ROLE OF VITAMIN D IN PREVENTION OF CHRONIC DISEASES

Sofia Khanam

Department of Pharmacology, Calcutta Institute of Pharmaceutical Technology and Allied Health Science, Uluberia, Howrah-711316, West Bengal, India

ABSTRACT

Vitamin D is one of the essential nutrients to sustain the human health. Vitamin D functions in the body through both an endocrine mechanism (regulation of calcium absorption) and an autocrine mechanism (facilitation of gene expression). The role of Vitamin D deficiency in increasing the risk factor of many common and serious chronic diseases, including cancers, type 1 diabetes, cardiovascular disease and osteoporosis. Numerous epidemiologic studies suggest that exposure to sunlight, which enhances the production of Vitamin D₃ in the skin, is important in preventing many chronic diseases. 25(OH)D (25-hydroxyvitamin D) is the metabolite that should be measured in the blood to determine Vitamin D status. 25(OH)D deficiency is prevalent in infants who are solely breastfed and who do not receive Vitamin D₃ supplementation and in adults of all ages who have increased skin pigmentation or who always wear sun protection or limit their outdoor activities. It is therefore necessary to know the adverse health effects of 25(OH)D deficiency and to design intervention and early treatments for those who are likely to have low levels of 25(OH)D.

VITAMIN D: OVERVIEW

Vitamin D, a fat-soluble vitamin, is now recognized as a prohormone because the body can synthesize vitamin D from its precursor (7-dehydrocholesterol) when exposed to ultraviolet light at a wavelength between 290-315 nm. Adequate circulating 25-hydroxy vitamin D concentrations need to be maintained for functioning of the metabolic, immune, reproductive, muscular, skeletal, respiratory and cutaneous systems of men and women of all ages.

There are two main forms of Vitamin D, Vitamin D₃ (cholecalciferol) and Vitamin D₂ (ergocalciferol). Following the absorption from the intestines or/and the synthesis by skin, Vitamin D is transferred to the liver where it is metabolically converted into 25(OH)D in the liver, 25 (OH)D has a further metabolic conversion in the kidney. The active metabolites 1, 25 (OH) 2D₃ and 24R (OH) D can be converted by 25 (OH) 1 α -hydroxy-D (CYP27B1) or 24R hydroxylase (CYP24A1 or CYP24) in the kidney, respectively.

RELATIONSHIP BETWEEN 25OHD DEFICIENCY AND A VARIETY OF CHRONIC DISEASES

In recent years, accumulating epidemiological and laboratory evidence has documented that 25OHD deficiency is correlated to the onset and progression of many chronic diseases.

Vitamin D and cancer

Vitamin D binding protein (VDBP) as a carrier of Vitamin D can be combined with Vitamin D and its metabolites to play a crucial role in transport to the cell. Deficiency in VDBP also affects the function of Vitamin D. For example, studies have demonstrated that low level of VDBP is related to a variety of malignant tumors, including breast, prostate and colorectal. Both prospective and retrospective epidemiologic studies indicate that levels of 25OHD below 20 ng/ml are associated with a 30 to 50% increased risk of incident colon, prostate, and breast cancer, along with higher mortality from these cancers. The report that postmenopausal women who increased their vitamin D intake by 1100 IU of vitamin D₃ reduced their relative risk of cancer by 60 to 77% is a compelling reason to be vitamin D sufficient. Similarly, a recent study observed that 25 (OH) D progressively decline during the course of the development of liver fibrosis, cirrhosis to liver cancer.

Vitamin D and cardiovascular diseases

The pathogenesis of chronic cardiovascular disease is affected by a variety of risk factors. Clinical studies found that in addition to high cholesterol, smoking, obesity, high blood pressure and diabetes, low serum levels of 25OHD are also closely related to the occurrence of cardiovascular diseases. In addition, hypertension incidence may be related to low levels 25OHD. The role of vitamin D in the cardiovascular system is noticeable since the presence of its receptors not only the heart but also in the entire cardiovascular system. The 1, 25(OH)2D₃ active form of Vitamin D combines with VDR and then regulates the expression of many genes. Vitamin D metabolites act on multiple domains of cardiovascular function including those related to inflammation, thrombosis and the renin angiotensin aldosterone system (RAAS) pathways. Vitamin D has well known effects in endothelial cells, where it stimulates nitric oxide (NO) production, protects against oxidative stress and prevent endothelial apoptosis by diverse genomic and non genomic pathways. As endothelial function has emerged as a key factor for initiation and progression of atherosclerotic process, vitamin D may contribute for reversing atherosclerosis burden. A broad series of in vitro studies have also suggested that vitamin D and its analogs consistently suppress pro-inflammatory cytokines and increases anti-inflammatory cytokines, which mechanisms involved seem to be related to the inhibition of NF- κ B and p38 pathways by VDRs.

Vitamin D and diabetes

25OHD deficiency has been shown to be related to the development of diabetes. Recent studies have shown that 25 (OH) D levels are negatively correlated to prevalence of diabetes mellitus type 2(T2DM), islet beta cell function, insulin resistance, body fat, and BMI levels. Conversely, 25(OH)D levels were positively correlated with insulin sensitivity. 25OHD deficient individuals have a higher insulin resistance and type 2 diabetes risk. 1, 25 (OH) 2 D₃ can be combined with Vitamin D₃ receptor on the islet β cells, increasing insulin sensitivity, inhibiting inflammatory factors, alleviating chronic inflammation process of the pancreas to improve the function of islet β cells; Additionally, it also inhibits the action of the renin-angiotensin system, which promotes insulin secretion. Vitamin D supplementation can improve islet β cell function and glucose tolerance.

Vitamin D and immune system diseases

Vitamin D can play a role in regulating immune function, inhibiting inflammatory reactions and autoimmune diseases. 1, 25(OH) 2D₃ combined with Vitamin D receptor plays an important role in immune cell biology. Many immune cells in the human body such as monocytes, macrophages, dendritic cells, T cells, and B cells express VDR. Vitamin D₃ in combination with VDR in T cells can inhibit the activity of Th1 cells, thereby reducing the CD4 + T cells to release IL-2, interferon γ and tumor necrosis factor (TNF) α , β , and to delay the progress of chronic inflammatory autoimmune diseases. In addition, it can promote the differentiation of mononuclear cells into macrophages, and strengthen their chemokine production and ability to control infection. It also inhibits the major histocompatibility complex II (MHC II) expression on antigen-presenting cells to prevent the activation of immune system. Vitamin D also induces B cell proliferation and the secretion of immunoglobulins E and M, leading to the formation of memory B cells and B cell apoptosis promotion. These results have demonstrated that 1, 25- (OH)2D₃ has an important role in the anti-inflammatory response and immune regulation.

CRITERIA FOR VITAMIN D LEVELS

Although there are different methods and criteria on defining Vitamin D levels, the criteria Holick proposed has been widely accepted. In this proposal, it is suggested as Vitamin D deficiency if the level of 25 (OH) D in circulating blood in human is less than or equal to 20 ng/ml (50 nmol/L), insufficiency if between 21 to 29 ng/ml and sufficiency if greater than or equal to 30 ng/ml. 25OHD level is also generally low in infants, children and women in menopause. The proportions of deficiency and insufficiency among these populations vary between 30% to 80%, and even teenagers in the sunny plateau area. Recent study observed that population in sunny plate area still have an incidence of 25OHD deficiency between 23%-44%. There is a low 25OHD level in the populations from developing countries even in sunny climates, suggesting that the 25OHD deficiency is not only due to the lack of sunshine.

CONCLUSION

25OHD deficiency predominately affects the occurrence and development of many chronic diseases. With an aging population, the numbers of patients with osteoporosis, cardiovascular diseases, cancers, diabetes and other chronic diseases dramatically increasing year by year. These outcomes result in the loss of life of the population, reduced quality of life and significant social and economic burdens. Since these chronic diseases lack specific treatment or the treatment effects are not curative, strategies for the control of chronic diseases should focus on the prevention. Vitamin D deficiency is associated with chronic disease. Hence, it is challenging to clarify whether vitamin D deficiency is the cause or only the consequence of various chronic disease.

REFERENCE

- Wang H, Chen W, Zhang H, Yin X, Olsen N, Zheng SG, et al. Vitamin D and Chronic disease: Review. Aging and Disease. 2017 June;8(3):346-53.
- Tiwari P, Sharma S. Role of vitamin D in various illness: A Review. Journal of Pharmaceutical care and health system. 2017;4(3):176-9.
- Heaney RP. Vitamin D in health and disease. Moving points in nephrology. Creighton University, Omaha, Nebraska. 2008: 1535-41.