

Effect of Vitamin D on Multiple Sclerosis: A review

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Abstract:

Multiple sclerosis (MS) defines a typical nervous disorder, and therefore the causes unknown. In recent years, many studies have been shown that vitamin D deficiency could associate with MS. Many important factors could aggravate MS and could concenter as MS risk factors, such as genetic factors and environmental factors together. Vitamin D is assumed to have an immunomodulatory effect within the central nervous system besides maintaining bone health and Ca metabolism. Many previous studies declared that there is a correlation between serum level of vitamin D and MS. They found that reduced levels of vitamin D (15 -63)nmol/L had a significantly higher incidence of multiple sclerosis more than those with higher levels of vitamin D (99 – 152) nmol / L. Some studies showed that humans with higher dietary vitamin D intake have lower incidence of MS. Here, we have a tendency to tend to review these studies that investigate the effect of vitamin D levels on MS progression. However, despite the shortage of proof for the results of vitamin D effect on MS progression. Previous research shows that there is a correlation between vitamin D deficiency and increased risk of MS

Keywords: multiple sclerosis, Vitamin D, immunomodulatory effects.

Introduction

Vitamin D is a lipid-soluble vitamin, in the human body vitamin D acts as a hormone ^[1], Vitamin D has two main forms of plant origin which is ergocalciferol (vit.D2) and animal origin which is cholecalciferol (vit.D3). Vit.D3 is considered more bioactive than vit.D2. The sources of Vit. D in our body are sunlight, which help conversion of 7-dehydrocholesterol to vit.D in the skin, foods like

fatty fish and fortified food, or dietary supplement. However, a large percentage of human Vitamin D intake is skin exposure to sunlight while a small amount of human Vitamin D intake is from the diet [2]. After vitamin D intake either orally or by skin from sun exposure, is metabolized by the liver to the active form, 25-hydroxyvitamin D (25-OH-vitamin D). Dietary intake of Vitamin D and exposure to sun light could affect 25(OH)Vit.D level in human body, for this reason measuring of 25(OH) D could be reflect the availability and status of Vitamin D in the body. However, level higher than 80 nmol/l (approx 30 ng/ml) of the blood concentrations of the 25 OH vitamin is important for increasing of calcium absorption and production of 1, 25 dihydroxy vitamin D by the extra-renal 1 alpha hydroxylase that is present in most tissues. Vitamin D act as an immunomodulator factor in the central nervous system (CNS). Hypovitaminosis of Vitamin D is presently as one of the most studied environmental risk factors for multiple sclerosis (MS) and is probably the foremost promising in terms of recent clinical therapeutic implications [3] (MS) is, autoimmune disease and it is a chronic inflammatory disorder [4], characterized by central nervous system (CNS) lesions which will result in severe physical or cognitive incapacity in addition as neurologic defects [5]. The name refers to 2 options of the disease: multiple describe the amount of central nervous system lesions, and pathology refers to the demyelinated lesions. The illness occurring between the ages of 20 and 50 years with a mean age of 30 years. Over two million individuals worldwide suffered from MS. [6], the association of vitamin D deficiency and many other diseases, as well as multiple sclerosis (MS), has been investigated extensively in recent years within the medical community. The risk of MS, also as illness severity has been related to vitamin D during a many studies [7], higher vitamin D levels were related to lower resultant risk of MS [8].

Effects and mechanisms of action of Vitamin D

Vitamin D effect on multiple sclerosis was extensively investigated in many studies performed on animals and human models, using different doses, duration of treatment and treatment times. Guo et al study, one of the important studies that concerning the utilizing effect of Vitamin D on MS, using animal models to determine the effect of vitamin D in MS, showed that dietary supplements of vitamin D with a level of (700ng / week) extended to four weeks, multiplied the spread of neural stem cells, and this helps within the repair of injury nervous by demyelination of the nerve fiber, low lesions, that improves clinical MS symptoms. However, the ability of neural stem cells to multiply and regenerate itself have an important role in restoring the affected tissue.

In the study of the Golan et al, with the use of an oversized dose (30,600 IU / week) and low-dose unit (5,600 IU /week) of vitamin D for a period of 12 months in each sex with the treatment of RRMS IFN β . It found through this study that the high dose, 4,370 IU / day have a very important role in increasing blood serum levels of 25(OH) D and decreasing serum levels of parathyroid hormone, this may help in the prevention of osteoporosis, which is a common illness in multiple sclerosis Patients. Regarding the other groups that administered a lower dose of vit. D, 5,600 IU / week, it had been observed that there was an associated IL-17 increase in this group. Relying on these results, the study hypothesized that vitamin D administration in high doses may reduce IL-17 levels. Ashtari et al. during this study, taking vitamin D supplementation (50,000 IU / day) in patients with MS for twelve weeks resulted in rapidly increasing of 25 (OH) D levels in blood serum, in addition they found that vitamin D dose correlated positively with interleukin 10 (IL-10) levels, a very important cytokine that's important in such conditions because it plays an anti-inflammatory response. Through this study, it shows that MS have a negative result on the levels of IL 10 and this ends up in the decreasing of the immune system within the body, therefore the use of dietary supplements of vitamin D may have an essential role in reducing complications in these patients, as a result of that vitamin D could contribute to increasing the body immune system. Sotichos et al. estimated that vitamin D₃ supplementation as doses of 10,000 IU and 400 IU/day in RRMS patients, he declared that 10,000 IU/ day dose of vitamin D₃ may double 25(OH)D serum level, in addition it could reduce IL-17 serum levels. However, these findings showed the

Importance of vitamin D dietary supplementation in MS patients, through its positive results effect on decreasing the levels of IL 17 within the blood and this helps to reduce inflammation and exacerbation of the illness. Through all of these studies were found to be relevant to or related to immune function, as a result of vitamin D in MS contributes to the reduction of inflammation by regulation or increasing the effectiveness of the body's immune system and reducing the production of inflammatory cytokines, because one of the most causes of this illness is irregularity Or a defect in the immune system of the body, that causes the emergence of inflammatory cases during this illness ^[9].

Risk factor

Environmental and genetic factors might balance a number of the adverse effects of risk factors, and there are various factors that represent risk factors that increase the danger of the illness ^[10].

- 1. sun exposure :** The exposure to restricted periods or times to the sunlight will increase the danger of MS because sunlight is the main source of vitamin D3, that successively plays a very important role in stimulating regulatory T cells and inflammatory cytokines like IL-10 and TNF- α , which play a very important role within the regulation of body immune system in MS ^[11].
- 2. Latitude:** The spread of the disease is at its upper limit at the northern latitude or south whereas the spread is at its lowest level at the equator ^[10].
- 3. Vit.D& Diet:** Taking oral vitamin D in a variety of dietary supplements or fatty fish has a significant effect on the reduced risk of MS. Wherever blood serum level 25(OH) D was clearly related to increased MS risk. Thus an integrated diet will be one of the necessary environmental factors for the low level of MS. there's a correlation between low MS risk and high fish intake, whereas intake of large amounts of linoleic acid with high-calorie intake supported animal material all result in an increased risk of MS. additionally to vitamin B12 and vitamin D are necessary factors within the production of myelin elements, therefore, the lack of those vitamins will increase the chance of MS ^[5].
- 4. Season of birth:** Some studies have found that the chance of MS is highest for births within the spring (especially in May) and the lowest chance for births in autumn (especially in November) as a result of it's related to vitamin D levels in pregnant women. the levels of blood serum 25 (OH)) D are at their lowest within the spring and highest in the autumn ^[10].
- 5. Gestational diabetes:** In a prospective study, there was a clear correlation between decreasing level of vitamin D in pregnant women and an increased probability of gestational diabetes ^[12].
- 6. Smoking:** Smoking is one of the most serious causes of the risk of MS, because of nitric oxide (NO) and also the production of carbon monoxide (CO). nitric oxide (NO) is a soluble toxic gas and is considered one of the harmful agents of nerve cells and oligodendrocytes, that will increase the negative effects of MS. Nitric oxide (NO) also causes a rise in fat peroxide and mitochondrial injury and this leads to oligodendrocytes apoptosis, nerve fibre degeneration, and demyelination. In addition to risk exposure to CO, where this causes the lack of oxygen levels in tissue, damage the myelin basic protein (MBP), further as also causes damage axon, and this results in increased inflammatory response, together with the

stimulation of microglia and CD4+ lymphocyte that invade the central nervous system, resulting in demyelination^[5].

7. **Infections:** Exposure to viral and bacterial factors in adolescence, like the Epstein Barr virus (EBV), human herpesvirus type 6, herpes zoster virus, and respiratory disease, in such cases the danger of MS doubles 20 to 30 times because of the immunologic response of Epstein-Barr virus, could interact with myelin antigens that include each T cells and B cells^[5].
8. **Genetic risk factor:** The genetic factor plays a very important role in MS by sharing genetic information to members of the family. Chromosomes are responsible for this genetic information, specifically the human leukocyte antigen chromosomes. 5% represents the danger of the genetic factor of family members with this disease. Genomic changes have an impact effect that could affect metabolism of vitamin D, which in turn affects the distribution of 25 hydroxyvitamin D concentrations. Also genetic changes have an effect on vitamin D receptors and genes, which affects the effectiveness of vitamin D and its role within the body's immune system.^[12].

Effect of Vit. D on the treatment of MS

Through previous studies that included randomized clinical trials in order to establish therapeutic benefit of vitamin D in patients with MS.

- Observed through an open study with 156 patients with MS, there's a strong inverse relationship between the rate of relapse and blood serum levels of 25(OH)D. It absolutely was found that after correcting the low levels of serum 25(OH)D by taking vitamin D supplements orally, this was related to lower annual relapse rate (ARR).^[10]
- There are few studies on the effect of vitamin D supplementation on the results of MRI within the treatment group for vitamin D3 in the Commonwealth of Independent States (CIS). After the increase in doses of vitamin D3, the number of T1GD lesions reduced and therefore the rate of T2, T1GD reduced, leading to reduced inflammation.
- In Finland clinical trial that performed on MS patient group. The whole number of patients was 66, 34 patients treated with 3000 IU / day of vitamin D with interferon beta-1b (IFN β -1b) on the other hand, the other group of 32 patients treated with interferon beta-1b (IFN β -1b) only. In that study Preliminary results from this study enclosed endurance and safety aspects, a number of new lesions and gadolinium enhancement lipids in magnetic resonance imaging. The researchers found that within the group treated with vitamin D, there have been fewer

new lesions T2, with the differences are not statistically significant between the two groups after twelve months. However, gadolinium enhancing lesions was significantly decreased in vitamin D treated group^[4].

Conclusion

The underlying causes of MS are unknown. However, genetic factors, together with environmental factors, play a very important role within the incidence of the disease. These studies show that vitamin D has a positive correlation with strengthening the immunity of the body from the regulation of the immune system and inflammation because it works to recover the cells of the central nervous system, reduces relapse rates and brain lesions, and modify the clinical course of MS. Therefore, it's necessary to monitor the levels of vitamin D blood serum in patients with multiple sclerosis and provide them with a necessary recommendation concerning the requirement to sun exposure as one of the most sources of vitamin D, intake the dietary sources rich in vitamin D and supplements so as to maintain adequate blood serum levels of vitamin D as a result of vitamin D deficiency cause negative effects in this population

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