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Review

Average levels of vitamin D in different continents

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Abstract

Vitamin D is a group of fat-soluble hormone precursor that enters the body through food and nutritional supplements. Vitamin D has two important forms which are vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). This vitamin is activated in the body through two hydroxylation reactions and produces calcitriol (1,25-dihydroxycholecalciferol), which is its active form. The metabolites and other analogues of these substances also refer to vitamin D. Vitamin D plays a significant physiological and essential role in maintaining the levels of extracellular calcium ions. The most important role of extracellular calcium is its contribution to muscle contractions. Around 10% to 20% of vitamin D is supplied by the foods. Vitamin D sources include salmon, cod liver oil, wild mushroom, milk, and meat and also egg yolk. However, 80% of vitamin D comes from sunlight. Vitamin D has an important role in the process of bone metabolism, regulation of proliferation and cellular differentiation, as well as the regulation of immune responses. The purpose of this review article is to study the importance of vitamin D and its use in the body as well as examining the vitamin D levels in different continents.

Keywords: vitamin D, vitamin D3, Cholecalciferol

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Introduction

Vitamin D plays a significant physiological and essential role in maintaining the levels of extracellular calcium ions. The most important role of extracellular calcium is its contribution to muscle contractions. Around 10% to 20% of vitamin D is supplied throughout the foods (1,2). Vitamin D sources include salmon, cod liver oil, wild mushroom, milk, and meat and also egg yolk (1). However, 80% of vitamin D supplies from sunlight (3). Vitamin D has an important role in the process of bone metabolism, regulation of proliferation and cellular differentiation, as well as the regulation of immune responses. Vitamin D receptors are widely present in immune system cells, and the active form of this vitamin, which is 1,25-dihydroxycholecalciferol, has the ability to change and modify dendritic cells and increase the resistance of these cell against the exchange of severe immune responses in the body (4). Vitamin D also plays a role in controlling the absorption of calcium in the body through bone absorption by secretion of PTH (5). Vitamin D receptors not only regulate calcium levels in the body, but also play a key role in differentiating stem cells into other cells (6). Studies have shown that vitamin D deficiency during maturity leads to osteoporosis and osteomalacia (a role in bone infections), and daily intake of 20 µg of vitamin D and 1800 mg of calcium prevents colon cancer (7).

It has also been reported that vitamin D can be eliminated by inducing apoptosis in inflammatory cells. As mentioned, vitamin D is a nerve-activating hormone (1). The vitamin D receptor and its enzymes are found in the nerve cells (black body) of the hippocampus, the hypothalamus, and prefrontal cortex (8). Vitamin D plays a role in protecting against oxidative stress and regulating cerebral growth factor, in the proliferation and differentiation of the brain cells through various mechanisms and in increasing the antioxidant capacity (9). Vitamin D deficiency conducted in the culture medium and animal models leads to mild oxidative stress and an increase in proteolysis in the muscles, while, according to the results of these studies, this vitamin is known to be a potent antioxidant (10). Vitamin D is a group of fat-soluble hormone precursor that enters the body through sunlight, food and nutritional supplements. Vitamin D has two important forms which are vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). This vitamin is activated in the body through two hydroxylation reactions and produces calcitriol (1,25-dihydroxycholecalciferol), which is its active form. The metabolites and other analogs of these substances also refer to vitamin D (11).

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Implication for health policy/practice/research/medical education

Vitamin D plays a significant physiological and essential role in maintaining the levels of extracellular calcium ions. Vitamin D has an important role in the process of bone metabolism, regulation of proliferation and cellular differentiation, as well as the regulation of immune responses.

The chemistry of vitamin D

The chemical structure of the ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3) and its pre-vitamin, ergosterol and 7-dehydrocholesterol, is shown in Figure 1. All the sterols that have the features of vitamin D, have a similar steroid core, and their difference is in the side chain connected to carbon 17. In the body, cholesterol is converted into 7-dehydrocholesterol, which is also converted to cholecalciferol when animals' skin is exposed to the sun's ultraviolet rays. These precursors do not have anti-rickets effect, unless the B ring is formed between carbon 9 and 10 in steroids. This process is carried out by ultraviolet radiation, where a double bond is formed between carbon 10 and 19 in the new composition. Triennium is the result of vitamin D core (11).

High levels of irradiation to ergocalciferol or cholecalciferol produce various substances such as tachysterol, suprasterol I, suprasterol II and other compounds. Some of these substances have a relative vitamin D activity, some are poisonous, and some may have the ability to compete with vitamin D3 (11).

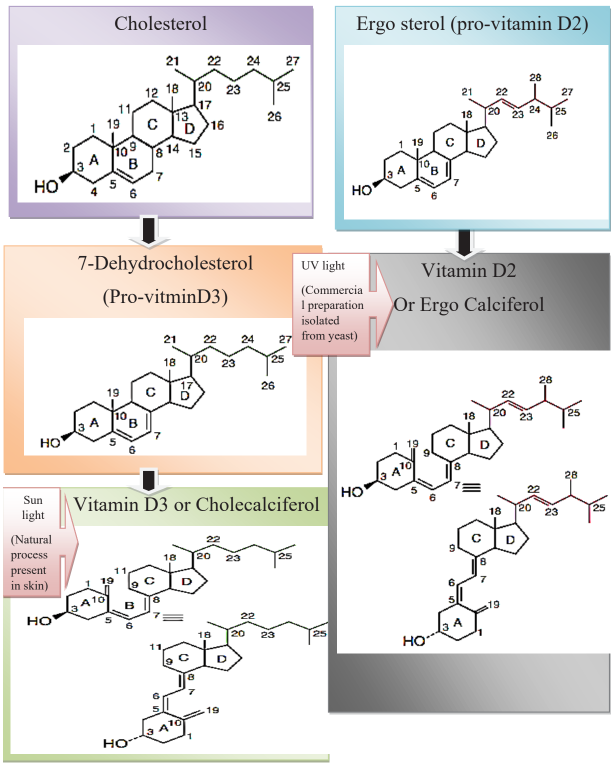

Figure 1. The structure of vitamin D_2 and vitamin D_3.

The conversion of vitamin D3 into the active form

In the late 1960s, a new phase of research on vitamin D began, which caused a complete change in the understanding of the functions of this nutrient in the body (12). The discovery that biological activity of vitamin D can be justified by a quasi-hormonal activity has led to a change in the research on vitamin D. Today it is known that vitamin D is a simple precursor for 1,25-dihydroxycholecalciferol (1,25(OH)$D_{2,3}$). It is observed that vitamin D_3 have a very strong anti-rickets effect (12,13). The first metabolite found in the liver was 25-hydroxyvitamin D_3 (25(OH)D_3), which was chemically synthesized by Blunt et al in 1968 (14,15).

This metabolite is naturally the main form of circulating vitamin D the body. Further studies have shown that (25(OH)D_3) is transmitted to the kidney and metabolically metabolized to some of the dihydroxy compounds, which the most important of them is 1,25(OH)$D_{2,3}$, where the kidney is the main source of this production. Existence of other amounts of this metabolite of vitamin D in the intestines was proven by some scientists. This metabolite of vitamin D is transmitted from the kidney to the intestine, bone and other areas of the body where is involved in the metabolism of calcium and phosphorus. Studies on the metabolism of vitamin D have shown that the functions of vitamin D_3 as a hormone (1,25(OH)$D_{2,3}$), is in the intestine and bone (15). Production of (1,25(OH)$D_{2,3}$) is precisely controlled by the parathyroid hormone (PTH) in response to the levels of calcium and phosphorus in the blood.

Previously. Barger-Lux et al introduced this metabolite as 1,25-dihydroxycholecalciferol and showed that the reaction of (25(OH)D_3) in calcium intestinal transplantation can be stopped by actinomycin D, while (1,25(OH)D_3) stimulate calcium intestinal transplantation, even in the presence of actinomycin D (16,17). Today it is known that vitamin D_3 is transferred from the skin into the liver and converted to the (25(OH)D_3). This metabolite is then transferred to the kidney through the bloodstream, and converted to the steroid hormone (1,25(OH)D_3) or one of the two metabolites of 24,25-dihydroxyvitamin D_3 and 1, 24 and 25-trihydroxyvitamin D_3 (16). The metabolic conversion of vitamin D is shown in Figure 2.

The PTH released due to the low levels of calcium in the blood leads to the excretion of phosphorus from the kidneys, which in turn stimulates metabolic change of kidney to produce (1,25(OH)$D_{2,3}$). When the levels of calcium and phosphorus of the kidneys are normal, PTH does not release and kidney converts 25-hydroxy to 24, 25-dihydroxy and then to 1, 24 and 25-trihydroxyvitamin D_3. These findings justify the mechanisms by which the body of the animal adjusts blood calcium absorption. It seems that the main controller of calcium absorption is the mechanism of reversal that stops the conversion of (25(OH)D_3) to (1,25(OH)$D_{2,3}$) by the kidney. This conversion is stimulated by low blood levels of calcium and the presence of PTH. This process is stopped when

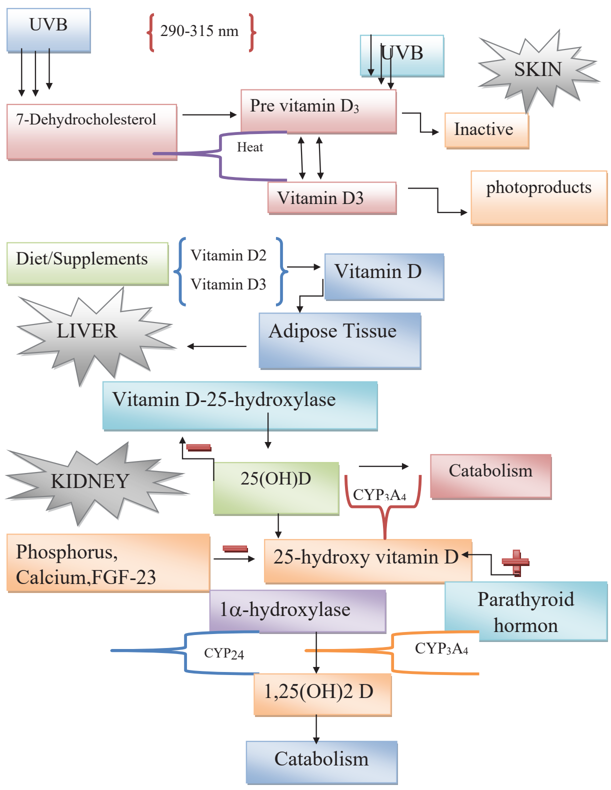

Figure 2. The metabolic conversion of vitamin D. Abbreviations: CYP3A4, CYP24 Cytochrome P450 3A4; CYP24, vitamin D 24-hydroxylase gene.

the level of calcium is normal and a decrease is observed in PTH concentration in the kidney (20).

The average levels of vitamin D in different continents

Asia

In recent studies on vitamin D in individuals living in different countries around the world, the levels of vitamin D have reported to be very low in Asian countries, like India (18,19). In the north of India, 96% of infants were deficient in vitamin D, 91% of healthy and educated girls were also deficient in vitamin D (20). Additionally, 78 percent of healthy employees in hospitals and 84 percent of pregnant Indian women were deficient in vitamin D. The remarkable issue with the lack of this vitamin was that it was prevalent among pregnant women and children, but in South India this feature was reported to be less (21-23). Similar data from Pakistan are available on newly born infants who are suffering from vitamin D deficiency (24). In Bangladesh, vitamin D deficiency is considered as a result of age, type of clothing and nutrition (25). The levels of vitamin D in Southeast Asia has been studied less. However, according to research conducted in these countries, vitamin D absorption is directly related to the amount of skin pigmentation of these individuals, and the type of clothing does not affect the intake of vitamin D, however, in any case, vitamin D deficiency is considered less (26,27).

The levels of vitamin D in Japan is generally much higher than other Asian countries due to the high consumption of fish, and this deficiency is most likely to be found in the elderly (28). According to a recent study, the level of vitamin D deficiency in postmenopausal women is 47% in Thailand, 49% in Malaysia, 90% in Japan and 92% in South Korea. The average levels of vitamin D in the blood serum of individuals in Indonesia was 48 nmol/L. A study conducted in part of Thailand near the equator showed high levels of vitamin D and proved that the geographic area in which people live, as well as the high levels of liver oil intake are very effective in increasing the levels of vitamin D (29). Osteomalacia is very common in Mongolia and China. Additionally, studies in the northern part of China showed that 89% of young Chinese girls suffer from vitamin D deficiency and have low levels of calcium as well. Around 48% of Chinese men suffer from severe vitamin D deficiency. In the comparison between the amounts of vitamin D in Chinese menopausal women, the deficiency of this vitamin was more common in Malaysia women. That is due to the low activity of their skin pigments. Accordingly, studies in two parts of China showed that 90 percent of Beijing and Hong Kong women have less serum vitamin D level than 50 nmol/L (32-36).

Middle East

Unlike the direct sunlight in the Middle East and Africa, we see the highest levels of osteomalacia in these areas. This issue is related to the restrictions on clothing due to cultural orientations. That is why the milk of lactating women contains relatively no amounts of vitamin D. In the African continent, dark skin and inadequate levels of calcium have also led to vitamin D deficiency. On the whole, both geographic areas suffer from vitamin D deficiency, while in these areas there is no correlation with the individuals' age. The vitamin D concentrations in a large population of adult girls in Iran (70%) and Saudi Arabia (80%) are less than 25 nmol/L. This rate is presented in 32% of Lebanese girls and 9% to 12% of Iranian adult boys. Severe diarrhea causes the loss of this vitamin in infants in the Middle East and Africa. Also, the type of clothing, type of season and economy that provides the basis for a nutritional model is one of the factors influencing the determination of vitamin D in people in the Middle East and South Africa. Many of these factors are also important determinants of calcium levels.

A recent study in a group of university students in Saudi Arabia revealed that vitamin D level is between 10 and 30 nmol/L. This rate was 25 nmol/L among Iranian girls and women, and Lebanese women. In the Lebanese elderly, the average level of vitamin D was less than usual, and the average level of vitamin D in 35% of them is less than 25 nmol/L. The vitamin D level in the Iranian elderly population is between 60% and 65%. The cutoff for vitamin D in Tunisia is 37.5 nmol/L, of which the vitamin levels of 48% of the Tunisian elderly is less than this. According to studies conducted in women with osteoporosis, women in the Middle East had the highest percentage of osteoporosis. Also, studies in Saudi Arabia, Kuwait and Iran showed that 10% to 60% of mothers and 40% to 80% of their infants have vitamin D deficiency (30,38).

Latin America

In 2006, the population of Latin America and the Caribbean region was reported to be around 556 million, with an average age of 73 years (31). We see a large population of the elderly in the area. The pattern of diet in the area testified the malnutrition and the lack of vitamin D in the various classes, especially in poor persons. A series of studies in different regions of Argentina showed a large difference in the amount of vitamin D in the northern and southern parts of the country. The average levels of vitamin D in northern Argentina were 52 nmol/L, however, in the southern provinces of Argentina it was 36 nmol/L. The sampling of different studies in Argentina revealed seasonal differences in the levels of vitamin D in the body. This rate in a group of women in summer was 63 nmol/L and in winter was 53 nmol/L. During other studies, the levels of vitamin D in the southern provinces of Argentina in mothers and infants were less than 25 nmol/L. The results of an international research found that vitamin D deficiency in postmenopausal women in 3 countries, Mexico, Chile and Brazil, was 67%, 50%, and 42%, respectively. In addition, severe osteoporosis in postmenopausal women in Mexico influenced the rate of vitamin D deficiency in that country (32).

Europe

Vitamin D deficiency in Europe is more dispersed and more diverse (30). The serum levels of vitamin D are found to be less than 25 nmol/L in 2% to 30% of adults, reaching 75% in the elderly (31). In a series of international studies, the levels of vitamin D in southern Europe were between 20 and 30 nmol/L and in northern Europe were 40 to 50 nmol/L. Also, the level of vitamin D in men is higher than women. According to investigations and statistics, the conclusion was that ultraviolet radiation was more effective in southern Europe than in the north (32).

North America

In North America, the average level of vitamin D was measured in a two-year process between 2002 and 2004. Among the men selected from those who were 1 to 5 years old, 20 to 49 years old and the third group, which includes men who aged more than 70 years, the level of vitamin D deficiency was 2%, 13% and 16% respectively. In addition, among a group of women with this age, the percentage of vitamin D deficiency, which is lower than 37.5 nmol/L, was reported to be 3%, 19% and 16.5%, respectively.

Available information among women in the Toronto, aged between 18 and 35, in Canada states that the level of vitamin D in 21% of white women, 32% of immigrant women, including South Asian, Indian, and East Asian, and 25% of black women is less than 40 nmol/L. Also, according to seasonal studies conducted in this country, it was reported that people exposed to a limited amount of sunlight per day and the level of vitamin D deficiency in these individuals increases to 90%, and in winter it will increase to 18%. Those with vitamin D deficiency have an increase of 38% in the autumn and 60% in winter (37).

Oceania

A lot of researches have been done on the lack of vitamin D in Oceania, and has shown that the population suffers from a more acute deficiency of vitamin D than other continents and is addressed as a type of crisis (36). Serum concentrations of vitamin D in women were reported to be 25 nmol/L in the northern Sydney area and the mean serum concentrations of vitamin D was 17 nmol/L in total. In Tasmania, around 67% of men population suffer from vitamin D deficiency. Accordingly, vitamin D deficiency is higher among different immigrant peoples than Australians, and this gap is three times higher among Vietnamese compared to Europeans. Studies conducted among young immigrant Chinese people have also revealed that 28% of them are suffering from vitamin D deficiency. In another comparison between Vietnamese and Australian-British individuals, the serum levels of vitamin D was reported to be 63% and 37%, respectively. According to studies conducted in New Zealand, unfortunately vitamin D deficiency is a growing problem (38).

Conclusion

Vitamin D plays a significant physiological and essential role in maintaining the levels of extracellular calcium ions. Vitamin D has an important role in the process of bone metabolism, regulation of proliferation and cellular differentiation, as well as the regulation of immune responses.

Authors' contribution

MI and HI searched the data and prepared the draft of the manuscript. HN edited and finalized the paper. All authors read and signed the final manuscript.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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