerosis was 50% less in the summer, compared with that in the winter [45,47].

Diagnostic Tests: Serum is obtained for calcium, albumin, phosphate, alkaline phosphatase, PTH, and 25[OH]D_3 determinations[48]. Bone densitometry helps document the degree of osteopenia. Radiographs may show diagnostic features [49]. In one series of biopsy-proved osteomalacia, alkaline phosphatase was elevated in 94% of patients; the calcium or phosphorus was low in 47% of patients; 25(OH)D_3 was low in 29% of patients; pseudofractures were seen in 18% of patients; and urinary calcium was low in 18% of patients. 1,25(OH)2D_3 may be low even when 25(OH)D_2 levels are normal[50].

Prevention and Management: Measurements of 25(OH)D, a wide consensus exists that 25(OH)D levels below 20 ng/ml (50 nmol/l) are insufficient and should thus be prevented and treated[47-54]. Considering that vitamin D treatment is mainly justified due to beneficial effects on bone health, it seems reasonable to use vitamin D doses ranging from 800 to 2000 IU per day, because these doses have been shown to significantly reduce fractures [55]. It has been shown that daily, weekly or monthly vitamin D dosing regimens can equally raise 25(OH)D levels; but not support the use of single doses exceeding approx 100,000 IU vitamin D[56,57]. The safe tolerable upper intake level for vitamin D is 4000 IU per day in adults [52,58]. Some individuals with morbid obesity or vitamin D absorption problems such as in inflammatory bowel disease may require higher dosages. For such specific patients with still insufficient 25(OH)D levels after supplementation with 4000

IU per day, doses up to 10,000 IU per day may be used.[53,59] . Vitamin D is frequently given in combination with calcium, it should be noted that concomitant calcium supplementation can reduce the compliance of vitamin D supplementation [60].

Conclusion: Vitamin D should be considered essential for overall health and well-being. Vitamin D deficiency and decreased exposure to solar UVB radiation have been demonstrated to increase the risks of many metabolic bone diseases among children and adults, common cancers, autoimmune disease like rheumatoid arthritis and multiple sclerosis, dementia, cardiovascular disease. So vitamin D has evolved into such an important and necessary hormone, which acts as an indicator of overall health and wellbeing. Vigilance in maintaining a normal vitamin D status, i.e. 25(OH)D concentrations of 75–125 nmol/L, should be a high priority. Surveillance for vitamin D deficiency, with measurement of 25(OH)D concentrations, should be part of normal yearly physical examinations.

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