The Impact of Serum Vitamin D Concentration on Median Nerve Conduction

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ABSTRACT

Objectives: To perform nerve conduction studies (NCS) and to evaluate distal latency, amplitude and conduction velocity values of the median nerve in relation to serum vitamin D levels in patients with neuropathic symptoms compared to controls.

Patients and Methods: Patients with neuropathic symptoms of numbness, tingling and burning sensation were included in the study. Serum 1,25(OH) D3 levels were measured and patients were stratified by vitamin D status into three subgroups. Electrophysiological assessments of the median nerve were performed as recommended by the American Society of Electrodiagnostic Medicine. SPSS for Windows, version 24 was used for statistical analyses. Median nerve conduction values were compared between patient and control groups in relation to vitamin D concentration.

Results: The study enrolled 39 patients including 24 (61.5%) males and 15 (38.5%) females and 39 control subjects including 22 (56.4%) males 17 (43.6%) females. Patient and control groups had a mean age of 45 years. Average vitamin D concentration was 8.5 ng/ml in the patient group and 8.8 ng/ml in the control group. There was no statistically significant difference between two groups with respect to age and average vitamin D concentration (p=0.552). Greater distal latency values and a statistically significant association between median nerve distal latency and vitamin D deficiency were found in the vitamin D-deficient subgroup (p=0.024).

Conclusion: Given the neuroprotective action of vitamin D and the involvement of vitamin D deficiency in several neurological diseases as well as evidence that it might be an independent risk factor and a potential biomarker for neuropathy, we believe that patients presenting with mononeuropathy or polyneuropathy to a healthcare facility should be screened for vitamin D deficiency.

Key words: 25-hydroxyvitamin D, median nerve, conduction

INTRODUCTION

Studies suggest that vitamin D has a role in neuroprotection. In recent years, vitamin D deficiency emerged as a global public health problem and became the focus of widespread discussions due to its role in the development of various neurovascular disorders. Despite seasonal changes, the reported prevalence of vitamin D deficiency varies from 30% to 80% in the global population [1-4]. Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremity that involves the entrapment of the median nerve in the carpal tunnel and causes pain, numbness and weakness in the hands. It is more common in the third and fifth decades of life and affects women more often than men [5,6]. Despite being a well-recognized condition, CTS is mostly idiopathic with no clearly established etiology [7]. Age, gender, diabetes mellitus, thyroid disorders, connective tissue diseases, amyloidosis, acromegaly and repetitive hand movements were demonstrated to be risk factors for CTS.
PATIENTS AND METHODS

Patients were randomly enrolled for the present study. The study was conducted at the neurology department of a university hospital in Gaziantep. A retrospective chart review was performed for each patient.

The control group was selected from equally voluntary hearts of similar age and gender.

Approval for the study was obtained from the institutional ethics committee.

Patients with neuropathic symptoms of numbness, tingling and burning sensation were included in the study. Pregnant patients, patients with diabetes mellitus, cervical radiculopathy/plexopathy, generalized peripheral neuropathy, amyloidosis, other vasculitic conditions or thyroid disease and patients with a history of trauma were excluded.

Biochemical Assessment

To assess serum levels of vitamin D, 1,25(OH) D3 was measured by enzyme-linked immunosorbent assay (ELISA). Patients were categorized into three subgroups according to the World Health Organization definition, as follows based on the results of serum vitamin D measurements: deficient (serum vitamin D less than 12 ng/ml); insufficient (serum vitamin D between 12 and 30 ng/ml); and sufficient (serum vitamin D more than 30 ng/ml). Calcium, phosphorus, and albumin levels were measured for the differential diagnosis of primary hyperparathyroidism.

Procedure for Nerve Conduction Study

Nihon Kohden MEB-9400K (Nihon Kohden Corp., Tokyo, Japan, 2015) EMG system was used. In our EMG laboratory, filter settings were adjusted to a range of 20 Hz - 10 kHz for motor nerve conduction studies with a stimulation frequency of 1 Hz and stimulation duration of 0.2 msec and to a range of 20 Hz- 2 kHz for sensory nerve conduction studies with a stimulation frequency of 1 Hz and stimulation duration of 0.2 msec. As with routine EMG examinations, room temperature was maintained constant at 25°C and skin temperature varied between 31°C and 34°C throughout the procedure. The guidelines published by the American Society of Electrodiagnostic Medicine are followed at our laboratory for electrophysiological assessments. In line with conventional EMG examinations, upper extremity nerve conduction studies were performed using standard techniques for supramaximal percutaneous stimulation with a constant current stimulator and surface electrodes for recording. Median nerve sensory conduction was measured by placing recording electrodes on the index finger and stimulating electrodes on the wrist using antidromic technique. For the median nerve motor conduction study, recordings were obtained from the abductor pollicis brevis and distal latency, amplitude and nerve conduction velocities calculated.

Statistical Analysis

Normality of numerical data was tested by Shapiro-Wilk test and Mann-Whitney U test was used for non-normally distributed data to compare 2 independent groups. Relationships between numerical variables were tested by Spearman rank correlation test and relationships between categorical variables were tested by Chi-square test. Frequency, percentage (%) and median [25%-75%] were presented as descriptive statistics. All analyses were performed using SPSS for Windows, version 24 and a P value smaller than 0.05 was considered significant.

RESULTS

The study enrolled 39 patients including 24 (61.5%) males and 15 (38.5%) females and 39 control subjects including 22 (56.4%) males 17 (43.6%) females. Patient and control groups had a mean age of 45 years. Average vitamin D concentration was 8.5 ng/ml in the patient group and 8.8 ng/ml in the control group. There was no statistically significant difference between two groups with respect to age and average vitamin D concentration (p=0.552) (Table 1). Among subgroups of vitamin D deficiency, 23 participants from each group had severe vitamin D deficiency (59%), and 16 (41%) patients and 11 (28.2%) controls were vitamin D-deficient. Vitamin D insufficiency was present only in 5 (12.8%) control subjects.

Comparing vitamin D-deficient subgroups with the control group, a statistically significantly difference was found in vitamin D level in the patient group (p=0.020) (Table 2).

Vitamin D status and median nerve conduction study: For the study, distal latency, amplitude and conduction velocity of the median nerve were obtained. A positive correlation and a significant association were found between average vitamin D concentration and prolongation of the median nerve distal latency (r=0.370, p=0.020) (Table 3). In addition to this finding, vitamin D-deficient subgroup showed greater distal latency values and a statistically highly significant association was observed between vitamin D deficiency and median nerve distal latency (p=0.024) (Table 4, Figure 1)

| Table 1. Average vitamin D levels of patient and control groups |
|-----------------|-----------------|-----------------|
| Variables       | Patients         | Controls         | P     |
| Age             | 45 (28-56)       | 45 (28-56)       | 0.384 |
| Vitamin D       | 8.5 (5.2-11)     | 8.8 (6.1-12.6)   | 0.552 |

1 Median (25%-75%); Mann-Whitney U test
Table 2. Gender distribution and vitamin D status of patients and controls by subgroups

| Groups               | Patients | Controls | P  |
|----------------------|----------|----------|----|
|                      | n        | %        | n  | %      |    |
| Gender               |          |          |    |        |    |
| Female               | 24       | 61.5     | 17 | 43.6   | 0.112 |
| Male                 | 15       | 38.5     | 22 | 56.4   |    |
| Vitamin D Status     |          |          |    |        |    |
| Insufficiency        | 0        | 0.0      | 5  | 12.8   |    |
| Deficiency           | 16       | 41.0     | 11 | 28.2   | 0.020 |
| Severe Deficiency    | 23       | 59.0     | 23 | 59.0   |    |

* Chi-square test.

Table 3. Relationships between vitamin D level and median nerve conduction values and age among patients

| Vitamin D level | Median DL (Msec) | Median Amp (Mv) | Median Velocity (M/Sec) | Age |
|-----------------|------------------|-----------------|-------------------------|-----|
|                 | \( r \)          | \( P \)         |                         |     |
|                  | 0.370*           | **0.020**       |                         | -0.016 |
|                  | 0.106            | 0.520           | 0.439                   | 0.887 |
|                  |                  | 39              | 39                      | 39   |
|                  |                  |                 |                         | 78   |

* Spearman rank correlation coefficient; n: sample size
** Significant at 0.05 level.

Table 4. Association between median nerve conduction by vitamin D-deficient subgroups

|                | Deficiency (n=16) | Severe Deficiency (n=23) | \( P \) |
|----------------|-------------------|--------------------------|--------|
| Median DL      | 3.44 (3.14 -3.75) | 3.1 (2.92 -3.48)         | 0.024  |
| Median Amplitude | 3.01 (2.24 -5.2) | 4.37 (1.91 -6.42)        | 0.855  |
| Median Velocity | 47.85 (43.4 -51.2)| 49.2 (44.9 -53.4)        | 0.437  |

* Mann-Whitney U test.

DISCUSSION

Vitamin D has been suggested to be a neurotropic hormone. It was suggested that vitamin D exerts its neuroprotective effect through downregulation of L-type calcium channel expression or upregulation of vitamin D receptor (VDR) expression [11]. Thus, vitamin D deficiency has been identified as a factor associated with increased risk for development of neurological diseases. Increased VDR expression in the embryological stage was shown to induce higher apoptosis levels and decrease mitosis with effects on cell proliferation and neuronal development [12]. Another widely accepted mechanism to explain the neuroprotective action of vitamin D involves reduction of reactive oxygen species (ROS) by vitamin D [13].

1,25(OH)2 D3 was demonstrated to promote antioxidant activity in glial cells and neurons and reduce ROS in dead cells [14]. Vitamin D may interfere with nociceptor functions by causing diabetic nerve damage, which results in a decrease in the pain threshold in comparison with the nondiabetic population [15]. Alamdari et al. [16] demonstrated that a decreased level of circulating 25(OH)-D may contribute to an increased risk of large-fiber neuropathy in diabetic patients.

Interestingly, in a recent study, a non-linear contribution of serum vitamin D to symptomatic diabetic neuropathy occurrence was reported, which suggests careful monitoring of vitamin D administration [17]. In order to delineate a specific pathology, the current study focused on a single nerve. As mentioned above, several previous studies have mostly investigated the effect of vitamin D on the development of diabetic peripheral neuropathy. Despite seasonal changes, the reported prevalence of vitamin D deficiency varies from 30% to 80% in the global population [18-21].

In a study examining the relation between vitamin D level and neuropathic pain experienced by patients with carpal tunnel syndrome, vitamin D concentration was found to be markedly lower in patients with mild CTS [22]. However, a separate study involving the use of Boston Carpal Tunnel Questionnaire to assess symptom severity did not find an association between vitamin D level and pain symptoms and functional status [23]. In the current study, vitamin D was statistically significantly lower in the patient group versus control group. In another study, the severity of CTS was correlated with vitamin D levels in the deficiency group and a correlation was reported between weight gain and neuropathic pain intensity in vitamin D-deficient patients with carpal tunnel syndrome [24].

In our study, neither the Boston scale nor the neuropathic pain assessment scale was used. Vitamin D deficiency was shown to be an independent risk factor for development of diabetic peripheral neuropathy [25]. A study which supported this finding reported that vitamin D status may be associated with carpal tunnel syndrome in women under 50 years of age [26].

In our study, a strong positive correlation was found between average vitamin D concentration and prolongation of median
nerve distal latency in the overall patient group, which lends support the results of some of the previous studies. Similarly, vitamin D-deficient subgroup showed a more pronounced association between vitamin D deficiency and prolongation of median nerve distal latency.

In conclusion, vitamin D deficiency remains a significant public health concern which poses challenges for clinicians in all fields of medicine. Our current study and many previous studies demonstrated evidence that vitamin D deficiency plays a role in the development of both neuropathy and increased severity of neuropathic pain. Given the neuroprotective action of vitamin D and the involvement of vitamin D deficiency in several neurological diseases as well as evidence that it might be an independent risk factor and a potential biomarker for neuropathy, we believe that patients presenting with mononeuropathy or polyneuropathy to a healthcare facility should be screened for vitamin D deficiency.

Conflict of Interests: The authors declare that they have no conflict of interest.

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