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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/16626
DOI URL: http://dx.doi.org/10.21474/IJAR01/16626

RESEARCH ARTICLE

REVIEW ARTICLE ON (3B,5Z,7E)-9,10-SECOCHOLESTA-5,7,10(19)-TRIEN-3-OL (CHOLECALCIFEROL)

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Manuscript Info

Manuscript History
Received: 05 February 2023
Final Accepted: 09 March 2023
Published: April 2023

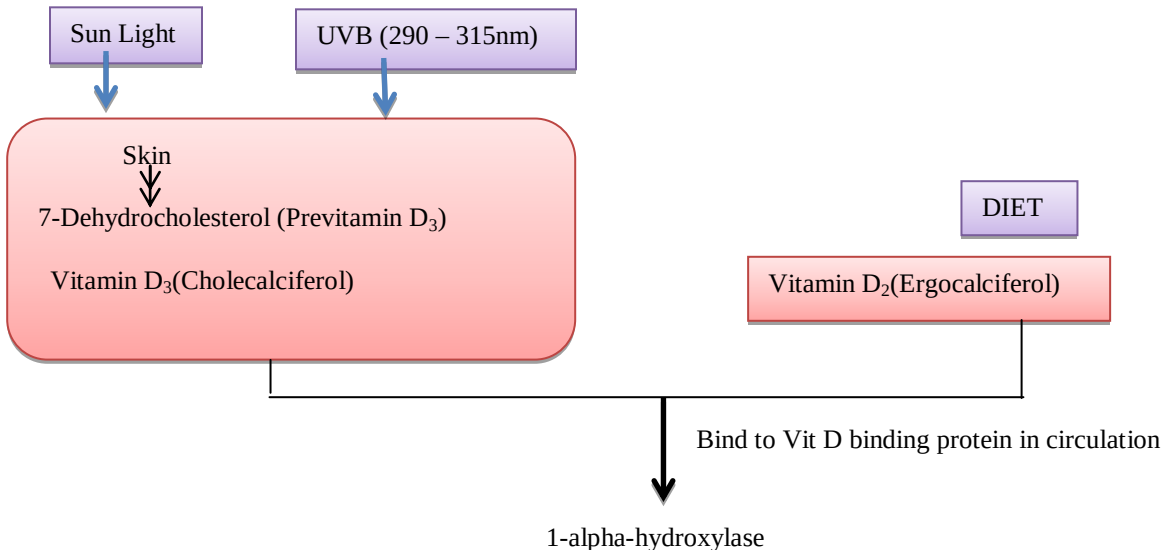
Key words:-
Vitamin D, Calcium, Osteoporosis, Osteomalacia, Cardiovascular System

Abstract

Vitamin D called as sunshine. There are varieties of sources available for cholecalciferol but mainly dairy, sea food and synthesized products are used. Calcitriol deficiency increased now days due to imbalanced life cycle and some desired and undesired effects of medications. We discuss about calcitriol life cycle from UV rays to immersion in the body as 7-Dehydrocholesterol to calcitriol. There are some parameters which effects on calcitriol absorption like age, skin color, disease, medications etc and discussed how to overcome calcium deficiency.

Introduction:-

Vitamin D is unique in that it is formed in the skin when exposed to sunlight[(1)].Vitamin D3 is synthesized in the skin by exposed to UV light with wavelengths between 290 and 315 nm, which stimulates the conversion of 7-dehydrocholesterol to previtamin D[(2)].This vitamin D sources varies by season, time of day, length of exposure, sunscreen use, skin pigmentation, and latitude [(3)(4)].Vitamin D from diet or skin synthesis is converted in the liver to 25-hydroxyvitamin D [25(OH)D], the major circulating form, and then in the kidney s to 1,25-dihydroxyvitamin D, which is converted into calcium, and optimize phosphate absorption. Hydroxylated from the gut, direct effect on bone cells[(5)(6)].



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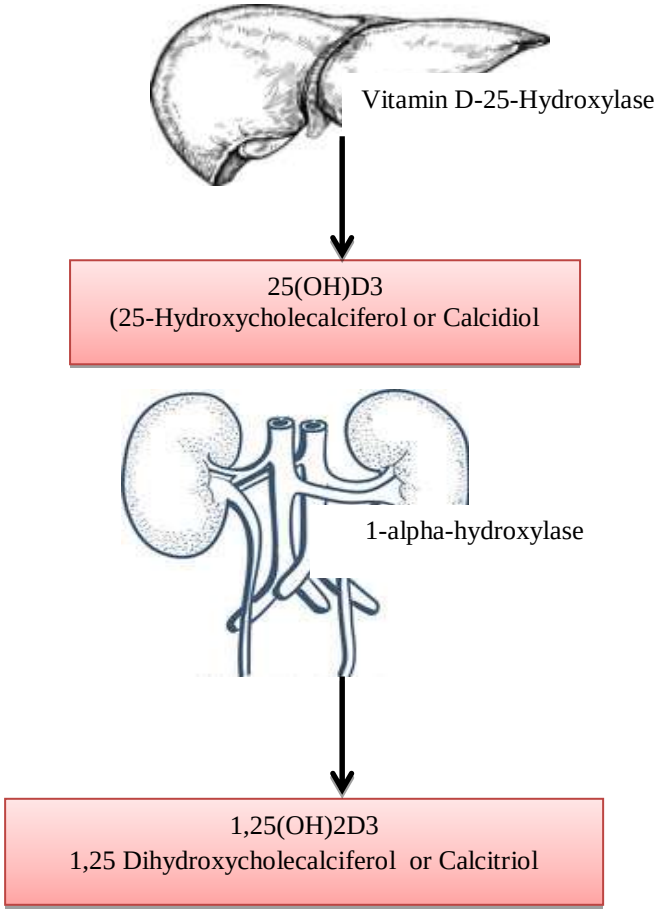

Very few foods contain vitamin D naturally; Meat from fatty fish (trout, salmon, tuna, mackerel, etc.) and cod liver oil are among the best sources [7,8]. An animal's diet affects the amounts of vitamin D in it tissues. Beef liver, egg yolks and cheese contain small amounts of vitamin D, mainly in the form of vitamin D3 and its metabolite 25(OH)D3. Mushrooms provide varying amounts of vitamin D2[9].Most authors consider vitamin D deficiency to be the range of serum/plasma 25(OH)D concentrations below 75 nmol/1 (or 30 ng/ml)[10,11].

Causes of cholecalciferol deficiency

The elderly

Elderly people are particularly at risk of developing vitamin D deficiency due to the reduced presence of 7-dehydrocholesterol in the skin, a precursor for UVB-mediated vitamin D synthesis. In addition, restrictions on movement and institutionalization that discourage sun exposure, reduced renal production of 1,25-dihydroxyvitamin D, and reduced intake of fortified foods pose significant challenges to vitamin D synthesis in the body, brings [12,13].

Dark skin

People with dark skin have great amounts of melanin in their epidermis. Melanin competes with 7-dehydrocholesterol for absorption of UVB photons. Therefore, people of color are less efficient in producing vitamin D than are whites. It is reported that a person with skin type 5/6 (dark skin) requires 10-50 times the exposure to sunlight to produce the same amount of vitamin D as does a white person with skin type 2/3[14].

Sunscreen users

Sunscreens can effectively absorb UVB radiation. This dramatically prevents UVB from interacting with 7-dehydrocholesterol, a process that produces previtamin D3. When used correctly, a sunscreen with a sun prection factor of 8 has been shown to reduce previtamin D3 production by 95%, and a sunscreen with a sun protection factor of 15 by as much as 99%[15,16].

Anticonvulsant use
Anticonvulsant, also called antiepileptic, has been used to treat epileptic seizures and bipolar disorder. It is well established that long-term use of some antiepileptic drugs, including phenobarbital, phenytoin, carbamazepine, and the antibiotic rifampicin (RIF), can lead to osteomalacia[17,18].

Chronic kidney disease
To become biologically active vitamin D, the kidneys play an important role in this conversion process. Chronic kidney disease, such as those with stage 4 to 5 chronic kidney disease or those requiring dialysis, are unable to produce enough 1,25-dihydroxyvitamin D, which has the effect of directly inhibiting parathyroid hormone expression[19,20].

Influence variety of disease due to level fluctuation
Clinical manifestation of vitamin D deficiency
Several studies have shown that low 25(OH)D levels are associated with other pathological disease (CVD)[21,22].Vitamin D is a fat-soluble prohormone steroid with endocrine, autocrine, and paracrine functions[23].

Nutritional rickets
A review of rickets cases published in the United States found most in children under 30 months [24].

Osteomalacia
Osteomalacia refers to the failure of organic osteoid formed by osteoblasts to mineralize with calcium and phosphorus. Although histological osteomalacia is characteristic of rickets, the term osteomalacia is commonly used to describe bone disease caused by vitamin D deficiency in adults whose bones are no longer growing. The clinical manifestations of these two conditions are different.

An x-ray may show a pseudofracture of the outer edge of the pelvis, femur, metatarsal, or scapula. The biochemical features of osteomalacia most often resemble those of rickets, with elevated serum alkaline phosphatase and PTH and low calcium, phosphorus, and 25(OH)D. In a review of all archived cases of bone biopsy-proven osteomalacia observed by the Bone Histomorphometry Laboratory at the Mayo Clinic, in patients with clinical features suggestive of osteomalacia, radiographic and serum it was concluded that calcium, phosphorus, and alkaline phosphatase assays are suitable screening tests. 25(OH)D levels may be normal[25].

Vitamin D and cardiovascular diseases
The etiology of chronic cardiovascular disease is influenced by various risk factors. Clinical studies have shown that in addition to high cholesterol, smoking, obesity, hypertension and diabetes, low serum levels of 25OHD are also closely associated with the development of cardiovascular disease [26].Furthermore, development of hypertension may be associated with low 25OHD levels [27].The role of vitamin D in the cardiovascular system is noteworthy. This is because vitamin S receptors are present throughout the cardiovascular system, not just in the heart[28].Vitamin D metabolites act on multiple domains of cardiovascular function, including those associated with inflammation, thrombosis, and the renin-angiotensin-aldosterone system (RAAS) signaling pathway[29].Extensive in vitro studies have also shown that vitamin D and its analogues consistently suppress pro-inflammatory cytokines and increases anti-inflammatory cytokines, the mechanism involved being NF-kB and p38 by VDR. It seems to be related to pathway inhibition[30].Vitamin D also has anticoagulant properties [31].

Vitamin D and diabetes
Recent studies have shown that 25(OH)D levels are negatively correlated with the prevalence of type 2 diabetes (T2DM), islet-cell beta-cell function, insulin resistance, body fat and BMI levels [32,33].1,25(OH)2D3 can bind ti vitamin D3 receptors on pancreatic islet β-cell, thereby enhancing insulin sensitivity, suppressing inflammatory factors, alleviating chronic inflammatory processes in the pancreas, and reducing islet β-cell. Improve cell function [34].It also inhibits the action of the renin-angiotensin system, which promotes insulin secretion[35].Vitamin D supplementation may improve islet β-cell function and glucose tolerance [36].Studies have received that vitamin D-dependent calcium-binding proteins are presents are present not only in islet β-cells, but also in PP and D cells, with the highest abundance in islet α-cells[37].Its main action is to regulate intracellular calcium concentration via vitamin D-dependent calcium-binding proteins, thereby influencing endocrine and metabolic processes in various cells of the pancreas. In other studies, glucagon hormone release in islets isolated from 25OHD-deficient mice was normalized to normal vitamin D levels after in vitro stimulation with 10mmol/L arginine or hyperglycemia (glycemic control

<1.7 mmol/L) was found to be significantly higher than that isolated from mice. L.Additionally, 1,25(OH)2D3 supplementation may restore glucagon to normal levels [38]. Therefore, 25OHD deficiency not only suppresses insulin secretion by weakening islet β-cells function, but also increased blood glucose by enhancing islet α-cells function.

Vitamin D and immune system

Vitamin D may play a role in regulating immune function, suppressing inflammatory responses, and autoimmune diseases [39].Many immune cells in the human body express VDR, including monocytes, macrophages, dendritic cells, T cells, and B cells. Vitamin D3, coupled with the VDR of T cells, inhibits the activity of Th1 cells, thereby depleting CD4+ T cells to release IL-2, interferon-γ, and tumor necrosis factor (TNF) αββ, leading to chronic inflammation can slow the course of autoimmune diseases[40].Vitamin D also induces B-cell proliferation and secretion of immunoglobulins E and M, leading to the formation of memory B-cells and promotion of B-cell apoptosis [41]. These results indicate that 1,25-(OH)2D3 plays an important role in anti-inflammatory responses and immunomodulation.

Vitamin D and neuropsychiatric disorders

Vitamin D is closely associated with CYP27B1 metabolism. CYP27B1 is expressed in both fetal and adult neurons and glial cells, particularly in the paraventricular tissue of the highly sapraopticsubstanianigra and hypothalamus. Furthermore, VDR was highly expressed in the hypothalamus, pons, basal ganglia, hippocampus, and developing brain tissue, suggesting that vitamin D may be involve in brain development and function[42].Vitamin D may be involved in processes of neurotransmitter synthesis, inflammation, and calcium balance. Other studies have shown that vitamin D can protect nerve cells through its antioxidant effects[43].There is evidence that 1,25(OH)2D3 may increase the expression of calcium-binding proteins [44], but this has not been demonstrated in all studies.1,25(OH)2D3 may also work by increasing serotonin levels in the brain [45].The antitumor effects of vitamin D are the result of inhibition of cell cycle genes, induction of apoptosis, and reduction of tumor invasiveness and angiogenesis. Colon cancer cell cultures show a significant reduction in proliferation in the presence of 25(OH)D3 or 1,25(OH)D3 [46].A possible role for vitamin D is also associated with several other diseases and chronic kidney disease[47].

How To Overcome Calcium Deficiency

All studies demonstrating the efficacy of vitamin D in fracture prevention used at least 800 IU of cholecalciferol, primarily in vitamin D deficiency populations. Ergocalciferol is probably effective in preventing fractures, but evidence is limited. In addition, 25(OH)D levels should be taken with 1000-1200 mg of calcium per day [48].

Whether calcium absorption differs among common calcium supplements (i.e., calcium citrate or calcium carbonate) is a matter of debate. Most forms of calcium are best absorbed on divided dosages of 500 mg or less given two times daily [49].

Calcium citrate may be slightly better absorbed than calcium carbonate in patients with achlorhydria[50].Calcium absorption does not appear to differ between different food sources such as milk, yogurt, and cheese[51].Dairy products provide 200-300 mg of calcium per serving (1 cup milk, ¾ cup yogurt, 1.25 inch cube of cheese). Calcium absorption from cow's milk is the same as that of the increasingly popular beverage when soy milk is fortified with calcium carbonate., oily fish such as blue fish[52].

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