



The adverse effects of vitamin D deficiency on health

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Abstract

Vitamin D has been demonstrated to play the important roles on the muscular, immune, endocrine and also central nervous systems. Furthermore, vitamin D deficiency is one of the global problems because of the prevalence of osteoporosis, rickets, diabetes mellitus, hypertension, cancer, and cardiovascular and also renal diseases. On the other hands, vitamin D toxicity is widespread that negatively affects on gastrointestinal disorders and kidney stones. Thereby, the aim of this mini-review paper is to illustrate the negative effects of vitamin D deficiency on the health.

Keywords: Vitamin D, Hypertension, Cardiovascular disease, Stroke, Osteoporosis, Rickets, Diabetes mellitus

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Introduction

Vitamin D has been advised to prevent rickets in children and osteoporosis in elderly (1,2). It affects the bone regulation and mineral metabolism via modulation of calcium absorption in the gut and also bone mineralization (3). Vitamin D is endogenously synthesized in skin by ultraviolet sunlight exposure. Vitamin D status is attributable to the severity of sunlight, nutrition, parathyroid hormone (4,5).

Approximately 40% to 80% of people in Iran suffer from vitamin D inadequacy as demonstrated by a recent investigation (6). The outbreak of vitamin D deficiency is observed as the level of vitamin D in serum is below 30 ng/mL (7). Vitamin D deficiency is demonstrated to be attributable to chronic skeletal disease (3), cardiovascular and renal diseases (8,9), autoimmune (10), cancer and also infectious disease (11).

On the other hands, vitamin D toxicity is an index of hypercalcemic and hypercalciuric status which arises from the excess $1, 25 (\text{OH})_2 \text{D}_3$ activity (12). The signs of excessive vitamin D include nervousness and kidney stones, and also gastrointestinal disorders such as anorexia, diarrhea and vomiting (13).

Since the disorders related to vitamin D and health are widespread, the objective of this mini-review is to clarify the adverse effects of vitamin D deficiency on human health.

Materials and Methods

For this mini-review we searched PubMed, EBSCO, Embase, directory of open access journals (DOAJ),

Scopus, Google Scholar, and Web of Science with key words as vitamin D, hypertension, cardiovascular disease, stroke, osteoporosis, rickets and diabetes mellitus.

Vitamin D biosynthesis and physiology

Vitamin D is frequently known as a pro-hormone rather than a vitamin (14). Approximately, 80% to 90% of vitamin D is endogenously synthesized in the skin by ultraviolet-B spectrum of sunlight that converts 7-dehydrocholesterol as a precursor to vitamin D (15). After that, vitamin D is converted to $(\text{OH})_2 \text{D}_3$ in the liver and finally this form is converted to $1, 25 (\text{OH})_2 \text{D}_3$ in the kidney (its active form) by the enzyme 25-hydroxylase (14,16). In addition, the minor amount of vitamin D is provided from nutrition (17). Some foods are rich in vitamin D including fish, milk and orange juice. Serum $1, 25 (\text{OH})_2 \text{D}_3$ content is linked to its renal production that depends on calcium and phosphorus levels (18).

Vitamin D functions

Adequate vitamin D not only regulates calcium homeostasis but also improves musculoskeletal activity (19). Vitamin D plays the important role on the regulation of intestinal calcium absorption (20,21). Thus, it affects skeletal health. Furthermore, vitamin D has a vital role on regulation of cell growth and differentiation (22,23). Additionally, vitamin D regulates blood pressure and heart health (24).

Vitamin D deficiency and hypertension

Vitamin D has anti-hypertensive activity via several

■ Implication for health policy/practice/research/medical education

Vitamin D plays vital roles on many organs including muscle, endocrine, bone and immune systems. Thus, vitamin D status either deficiency or toxicity adversely affects human health.

proposed mechanisms. First, vitamin D suppresses the rennin-angiotensin-aldosterone system (25). These hormones are the most important hormones for controlling blood pressure (26). Resnick et al (27) studied the effects of vitamin D on plasma rennin activity in 51 hypertensive subjects. They found an inverse association between the serum $1, 25 (\text{OH})_2 \text{D}_3$ concentration and the plasma rennin activity. In addition, Li et al (28) noticed that $1, 25 (\text{OH})_2 \text{D}_3$ supplement down-regulated rennin gene expression in wild-type mice. Second, vitamin D modulates the cardiovascular risk factor. In this case, vitamin D suppresses nuclear factor- κB arising from its anti-inflammatory action (29). Third, vitamin D manifests anti-atherosclerotic action (30) through the reduction of endothelial adhesion molecules, the increase of nitric oxide generation and also the inhibition of macrophage to foam cell formation (31,32). In this case, Sowers et al (33) detected an association between vitamin D and hypertension. Interestingly, it was detected that combination therapy of vitamin D and calcium were more efficient in decreasing blood pressure in comparison to intake of calcium alone (the clinical trial with 148 elderly women, by Fahrleitner et al) (34). Likewise, Chandana et al (35) showed that the outbreak of hypertension including systolic and diastolic blood pressure was elevated when women are exposed to vitamin D deficiency (less than 50 nmol/L). Scragg et al (36) noticed that vitamin D supplementation decreased systolic and diastolic blood pressure in elderly hypertensive patients. Moreover, Nasri et al (37) showed that oral vitamin D administration reduced blood pressure in subjects with diabetes mellitus. In contrast, Jorde and Bona (38) found no relation between vitamin D and the incidence of blood pressure. Also, Forman et al (39) observed that consumption of vitamin D had no adverse effects on the incidence of hypertension.

Vitamin D deficiency and cardiovascular disease

Vitamin D deficiency is linked to cardiovascular risk factors (11). Previously, Lindén (40) found the increased vitamin D intake in patients with myocardial infarction. Vitamin D inadequacy leads to an increase in rennin-angiotensin-aldosterone system that negatively influences cardiovascular system (41). Moreover, low vitamin D level has adverse effects on the induction of cardiovascular disorders including coronary artery disease and heart failure (22). Interestingly, vitamin D also influences the proliferation of the vascular smooth muscle cells and also the expression of vascular endothelial growth factor (42). These changes result in the sustained increased pulmonary vascular resistance (43).

Vitamin D deficiency and stroke

There is association between low vitamin D and stroke severity (44). In this context, it was observed that sunlight exposure improved stroke patients and also bone mineral density (45). Similarly, evidences show that administration of vitamin D inhibits musculoskeletal disturbance in stroke patients (45,46).

Vitamin D deficiency and renal disease

Vitamin D plays the important role in the kidney function (47). Experimental data showed that vitamin D deficiency is linked to the renal disorders (47). The abnormalities in vitamin D metabolism participates in the prevalence of mineral and skeletal disturbances and the induction of hypertension that leads to renal damage as the result of the lack of conversion of $25 (\text{OH}) \text{D}_3$ to $1, 25 (\text{OH})_2 \text{D}_3$ (48,49).

Vitamin D deficiency and diabetes

Vitamin D exerts immunomodulatory activity through decreasing cytokine production and lymphocyte proliferation; as a result, it depresses the destruction of β cells in the pancreas, which is responsible for insulin secretion, and hence develops type 1 diabetes mellitus (50). Similarly, Mathieu et al (51) observed that intake of vitamin D in mice suppresses the outbreak of type 1 diabetes mellitus. Notably, in an investigation with 10366 children in Finland, Hypponen et al (52) reported that administration of high dosage of vitamin D (2000 IU/d of vitamin D) in the first year of life markedly decreased the risk of type 1 diabetes mellitus. Moreover, its deficiency is closely attributed to obesity (53), type 2 diabetes and also disorder of glucose metabolism (54).

Vitamin D deficiency and cancer

Numerous studies have reported that vitamin D manifests the anti-proliferative role on breast, colon and prostate cancer cells (55,56). The impact of vitamin D₃ on cancer and regulation of cell growth proliferation include the reduction of angiogenesis (57), increase of cell differentiation and apoptosis of cancer cells (58) as well as the decline of cell proliferation and metastasis (59,60). Various studies have found that the risk of prostate cancer is decreased as the level of vitamin D₃ in serum is more than 20 ng/mL (61-63).

Conclusion

Vitamin D plays vital roles on many organs including muscle, endocrine, bone and immune systems. Thus, vitamin D status either deficiency or toxicity adversely affects human health.

Author's contribution

HN was the single author of the manuscript.

Conflicts of interest

The author declared no competing interests.

Ethical considerations

The author of this manuscript declares that he has followed the

ethical requirements for this communication. Also, Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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