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Increasing Indications of Treatment with Vitamin D, The Magic Hormone of Present Time

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Vitamin D

Vitamin D is known as sunshine vitamin. Vitamin D exists as two forms - Vitamin D3 and Vitamin D2. Vitamin D3 or cholecalciferol is an inactive form which is synthesized from the skin on exposure to UVB radiation. Vitamin D2 or ergocalciferol is synthesized from plants. Fatty fishes, such as salmon, tuna, and mackerel, as well as beef, liver, and eggs comprise the primary dietary sources of Vitamin D3. The previous literature shows that Vitamin D is indeed a hormone not a nutrient. The body synthesizes Vitamin D after sun exposure, and it is activated by liver and kidneys. During exposure to sunlight, 7-dehydrocholesterol in the epidermis and dermis absorb ultraviolet B radiation resulting in the production of pro vitamin D3.

Pro vitamin D3 is rapidly converted by thermally induced rearrangement of the double bonds to form vitamin D3. Vitamin D3 enters the circulation and is bound to the vitamin D binding protein. It enters the liver where it is converted to 25-hydroxyvitamin D3 [25(OH) D3] Both vitamin D2 and vitamin D3 are converted to their respective 25-hydroxymetabolites, and are known collectively as total 25-hydroxyvitamin D [25(OH) D]. 25(OH) D is the major circulating form of vitamin D that is measured by clinical laboratories to determine a patient's vitamin D status. 25(OH)D is biologically inactive and is transported on the vitamin D binding protein to the kidneys where it is converted to 1,25-dihydroxyvitamin D [1,25(OH)2D] which is considered to be the biologically active form of vitamin D. It is responsible for regulating serum calcium and phosphorous and is essential for bone metabolism by enhancing intestinal calcium absorption and mobilizing calcium from the skeleton [1]. Researchers consider 1_,25(OH)2D3 to be steroid hormone and believe that it functions the same way as other steroid hormones by interacting with its cognate vitamin D receptor (VDR) [2].

Vitamin D receptor (VDR) is present in most tissues and cells in the body.1,25(OH)2D has a wide range of biological actions, such as inhibition of cellular proliferation and inducing terminal differentiation, inhibiting angiogenesis, stimulating insulin pro duction, and inhibiting renin production [3]. Dermal synthesis of vitamin D3 decreases with increasing latitude, increasing age, use of sunscreen, and darker skin pigmentation. Dark skinned populations in temperate climates have been found to demonstrate low levels of vitamin D3. Fair-skinned individuals need approximately 6 to 7 minutes of direct sunlight daily to the face, arms, and hands during summer months and up to 30 minutes in the winter. Darker-skinned individuals require 3-6 times longer exposure than white skinned individuals. This is because of melanin pigment in dark skinned individual doesn't absorb as much UV radiation [4].

Vitamin D and Skin

Vitamin D is widely used in dermatology for various skin disorders like psoriasis, urticaria, vitiligo and alopecia. The skin is the unique organ that is able to synthesize Vitamin D by exposure to UV rays. Vitamin D receptors present in the skin also help in prevention of skin cancer. Vitamin D also improves the immunity of skin and act as a physical barrier. The keratinocytes are the cells expressed in vitamin D receptor (VDR). The biologically active form of vitaminD3 or calcitriol plays a role in keratinocyte regulation by inducing differentiation and limiting keratinocyte proliferation. In psoriasis, keratinocyte proliferation occurs in a very high rate. The current therapy of vitamin D3 aims in controlling keratinocyte proliferation [5].

VDR is found in almost every cell in the immune system, including monocyte, macrophage lymphocyte, mast cell, natural killer cell, and dendritic cell. Aside from having VDR, those cells also have CYP27B1 enzyme activity and therefore are able to synthesize and secrete calcitriol. In natural immunity, Calcitriol stimulates antigen presenting cell (APC) to produce anti-microbial peptides cathelicidin and defensin and increases phagocytic capacity of APC. Calcitriol maintains mast cell stability and reduces histamine production. This action is helpful in treatment of urticaria. In adaptive immunity, CYP27B1 enzyme activity increases when T and B lymphocytes are activated. Calcitriol inhibits adaptive immune system by limiting proliferation and differentiation of B lymphocyte to plasma cell. Calcitriol inhibits proliferation and function of T helper-1 and T helper-17.

Calcitriol's effect in suppressing adaptive immune system is beneficial for several conditions such as autoimmune diseases [6]. In 2013, Danilo et al. conducted an open-label study in sixteen vitiligo patients aged 18 years old and above in Sao Paulo Brazil. In this study, 35,000 IU oral vitamin D3 was administered daily for six months and demonstrated satisfactory result. This study found 32% patients had up to 75% repigmentation, 32% had 50% repigmentation, and the remaining number had up to 25% repigmentation [7] The studies have shown that mutation occurring in VDR both in human and in mice resulted in alopecia [8]. Alopecia aerata is an autoimmune disorder where the vitamin D3 has a role in etio-pathogenesis and oral supplementation of vitamin D3 had shown an improvement of outcome [9].

Vitamin D in Obesity, Diabetes Mellitus, & CKD

As VDRs in pancreatic β-cells play an important role in the progression of type 2 DM Vitamin D deficiency is related to insulin secretion, insulin resistance, and β-cell dysfunction in the pancreas. The secretion of pancreatic insulin is inhibited by vitamin D deficiency in the diabetic animal model. Insulin sensitivity is also associated with vitamin D. By stimulating the expression of insulin receptors, vitamin D regulates insulin sensitivity [10]. Low serum levels of 25(OH)D have been linked through observational studies to the patho-physiology of Obesity, Diabetes Mellitus, and Metabolic Syndrome. A number of mechanisms are explained. First, the VDR is highly expressed in adipocytes and is responsive to activation by 1,25-(OH)2D Second, vitamin D is fat soluble and can be stored in adipose tissues, Third, large cohort studies have shown that an increased percentage of body fat and high body mass index (BMI) are strongly and inversely correlated with serum 25(OH)D concentrations, particularly in Caucasians. Fourth, in rodent models, vitamin D modulates insulin synthesis and secretion. Importantly, 1,25-(OH)2D regulates calcium trafficking in _-cells in vitro and in mouse models. (3) In a randomized controlled trial Vitamin D was supplemented the diets of non-diabetic overweight South Asian women with 4000 IU/d for 6 months and found a significant improvement in insulin sensitivity compared with a placebo group [11].

Vitamin D deficiency has been linked with the renin-angiotensin system and inflammation, which may be associated with the cause and progression of CKD. According to the Kidney Disease Improving Global Outcomes guidelines, 25(OH)D levels should be determined in patients with CKD stage 3-5, and if levels are low, physicians should consider vitamin D supplementation. Low 25(OH)D levels are associated with all-cause mortality and cardiovascular disease in patients with CKD as well as in patients undergoing dialysis [12].

Vitamin D and CAD

Accumulating evidence suggests that altered vitamin D homeostasis may also contribute to an increased cardiovascular disease risk in obese subjects. The major observation involves the association between low 25-hydroxyvitamin D [25(OH)D;,43 nmol/L] and obesity [7]; 25(OH)D concentrations ,33–37.5 nmol/L are independently related to a higher risk of myocardial infarction, cardiovascular mortality, and all-cause mortality than are 25(OH)D concentrations of 71–75 nmol [13,14]. In addition, low 25(OH)D concentrations are predictive of elevated concentrations of parathyroid hormone (PTH) (another biochemical variable that is related to cardiovascular disease [15]. The previous RCT shows that vitamin D supplement of 83 mg/d does not adversely affect weight loss and is able to significantly improve several cardiovascular disease risk markers in overweight subjects.

Vitamin D and Cancer

In recent years it has been recognized that calcitriol exerts anti-proliferative and prodifferentiating effects in many malignant cells and retards the development and growth of tumours in animal models raising the possibility of its use as an anticancer agent [16]. Epidemiological studies that identified beneficial associations of serum 25(0H) D with incidence and case-fatality rates of breast and colon cancer are supported by confirmatory laboratory results from studies that have investigated the biological mechanisms accounting for the action of vitamin D and its metabolites in prevention of malignancy. For example, oral administration of Vitamin D3 substantially reduced incidence of colon cancer in rats fed with high-fat diets [17]. Another study found that administration of either UVB irradiance or the raising of vitamin D metabolites with oral supplementation blocked growth of mammary cancer in mice inoculated with cancer xenografts that express vitamin D receptor (VDR) [18].

Vitamin D and Dementia

Recent systematic reviews and meta-analyses from cross-sectional analyses suggest that low serum vitamin D concentrations may be associated with Alzheimer's disease and other forms of dementia and cognitive impairment [19,20] However, other systematic reviews could not find an association between cognitive function and 25(OH)D concentration [21]. A Norwegian trial of overweight subjects showed that those receiving a high dose of vitamin D (20,000 or 40,000 IU weekly) had a significant improvement in depressive symptom scale scores after 1 year versus those receiving placebo [22]. The result determines a correlation between vitamin D and the risk of depression.

Conclusion

To conclude, there is increasing evidence to show that there is an increase in indications of Vitamin D therapy. Vitamin D is the 'talk' of today and the drug of the future. Vitamin D is a wonder hormone which will increase human healing and also longevity.

References

1. Norman, Anthony W (2008) From vitamin D to hormone D: fundamentals of the vitamin D endocrine system essential for good health. The American journal of clinical nutrition 88(2): 491S-499S.

2. Feldman D, Pike JW, Glorieux FH (2005) eds. Vitamin D. San Diego, CA: Elsevier Academic Press, USA.

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3. Rosen CJ, Adams JS, Bikle DD, Black DM, Demay MB, et al. (2012) The nonskeletal effects of vitamin D: an Endocrine Society scientific statement. Endocr Rev 33(3): 456–492.
4. Gupta A, March L (2016) Treating osteoporosis. Aust Prescr 39(2): 40-46.
5. Perez A, Raab R, Chen T, Turner A, Holick M (1996) Safety and efficacy of oral calcitriol (1,25-dihydroxyvitamin D3) for the treatment of psoriasis. Br J Dermatol 134: 1070-1078.
6. Holick M (2010) Vitamin D and health: evolution, biologic functions, and recommended dietary intakes for vitamin D. In: Vitamin D: physiology, molecular biology, and clinical applications. Holick M, editor. 2nd ed. Boston: Humana Press,US: p.3-33.
7. Danilo C Finamor, Rita S, Luiz C, Neves, et al. (2017) A pilot study assessing the effect of prolonged administration of high daily doses of vitamin D on the clinical course of J Gen Proced Dermatol Venereol Indones 2(1): 18-23.
8. Luderer HF, Gori F, Demay MB (2011) Lymphoid enhancer-binding factor-1 (LEF1) interacts with the DNA-binding domain of the vitamin D receptor. J Biol Chem 286: 18444–18451.
9. Rehman F, Dogra N, Wani MA (2019) Serum Vitamin D levels and Alopecia areata- A hospital based case-control study from North-India. Int J Trichol 11: 49-57.
10. Nakashima A, Yokoyama K, Yokoo T, Urashima M (2016) Role of vitamin D in diabetes mellitus and chronic kidney disease. World J Diabetes 7(5): 89-100.
11. Von Hurst PR, Stonehouse W, Coad J (2010) Vitamin D supplementation reduces insulin resistance in South Asian women living in New Zealand who are insulin resistant and vitaminDdeficient-a randomised, placebo-controlled trial. Br J Nutr 103: 549–555.
12. Kidney Disease: Improving Global Outcomes (KDIGO) CKDMBD Work Group (2009) KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney IntSuppl (113): S1-130.
13. Giovannucci E, Liu Y, Hollis BW, Rimm EB (2008) 25-hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. Arch Intern Med 168: 1174–1180.
14. Dobnig H, Pilz S, Scharnagl H (2008) Independent association of low serum 25-hydroxyvitamin d and 1,25-dihydroxyvitamin d levels with all-cause and cardiovascular mortality. Arch Intern Med 168: 1340–1349.
15. Zittermann A (2006) Vitamin D and disease prevention with special reference to cardiovascular disease. Prog Biophys Mol Biol 92: 39–48.
16. Deeb KK, Trump DL, Johnson CS (2007) Vitamin D signalling pathways in cancer: potential for anticancer therapeutics. Nat Rev Cancer 7(9): 684–700.
17. Pence B, Buddingh F (1988) Inhibition of diet ary fat promoted colon carcinogenesis in rats by supplemental calcium or vitamin 0 3• Carcinog enesis. 9: 187-190.
18. Valrance ME, Brunet AH, Welsh (2007) Vitamin D receptor-dependent inhibition mammary tumor growth by EB1089 and ultraviolet radiation in vivo. Endocrinology 148: 4887-4894.
19. Balion C, Griffith LE, Strifler L, Henderson M, Patterson C, et al. (2012) Vitamin D, cognition, and dementia: a systematic review and meta-analysis. Neurology 79(13):1397–1405.
20. Annweiler C, Llewellyn DJ, Beauchet O (2013) Low serum vitamin D concentrations in Alzheimer's disease: a systematic review and meta-analysis. J Alzheimers Dis 33(3): 659–674.
21. Barnard K, Colon-Emeric C (2010) Extraskeletal effects of vitamin D in older adults: cardiovascular disease, mortality, mood, and cognition. Am J Geriatr Pharmacother 8(1): 4–33.
22. Jorde R, Sneve M, Figenschau Y, Svartberg J, Waterloo K (2008) Effects of vitamin D supplementation on symptoms of depression in overweight and obese subjects: Randomized double blind trial. J Intern Med 264: 599–609.

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