Mini Review
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Non calcaemic & non osteogenic functions of vitamin d: a brief review

Abstract

Vitamin D insufficiency affects almost 50% of the population worldwide. This can mainly be attributed to lifestyle (for example, reduced outdoor activities, liberal use of sunscreen) and environmental (for example, air pollution) factors that reduce exposure to sunlight, which is vital for ultraviolet-B (UVB)-induced vitamin D production. Vitamin D deficiency is common in all age groups. High prevalence of vitamin D insufficiency is a particularly important public health issue as Hypovitaminosis-D is an independent risk factor for several non communicable & communicable diseases. Current studies suggest that we may need more vitamin D than presently recommended to prevent chronic disease like Diabetes & Hypertension. Present review focuses on the non-calcemic and non-osteogenic role of Vitamin D and how Vitamin D deficiency might be an important risk factor in increased disease incidence & prevalence.

Keywords: vitamin d, hypovitaminosis d, communicable disease, non communicable disease

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Introduction

Vitamin D was discovered in early 20th century while looking for a cure for rickets.[1] British doctor Edward Mellan[2] by noticed dogs that were fed cod liver oil did not develop rickets and concluded vitamin A, or a closely associated factor, could prevent the disease. In 1922, Elmer McCollum tested modified cod liver oil in which the vitamin A had been destroyed.[3] The modified oil cured the sick dogs, so McCollum concluded the factor in cod liver oil which cured rickets was distinct from vitamin A. He called it vitamin D because it was the fourth vitamin to be named.

Vitamin D refers to a group of fat-soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and multiple other biological effects. The major natural source of vitamin D is synthesis of cholecalciferol in the skin from cholesterol through a chemical reaction that is dependent on sun exposure (specifically UVB radiation). The 'sunshine vitamin' has always piqued the interest of scientists all over the world. This vitamin, which is a 'hormone' comes at no extra cost. We just have to expose our body to sunlight and our skin will generate the amount of Vitamin D that is needed for body. It's an irony that, even though Vitamin D comes at no cost.

Hypovitaminosis D is becoming a pandemic in paediatric & adult population in both developing & developed countries as well as in both children[4] and adults.[5] Vitamin D deficiency results in rickets and osteomalacia in children & adults respectively due to impaired bone mineralization and consequent bone damage. Recommendations for 25(OH)D serum levels vary across authorities, based on factors like age, gender, epidemiology etc.

Discussion

Vitamin D is known for long as a fat soluble vitamin which is involved in bone mineralization. But many tissues and cells in the body i.e., heart, stomach, pancreas, brain, skin, gonads, and activated T and B lymphocytes, have nuclear receptors for vitamin D (1,25(OH)2D) receptors.[6,7] Thus, it is not at all surprising that Vitamin D might have multiple biologic effects that are non-calcemic & non-osteogenic in nature. The increased incidence and risk of vitamin D deficiency, has motivated researchers & scientists to further evaluate intake requirements and this vitamin's role in preventing several other chronic diseases that might be affected or aggravated due to deficiency of the same.

Role of vitamin D in non communicable diseases

Diabetes mellitus

Type I diabetes mellitus: Several studies have proved that Vitamin D has important role in regulation of Insulin dependent diabetes mellitus (IDDM). When non-obese diabetic mice, who typically develop type 1 diabetes, received 1,25(OH)2D throughout their life, their risk of developing type 1 diabetes was reduced by 80% as studied by Gregori S et al.[8] and Mathieu C et al.[9] Recent observation by Hypponen et al.[10] that children receiving 2000 IU vitamin D from age 1year onwards tend to decrease their risk of getting type 1 diabetes by 80% which proves the importance & role of Vitamin D in Type I Diabetes.

Type II diabetes mellitus: Randomized trials of vitamin D supplementation and risk of type 2 diabetes didn't have consistent results. Studies of vitamin D supplementation with 4000 IU/d or 120000 IU every 2weeks in South Asian overweight women and obese men, respectively resulted in significant improvement of insulin sensitivity, compared with placebo.[11] Whereas, another study on overweight adults in Germany found no relationship between vitamin D supplementation (3300 IU/d) with glucose metabolism during weight loss.[12] So the picture remains unclear about the definitive role of Vitamin D in Non-insulin dependent Diabetes Mellitus (NIDDM).[13] Although the observational evidence might be suggestive of increased risks associated with low levels of serum 25-hydroxyvitamin D but that can also be due to behavioral or environmental effect.

Hypertension

Research shows that there is a link between vitamin D and hypertension. One researcher[14] found that by increasing 10ng/ml of Vitamin D levels, risk of developing hypertension lowers by 12%. People having highest Vitamin D levels were at 30% lower risk. Other researchers[15,16] in their studies have shown that increasing Vitamin D supplementation has resulted in lowering the blood pressure. Though the role of Vitamin D is found to be controversial in increased blood pressure but, it is proved that adequate Vitamin D lowers the risk of developing hypertension. Supplementing Vitamin D in hypertension may help in better blood pressure control.

Cancer

Vitamin D can effectively manipulate cell growth and maintain it in a normal proliferative state under most circumstances. Numerous epidemiologic studies have shown that higher intake or blood levels of vitamin D are associated with a reduced risk of colorectal cancer.[17] An inverse association between cancer mortality rates and regional solar UV-B radiation exposure has been found for cancers of the breast, colon, rectum, ovary, prostate, stomach, bladder, esophagus, kidney, lung, gallbladder, thyroid, rectum, pancreas, and uterus, as well as non- Hodgkin's lymphoma and multiple myeloma as shown by various researchers.[18–20]

Cardiovascular diseases

It was hypothesized way back in 1980's that sunlight exposure by increasing vitamin D levels, decreases the risk of cardiovascular diseases. 53% more incidence of myocardial infarctions were detected in winter than in summer as observed by Spencer PA et al.[21] Recent cohort studies done by multiple researchers[22–24] have also found that low vitamin D levels increase the risk of cardiovascular diseases.

Role of vitamin D in communicable diseases

Optimal Functioning of the Immune System is not complete without adequate amount of Vitamin D. Calcitriol (1,25(OH)2D) is a hormone that regulates both adaptive and innate immunity which in turn regulates the occurrence & severity of communicable diseases (Table 1).

Table 1 Summary reports by several researchers on role of Vitamin D

Researcher/s or Author/s	Effect of vitamin D	Physiological consequence/target	Disease/micro organism studied
Lucas et al.[25]	Stimulation of Toll like receptors, TGFβ , IFNγ, Synthesis of cathelicidin	Stimulates autophagy and the synthesis of antimicrobials, for bacterial killing.	Mycobacterium tuberculosis
Adams JS et al.[26]	Increased expression of both CP27B and VDR, and demonstrated autocrine induction of cathelicidin and bacterial killing in response to Vitamin D	Vitamin D and innate immunity are related	M. Tuberculosis
Liu PT et al.[27]	Activation of Toll-like receptors (TLRs)	Induction of the antimicrobial peptide cathelicidin and killing of intracellular Mycobacterium tuberculosis.	Tuberculosis
Aaranow C[28]	Suppresses T cell proliferation, inhibits monocyte production of inflammatory cytokines such as IL-1, IL-6, IL-8, IL-12 and TNFα	Important in the context of autoimmunity and the abrogation of self-tolerance	Respiratory tract infection, Influenza, Bacterial vaginosis
Snyman et al.[29]	Positive effects on levels of activated eosinophils and Schistosoma-specific antibodies	Significant increases in circulating lymphocytes, enhanced production of IgE, IgG & eosinophil vacuolization	Influenza

Vitamin D helps in activation of necessary intermediates which controls the killing & neutralization of micro-organisms. Vitamin D has been found to inhibit the adaptive immune system by suppressing immunoglobulin production and proliferation, and retarding the differentiation of B-cell precursors into plasma cells & T cell (Helper cells) in several studies.[30,31] By suppressing the adaptive immune response Vitamin D may account for the beneficial effect on various autoimmune disorders. This beneficial effect has also been studied on various experimental animals.[32] Thus the non-osteogenic & non calcemic function of Vitamin D is helpful in prevention as well as easier cure of infective/communicable diseases.

Functional implication

Various Scientists have proved that vitamin D is much more than just a nutrient needed for bone health. It is also an essential hormone required for regulation of a large number of physiologic functions other than bone health. It is clear that adequate levels of serum 25(OH)

2D are essential for optimizing human health. Adequate vitamin D is important in regulation of diabetes Mellitus (Both type I & II) & lowers the risk of developing hypertension. Optimum levels of the vitamin reduces the risk of various cancers (colorectal, breast, colon, rectum, ovary, prostate, stomach, bladder, esophagus, kidney, lung, gallbladder, thyroid, rectum, pancreas, and uterus).

Conclusion

Vitamin D is a multifaceted hormone which has multiple non-calcemic & non-osteogenic actions as well. Several studies as listed in Table 1 and many such studies will help the researchers as well as physicians to recapitulate the advancement in the field so that it helps to design future strategies to overcome multiple issues related to vitamin D deficiency in communicable and non-communicable disease. We need to assess more diseases and their correlation with vitamin D level needs to be optimized in relation to age, gender & ethnicity to confirm its impact on the larger community as a whole. As scientists continue to solve the mysteries related to vitamin D function and provide approaches for optimizing vitamin D status; it's time for us to stop shunning sun & enjoy the vital & essential sunshine as much as we can.

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Conflict of interest

Author declares that there is no conflict of interest.

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