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## Vitamin D: Is There a New Era?

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### ABSTRACT

**Background:** In recent decades, much interest has been focused on investigating new roles of vitamin D in human body beyond the mineral-ion homeostasis. **Methods:** By searching medical databases such as PubMed, over 16000 articles were found which have been published since 2000 on novel aspects of vitamin D in health and diseases. **Results:** Of great interest was the effects of vitamin D on decreasing the risk of several chronic illnesses, including common cancers, autoimmune, infectious, and cardiovascular diseases. In this review, the new roles of vitamin D that have recently been investigated were addressed. **Conclusions:** Due to the vast prevalence of vitamin D deficiency worldwide, it seems that time has come to conduct well-designed clinical trials and meta-analysis to explore the effectiveness of vitamin D supplementation in treatment of common diseases. Finally, the progression in cellular and molecular methods and technology will shed new lights on vitamin D roles in health and disease.

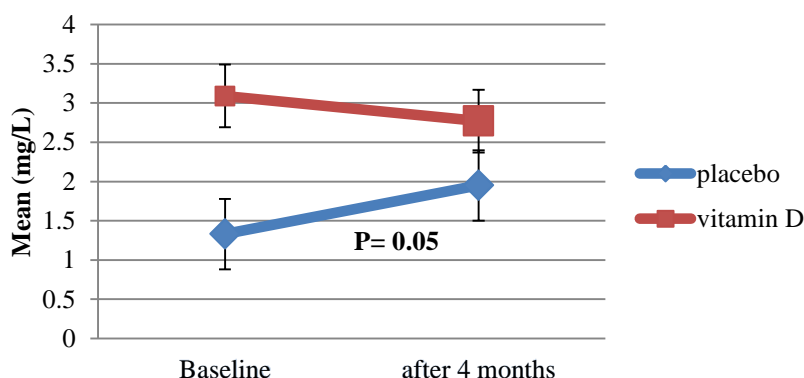
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### Vitamin D and chronic inflammation

Recently, non-calcemic functions of vitamin D, especially anti-inflammatory and immunomodulatory effects have attracted much attention. The beneficial effect of vitamin D intake on high-sensitive C-reactive protein (hs-CRP) was investigated in patients with non-alcoholic fatty

liver disease (NAFLD) (Figure 1) (Sharifi *et al.*, 2014). It has been found that 1,25(OH)<sub>2</sub>D inhibits the T-helper1 response and may promote T-helper2 response, in other words, it could reduce production of inflammatory cytokines and induce anti-inflammatory response (Cantorna *et al.*, 2004).

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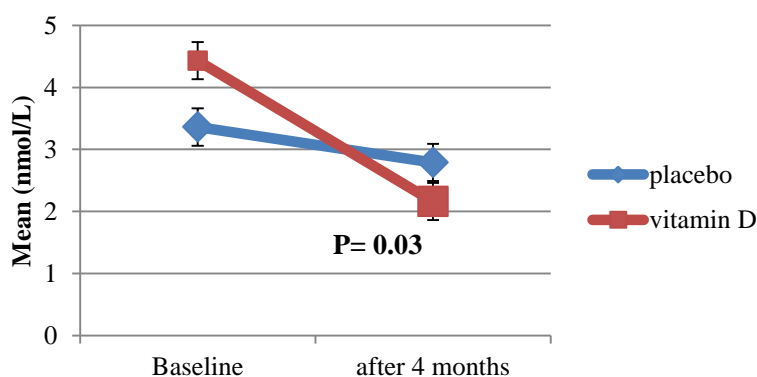


**Figure 1.** Mean serum levels of hs-CRP at the baseline and after supplementation with vitamin D compared with placebo in patients with NAFLD.

### Antioxidant effects of vitamin D

The antioxidant role of vitamin D was initially proposed by Wiseman in 1993; it was shown that vitamin D<sub>3</sub> and its active form 1,25(OH)<sub>2</sub>D<sub>3</sub> inhibited iron dependent liposomal lipid peroxidation (Wiseman, 1993). The structural similarity of vitamin D compounds to cholesterol

and ergosterol suggested for their membrane antioxidant ability (Wiseman, 1993). For the first time, it was found that improving vitamin D status in NAFLD patients could effectively reduce serum levels of Malondialdehyde (MDA) (Figure 2) (Sharifi *et al.*, 2014).



**Figure 2.** Mean serum levels of MDA at the baseline and after supplementation with vitamin D compared with placebo in patients with NAFLD.

It was reported in recent clinical studies on pregnant women that vitamin D supplementation could increase the serum total antioxidant capacity and glutathione levels (Asemi *et al.*, 2013). However, no association was found between 25(OH)D levels and activities of serum antioxidant enzymes in the study that assessed the relation between serum vitamin D levels and body

antioxidant status in ischemic stroke patients (Afshari *et al.*, 2015).

### Vitamin D and gastrointestinal diseases

Cumulative evidence has implicated the roles of vitamin D deficiency in increasing susceptibility to various gastrointestinal (GI) disorders, including colorectal disease, inflammatory bowel diseases (IBD), and irritable bowel syndrome (IBS)

(Ferguson *et al.*, 2016). A high risk of IBD has been associated with deficient or insufficient levels of vitamin D, unhealthy lifestyle, as well as presence of vitamin D related genetic polymorphisms (Basson, 2014). IBS is also a functional GI disorder. In this regard, it was demonstrated for the first time that supplementation with 50,000 IU vitamin D<sub>3</sub> every 14 days for 6 months improves the quality of life and clinical symptoms of patients with IBS (Abbasnezhad *et al.*, 2016).

### Vitamin D and depression

Vitamin D modulates the hypothalamic-pituitary-adrenal axis, regulating adrenalin, noradrenaline, and dopamine production through vitamin D receptors (VDRs) in the adrenal cortex and protects against the depletion of dopamine and serotonin centrally (Spedding, 2014). Therefore, a biological plausibility has been established for vitamin D effect on depression. Efficacy of vitamin D supplements in depression is controversial, awaiting further literature analysis. Premenstrual syndrome (PMS) is a condition with episodes of physical and psychological signs (Freeman, 2003). Based on the possible roles mentioned above, it seems that vitamin D status is associated with PMS

severity. However, there are a limited number of studies assessing the association of vitamin D with this condition. Thus, a cross-sectional study was designed to compare the nutritional status of vitamin D in young students affected by PMS with those of normal participants. The results, however, showed no significant differences in serum levels of vitamin D between the two groups (Saeedian Kia *et al.*, 2015). Further studies will reveal more facts in this area.

### Conclusions

In summary, vitamin D may exert important roles in prevention and treatment of many chronic diseases. As a result, it is necessary to maintain the sufficient serum levels of vitamin D among community members through food fortification and supplementation.

Due to the vast prevalence of vitamin D deficiency worldwide, it seems that time has come to conduct well-designed clinical trials and meta-analysis to explore the effectiveness of vitamin D supplementation in treatment of common diseases.

Finally, the progression in cellular and molecular methods and technology will shed new lights on vitamin D roles in health and disease.

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