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Prospective Evaluation of Vitamin D Supplementation on Peripheral Neuropathy in Type 2 Diabetes Mellitus -A Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Diabetic neuropathy is a long-term consequence of diabetes that can cause significant morbidity and a decline in quality of life in many individuals. Low vitamin D levels, in addition to causing rickets in infants and chondrosteoma in adults, may have a role in the development of DM and its underlying disorders, according to a growing body of evidence. Vitamin D deficiency has been linked to type 1 or type 2 diabetes, as well as the microvascular and macrovascular problems that come with it. Vitamin D insufficiency has been linked to diabetic peripheral neuropathy (DPN) as an independent risk factor. Vitamin D, both topical and oral, has been shown to considerably improve DPN symptoms and pain.

Keywords: Type 2 diabetes mellitus; neuropathy; vitamin D supplementation.

1. INTRODUCTION

Diabetic neuropathy is a long-term consequence of diabetes that can cause significant morbidity and a decline in quality of life in many individuals. Vitamin D deficiency [25-hydroxyvitamin D, 25(OH)D] is frequent in diabetic patients, and low concentrations have been linked to the presence and severity of sensory neuropathy [1,2,3,4].

PAINFUL diabetic neuropathy (PDN) is one of the most common and serious consequences in diabetic patients, and it not only hastens the development of diabetic foot ulcers and lower-extremity amputations, but it also has a negative impact on quality of life. Previous research has shown that PDN patients have an apparent vitamin D shortage, and that vitamin D therapy can significantly improve pain sensations and neurologic function. The evidence presented in these research, however, is inconclusive [5].

Vitamin D insufficiency has been linked to diabetic peripheral neuropathy (DPN) as an independent risk factor. Vitamin D, both topical and oral, has been shown to considerably improve DPN symptoms and pain. We expected that correcting a vitamin D deficit will improve DPN symptoms directly or indirectly [1,6-9].

2. SYMPTOMS AND RISK FACTORS

PDN is characterised by symmetrical lower limb paresthesiae, dysesthesiae, lancinating pains, and allodynia, as well as nocturnal exacerbation2 and severe sleep disruption, as well as a poor quality of life [10].

The main risk factors for DPN, according to epidemiological research, are high blood glucose and glycated haemoglobin levels, diabetes duration, higher albumin excretion rates, obesity, and hypertension. However, the pathological progression of DPN is still unknown. For a better understanding of DPN's process, it's critical to identify potential risk factors in diabetes mellitus. Vitamin D is a steroid hormone with a wide range of functions in the human body [10-15].

3. VITAMIN D AND NEUROPATHY IN DM 2

In earlier investigations, vitamin D has been linked to the regulation of bone metabolism. Vitamin D supplementation may have a therapeutic impact in decreasing the severity and progression of type 1 and type 2 diabetes. Vitamin D biomarker 25-hydroxyvitamin D [25(OH) D] is tested in blood samples to monitor vitamin D levels in patients. Vitamin D deficiency is defined as a 25-hydroxyvitamin D concentration of 20 to 30 ng/ml (50 to 75 nmol/L) or 50 to 75 nmol/L. Vitamin D insufficiency is defined as a 25(OH) D concentration of less than 20 ng/ml (50 nmol/L) in the blood. [15,16,17,18,19].

Several recent observational studies in diabetic patients have found a link between vitamin D deficiency and paraesthesiae and numbness, as well as between neurological impairments and electrophysiology and parasympathetic dysfunction. Furthermore, a recent systematic review and meta-analysis of 1484 patients with type 2 diabetes found a highly significant link between vitamin D insufficiency and diabetic peripheral neuropathy development. A more comprehensive investigation employing electrophysiology and Douleur Neuropathique 4 (DN4) scores revealed that serum vitamin D levels are considerably lower in diabetic individuals with peripheral neuropathy, but serum vitamin D-binding protein (VDBP) and vitamin D receptor (VDR) levels are equivalent. 15 Vitamin D deficiency was found in 50 percent of 9795 patients with type 2 diabetes in the FIELD

research, a multinational endeavour, and it predicted microvascular outcomes [10,20-26].

Vitamin D deficiency, a prevalent symptom in diabetic patients with distal symmetrical polyneuropathy, has been linked to type 1 or type 2 diabetes, as well as the microvascular and macrovascular problems that come with it [15,27-29].

According to a meta-analysis, vitamin D deficiency is linked to the onset and progression of DPN in Caucasian diabetes patients with T2DM, and diabetic patients with vitamin D deficiency are 1.22 times more likely to develop DPN than diabetic patients with normal vitamin D levels [15].

To relieve symptoms, a variety of symptomatic analgesic medicines are employed, including tricyclic antidepressants, selective serotonin-norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, anticonvulsants, and opioids. However, there is currently no effective treatment for PDN, with existing symptomatic treatments in western medicine only offering minimal pain relief and frequently causing major side effects that the patient cannot bear. Because of the advantages of having minimal side effects and excellent therapeutic benefits, alternative therapies have emerged as a new option for DPN treatment [5].

For symptom relief, national and international guidelines recommend a variety of treatments. 4/5 However, the therapeutic efficiency of all indicated drugs is restricted to a maximum of 50% pain alleviation and is limited due to undesirable side effects. 2 & 6 Aside from peripheral and cerebral changes, metabolic changes such enhanced glycemic flux8 and raised plasma methylglyoxal levels have been linked to PDN pathogenesis [10,30-35].

Although it is obvious that DPN patients have decreased serum vitamin levels, there are few instances of PDN patients. Vitamin D has a considerable impact on PDN as compared to DPN patients who are pain-free. Basit et alclinical .'s experiments have revealed that a high-dose intramuscular vitamin D injection can successfully reduce patients' pain sensations. There's also evidence that vitamin levels in DPN are lower, and that oral vitamin D treatment improves vitamin D status and peripheral nerve function. Vitamin D supplementation has been found in research by Razzaghi et al to improve wound healing in diabetic foot ulcers and the metabolic condition of diabetic individuals. Finally, there is a dearth of information of how vitamin D plays a role in neuropathic pain in people with PDN. Vitamin D supplementation may also be a useful "analgesic" in the treatment of pain in DPN sufferers. However, existing data of randomised controlled trials on vitamin D in the treatment of DPN available in the public domain is limited, and relevant systematic reviews and meta-analyses are uncommon [1,5,10,36-38].

In patients with painful diabetic neuropathy, a single intramuscular injection of 600 000 IU vitamin D is related with a considerable reduction in the symptoms of painful diabetic neuropathy according to study [10].

4. STUDIES COMPARISON

In a study A total of 112 type 2 diabetic patients with diabetic peripheral neuropathy (DPN) and vitamin D [25(OH)D] insufficiency took part in the placebo-controlled trial. A therapy group and a placebo group were assigned to patients in order. A neuropathy symptom score (NSS), a neuropathy disability score (NDS), and a nerve conduction study were used to assess both. The total 25(OH)D concentration in the blood was used to measure vitamin D status. For eight weeks, patients were given either oral vitamin D3 capsules or starch capsules once a week. Changes in NSS and NDS from baseline were the primary result. Changes in the NCS result were a secondary outcome. The result showed that when compared to the placebo group, serum 25(OH)D concentrations improved considerably after oral vitamin D supplementation in the treatment group. Similarly, in the treatment group, the improvement in NSS values was considerably greater than in the placebo group. After therapy, there was no difference in NDS and NCS between the two groups. [1].

In a study on 143 participants, the majority of whom had type 2 diabetes. The baseline 25-hydroxyvitamin D (25(OH)D) level was 31.7233.3 ng/mL, and 58 (40.5%) of patients had vitamin D deficiency, Vitamin D was administered intramuscularly, resulting in a considerable increase in 25(OH)D and a decrease in discomfort symptoms and neuropathy effects [10].

A research looked at The effects of vitamin D supplementation on peripheral neuropathy in

Egyptian prediabetic people, which included 178 prediabetic people who were screened for PN. Vitamin D levels were found to be inversely linked with neuropathy severity and score. In addition, vitamin D status was found to be an independent predictor of neuropathic severity. Vitamin D supplementation resulted in a considerable improvement in glycemic indices and lipid profile. Neuropathy score and severity before and after vitamin D administration were interestingly different. As a result, they came to the conclusion that vitamin D insufficiency is an independent risk factor for PN. Vitamin D deficiency is corrected, which improves glycemic indices, PN score, and severity [39].

In an Egyptian study looked at a total of 25 type 2 diabetic patients with diabetic peripheral neuropathy and 25 healthy controls. Sixty-four percent of the patients had vitamin D deficiency, 28 percent had vitamin D insufficiency, and only 8% had a normal serum vitamin D level. Females with diabetic peripheral neuropathy had a lower 25(OH) level than males, according to these findings. Female patients with type 2 diabetes mellitus exhibited lower 25-OHD levels than male patients, which is similar to Lebanese and Japanese research. In an Iranian study, however, there was no significant difference in vitamin D levels between men and women [11,40-42].

5. DISCUSSION

The sensation of neuropathic pain, particularly burning/hyperesthesia, was the symptom that improved the most. However, it is unclear if this was attributable to an increase in pain threshold, an improvement in the function of the afflicted nerves, or a combination of the two. Vitamin D is a strong inducer of neurotrophins and neurotransmitters, and its biological effects on the nervous system include the manufacture of enzymes involved in neurotransmitter synthesis and chemicals implicated in brain detoxification pathways. The nerve growth factor (NGF), a protein essential for the formation and maintenance of numerous populations of neurons in the peripheral nervous system, is potentiated when vitamin D is added [1].

When comparing diabetic peripheral neuropathy patients to controls, vitamin D insufficiency was shown to be very common. The link between vitamin D levels and diabetic peripheral neuropathy should be further investigated, as well as whether routine serum vitamin D testing should be performed in all diabetes mellitus patients [11].

Injections of vitamin D 200.000 IU intramuscularly three times a month for three months are in accordance with the guidelines for vitamin D supplementation and deficiency treatment in Central European individuals with proven vitamin D deficiency who require higher vitamin D doses than those recommended for the general population. Depending on the patient's body weight and age, the therapeutic dose for severe deficiency should be 1.000–10.000 IU/day (50.000 IU/week). Depending on the severity of vitamin D insufficiency, the treatment can last anywhere from 1 to 3 months. [39,43].

6. CONCLUSION

Serval studies shows strong connection between peripheral neuropathy in DM 2 and Vitamin D deficiency, all patients who have PDN should be analyzed for Vitamin D deficiency. Significant improvement in the symptoms of PDN after injection of Vitamin D for 8 weeks, the dosage should be adjusted according to the particular level of Vitamin D deficiency.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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