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Serum Vitamin D Level and its Relation with Clinical Parameters in Fibromyalgia as a Neuropathic Pain

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Abstract

The aim of this article is to examine the role of vitamin D on severity of pain in patients with fibromyalgia. Eighty premenopausal female fibromyalgia patients and 90 healthy controls were included in the study. The demographic characteristics of all subjects, including age, and body mass index, were recorded. The number of tender points was recorded, and the intensity of pain of the subjects was measured by Visual Analogue Scale (VAS). Fibromyalgia Impact Questionnaire (FIQ) was used to evaluate disease severity. The mean age was 44.86 ± 2.4 and 41.48 ± 4.1 years for the patient and control groups, respectively (p=0.08). The mean levels of vitamin D in patient and control groups were determined as 19.9 ± 4.5 and 32.97 ± 13.31 ng/ML, respectively (p<0.001). Apart from BMD in lumbar spine and femur which were significantly lower in the patients compared with healthy women. Vitamin D levels were negatively correlated with VAS (r=-0.653; p=0.001) and FIQ total scores in the fibromyalgia group (r=-0.344; p=0.030). Furthermore, the mean value of LANSS was 16.5 ± 0.4 in patient group.

In conclusion, the study confirmed high prevalence of hypovitaminosis D and osteoporosis in patients with FMS than in controls. Furthermore, vitamin D was closely related with pain and disease severity.

Keywords: Fibromyalgia; Vitamin D; Chronic pain

Introduction

Fibromyalgia Syndrome (FMS) is characterized by chronic diffuse musculoskeletal pain with unclear etiology. It is believed that patients with fibromyalgia may have alterations of the neuroendocrine function, characterized by mild hypocortisolemia, hyperreactivity of pituitary adrenocorticotropin hormone release in response to challenge, and glucocorticoid feedback resistance.

Studies suggested that vitamin D was the 'forgotten neurosteroid' which is required for normal brain homeostasis and development [1].

The role of vitamin D_3 as a vitamin or essential dietary component has achieved increasing prominence over the past 3 to 4 decades in the public health arena. Researchers consider 1α, 25 $(OH)_2$ D_3 to be a steroid hormone and believe that it functions the same way as other steroid hormones [2].

Vitamin D is a steroid hormone acts on the musculoskeletal system which associated with symptoms related to its deficiency could be responsible for diffuse muscle pain also in FMS. Tandeter et al. [3] reported a correlation between low serum 25 (OH) D levels and higher rates of muscle generalized pain in FMS patients.

In recent years, vitamin D deficiency has been linked to chronic pain including neuralgia and muscle pain. Studies have reported that an association between vitamin D deficiency and fibromyalgia and vitamin D replacement may have a therapeutic role in the management of fibromyalgia symptoms.

Neuroanatomy correlates with the psychological changes of pain. The studies suggested that chronic neuropathic pain was associated with impairment in the firing activity of the locus coeruleus and its expression of noradrenaline in ascending and descending pathways. This connection plays roles in not only pain perception, but mood, anxiety, attention and concentration, the sympathetic nervous system, and the activity of the hypothalamic-pituitary-adrenal axis [4].

The first of our aims was to evaluate vitamin D levels in patients with fibromyalgia in comparison to healthy controls, and the second one was to investigate the relation between clinical parameters and vitamin D level in fibromyalgia patients.

Patients and Methods

The study is a consecutive prospective case control study. Patients who were referred to the physical medicine and rehabilitation outpatient service for evaluating for fibromyalgia. Consent was obtained from all subjects who participated in the study. Eighty consecutive premenopausal female patients with FMS were recruited. FMS patients were diagnosed according to the ACR 1990 criteria of FMS [5]. Inclusion criteria included presence of nonspecific musculoskeletal pain for at least 3 months. We excluded postmenopausal women in this study. Subjects were excluded if they had a systemic metabolic disease, malignancy or pregnancy, endocrine disorders or drug therapy such as calcium, oral contraceptives or some other drugs. Patients using calcium or vitamin D in the past one year were also excluded.

At the same day of loco-motor examination, blood samples were obtained from all subjects after over-night fast. Full blood count, erythrocyte sedimentation rate, liver, kidney and thyroid function tests, serum phosohorus, calcium, alkaline phosphotase and parathyroid hormone and C-telopeptide were measured with routine laboratory methods in sera of all patients and controls. Serum 25-

hydroxyvitamin D level was measured by enzyme-linked immunoabsorbent assay (ELISA) method. 25 (OH) D_3 was used to determine vitamin D level. Vitamin D levels were measured during the summer period. Vitamin D deficiency is defined as levels<25 ng/mL.

The control group included 90 healthy women. The control group was matched to relative group for the age, education and gender. They had no chronic muscle pain, and had normal physical examination and had normal blood tests. The study was approved by the local ethics committee of Gaziantep University, Turkey.

BMD was measured at the lomber spine and femoral neck by dual-energy X-ray absorptiometry (DXA). Bone loss was defined according to the conventional World Health Organization (WHO) definition [6].

The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale was used to discriminate between neuropathic and nociceptive pain. The LANSS pain scale contains 5 neuropathic sensory disturbance domains complemented by 2 sensory examination items [7].

Statistical Analyses

The Statistical Package for Social Sciences (SPSS 11.5, SPSS Inc, Chicago, IL) was used for all statistical analyses. The differences among cases and controls were determined by independent samples t test. Values<0.05 were considered to be statistically significant. *Pearson's* correlation test was *used* to illustrate the *relationship* between variables.

Results

The demographic characteristics of the patient and control subjects are presented in Table 1. The mean age was 44.86 ± 2.4 and 41.48 ± 4.1 years for the patient and control groups, respectively (p=0.08). The mean values of BMI were 24.15 ± 4.15 and 25.37 ± 3.23 in patient and controls (p=0.07). The mean values of menarche age were 13.25 ± 1.1 and 12.97 ± 1.1 in patients and controls (p=0.06). The mean values of number of pregnancies were 4.4 ± 0.8 and 5.05 ± 0.9 in patients and controls (p=0.08). The mean disease duration was 4.17 ± 2.34 years in patient group.

	Patients (n=80)	**Control (n=90)**	**p**
25 (OH) D_3	19.9 ± 4.5	32.97 ± 13.3	< 0.001
LANSS	16.5 ± 0.4	2.5 ± 0.2	< 0.001
FIQ total	56.6 ± 19.9		
The mean number of tender point	12.4 ± 4.5		
Lumbar BMD (g/cm^2)	94.7 ± 3.2	103.9 ± 2.8	0.04
Femoral total BMD (g/cm^2)	98.9 ± 2.5	108.0 ± 2.2	0.01
PTH (pg/ml)	72.7 ± 5.2	74.4 ± 2.5	0.2
ALP (IU/l)	92.2 ± 4.2	92.3 ± 3.4	0.2
CTx (ng/ml)	17.5 ± 21.6	16.4 ± 13.9	0.2

Table 1: Clinical parameters in patients and controls

The mean levels of vitamin D in patient and control groups were determined as 19.9 ± 4.5 ng/mL and 32.9 ± 13.3 ng/mL in respectively, (p<0.001). PTH level were 72.7 ± 5.2 pg/ml and 74.4 ± 2.5 in patient and controls (p=0.2)

The mean value of LANSS was 16.5 ± 0.4 in patients. Table 2 presents the clinical characteristics of the patients with fibromyalgia. The mean number of tender points was 12.4 ± 4.5 and the mean total FIQ score was 56.6 ± 19.9 in patients group (Table 1).

The mean values of lumbar BMD were 94.7 ± 3.2 and 103.9 ± 2.8 g/cm2 in patients and controls. The mean values of femur total BMD were 98.9 ± 2.5 and 108.0 ± 2.2 g/cm2 in patients and controls (p<0.001). Vitamin D level was significantly negative correlated with FIQ and VAS (p=0.03, r=-0.344; p<0.000 , r =-0.623 in respectively) (Table 2).

	Vitamin D
FIQ	r =-0.344 p = 0.03
VAS	r =-0.623 p < 0.000

Table 2: Correlation between serum vitamin D levels, FIQ and VAS in patients with fibromyalgia

Discussion

Our study has demonstrated several interesting findings. The first of these is the greater proportion of FMS patients with hypovitaminosis D without any differences in parathyroid hormone. It is not clear whether low level of vitamin D contributes to FMS symptoms as a cause or whether it is a result of this clinical condition [8,9]. According to the first claim, vitamin D receptors are found in neurons and glial cells, in the brain, and vitamin D acts as other neuropeptides. In the second claim, patients with FMS are less exposed to sunlight due to their reduced functional capacity [10,11].

Low levels of vitamin D have been shown more often in FMS than in other rheumatological diseases. Plotnikoff et al. [12] have been reported that 89% of subjects with generalized muscle pain were deficient in vitamin D. Olama et al. [13] has been suggested that FMS patients with low level of Vitamin D were more likely to had impairment in memory, confusion, mood disturbance, sleep disturbance and restless leg syndrome.

In our study we found that BMD values in femur and lumbar spine were significantly lower than in controls. Jensen et al. [14] found that no significant differences in regards to lumbar spine and hip BMD values in FMS and controls.

Our patients with FMS had high LANSS scores and diffuse neuropathic pain complaints. Khasar and Simms [15,16] corroborated the extremely high prevalence of paresthesias in FMS. We used a questionnaire that is part of the Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale. This instrument was developed to recognize neuropathic pain and set it apart from nociceptive pain.

Our study showed that the patients with fibromyalgia had severe vitamin D deficiency and significant correlation was found between vitamin D level and mean FIQ score. So, we thought that quality of life

and pain severity may be related with vitamin D level in fibromyalgia patients.

Vitamin D deficiency should be considered in the differential diagnosis of patients with musculoskeletal pain especially fibromyalgia. Inflammatory cytokines might modulate central and peripheral pain perception in fibromyalgia [**17**]. The involvement of 1,25(OH) D_3 in immune system regulation could therefore link muscle pain with vitamin D deficiency.

In this study, we showed that a significantly higher prevalence of low vitamin D concentrations in women with fibromyalgia as compared with age-matched female controls. This result was similar with studies in before. If confirmed on a large sample size of fibromyalgia patients, these findings would have a significant impact on the investigation and management of this condition in the future.

The sample size of our study is small, but our results are important. The presence of low vitamin D levels has been described in fibromyalgia patients in various studies [18,19]. Our results have also indicated that fibromyalgia is associated with deficiency of vitamin D in women. Furthermore, we found vitamin D level was negatively correlated with pain level.

In a conclusion, vitamin D deficiency should be kept in mind in treating women with chronic musculoskeletal pain. There is a necessity for both education of health professional and the general public concerning the optimization of vitamin D status in the management of such patients. We want to say that an early prevention should be considered in FMS patients in terms of osteoporosis and hence pain severity. These results have led to a new understanding of the treatment in women with FMS.

These findings would have a significant impact on the investigation and management of this syndrome in the future. It might be thought that decrease in vitamin D level may be the mechanism responsible for chronic widespread pain in FMS.

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