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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

The relation between serum vitamin D levels and clinical findings of fibromyalgia syndrome

Serum vitamin D seviyelerinin fibromiyalji sendromunun klinik bulguları ile ilişkisi

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ABSTRACT

Objective: This study was performed to identify serum 25-OH vitamin D levels and to investigate the relationship between 25-OH vitamin D and clinical findings on patients with fibromyalgia syndrome (FMS).

Methods: Nineteen premenopausal women with FMS who were diagnosed according to ACR 1990 fibromyalgia diagnostic criteria and 24 premenopausal healthy women as control group were included in the study. Serum 25-OH vitamin D levels were determined in both patient and control groups. Widespread body pain, headache, fatigue, morning stiffness, sleep disorder, the number of tender points, Fibromyalgia Impact Questionnaire (FIQ) scores and Beck depression scores were evaluated as clinical findings in patients with FMS.

Results: Serum 25-OH vitamin D levels were significantly lower in patients with FMS than those in control group (p=0.01). There were significantly negative correlations between 25-OH vitamin D levels and widespread body pain (r=-0.731), Beck depression scores (r=-0.777), headache (r=-0.629), and sleep disorder (r=-0.767) in the FMS group (p<0.01).

Conclusion: It was concluded that 25-OH vitamin D deficiency may be related to the clinical findings such as widespread body pain, depression, headache and sleep disorder in patients with FMS.

Key words: Fibromyalgia, clinical finding, 25-OH vitamin D

ÖZET

Amaç: Bu çalışma, fibromiyalji sendromlu (FMS) hastalarda serum 25-OH vitamin D seviyelerini belirlemek ve 25-OH vitamin D seviyelerinin klinik bulgular ile ilişkisini araştırmak amacıyla yapıldı.

Yöntemler: Çalışmaya ACR 1990 fibromiyalji tanı kriterlerine göre tanı konulan ondokuz premenapozal kadın ve kontrol grubu olarak 24 premenapozal sağlıklı kadın dahil edildi. Yaygın vücut ağrısı, baş ağrısı, yorgunluk, sabah tutukluğu, uyku bozukluğu, hassas nokta sayısı, fibromiyalji etki anketi skorları ve Beck depresyon skorları FMS'nin klinik bulguları olarak değerlendirildi.

Bulgular: Serum 25-OH vitamin D seviyeleri FMS'li hastalarda kontrol grubuna göre anlamlı olarak daha düşüktü (p=0.01). FMS grubunda 25-OH vitamin D seviyeleri ile yaygın vücut ağrısı (r=-0.731), Beck depresyon skorları (r=-0.777), baş ağrısı (r=-0.629) ve uyku bozukluğu arasında (r=-0.767) anlamlı negatif korelasyonlar vardı (p<0.01).

Sonuç: 25-OH vitamin D eksikliğinin FMS'nin yaygın vücut ağrısı, depresyon, baş ağrısı ve uyku bozukluğu gibi klinik bulguları ile ilişkili olabileceği değerlendirildi.

Anahtar kelimeler: Fibromiyalji, klinik bulgu, 25-OH vitamin D

INTRODUCTION

Fibromyalgia syndrome (FMS) is a chronic pain syndrome causing widespread body pain, stiffness, and tenderness points on specific anatomic regions. It is also characterized by restless sleep, tiredness, fatigue, anxiety, depression, and disturbances in bowel functions [1,2].

The etiopathogenesis of fibromyalgia syndrome (FMS) remains unknown. The interactions of neuroendocrine, metabolic and immunological factors are assumed to play role in the induction and mainte-

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nance of FMS [3,4]. Neuroendocrine mechanisms, various hormones, serotonin, melatonin, substance P, endorphins, and vitamin D levels were researched on until now with respect to the etiopathogenesis of FMS [5-9].

The relationship between low levels of 25-OH vitamin D and non-specific skeletal-muscular pains including FMS is controversial. While a positive correlation was found between vitamin D levels and FMS in many studies, no relationship was found in others.

The aim of this study is to determine serum 25-OH vitamin D levels in patients with FMS and the control group of healthy individuals. Additionally, the correlations between 25-OH vitamin D levels and some of the clinical findings of FMS - widespread body pain, headache, fatigue, morning stiffness, sleep disorder, the number of tender points, Fibromyalgia Impact Questionnaire (FIQ) and Beck depression scores - were evaluated.

METHODS

Nineteen premenopausal women (aged 27-47 years, average 36.35±7.04 years) who were admitted to our outpatient clinic between 1 July - 30 August 2011 and met the 1990 American College of Rheumatology (ACR) criteria for the diagnosis of FMS were enrolled in the study. The control group was composed of twenty-four age and location matched healthy premenopausal women who had normal physical examination and routine test results and had no chronic and endocrinological diseases. 25-OH vitamin D levels were determined in FMS patients and controls.

Widespread body pain, headache, fatigue, morning stiffness, sleep disorder, the number of tender points, Fibromyalgia Impact Questionnaire (FIQ) and Beck depression scores were evaluated as clinical findings in patients. Fibromyalgia Impact Questionnaire (FIQ) was evaluated by Turkish version [10] of original FIQ [11]. The number of tender points was determined by ACR 1990 diagnostic criteria [12]. Depression scores were evaluated by Turkish version [13] of original Beck Depression Scale [14]. Widespread pain and fatigue were measured with 10-cm visual analog (VAS) scale [15]. Morning stiffness was evaluated by morning stiffness scale of Lequesne index (as 0=no stiffness, 1=low stiffness-less than 15 minutes, 2=severe stiffness-more than 15 minutes) [16].

Sleep disorder was evaluated sleep latency component of Pittsburgh Sleep Quality Index (as 0= no difficulty or difficulty falling asleep for ≤ 15 minutes, 1=difficulty falling asleep for 16-30 minutes, 2=difficulty falling asleep for 31-60 minutes, 3=difficulty falling asleep for more than 60 minutes) [17]. Headache was evaluated by 4 definitive words of Short-Form McGill Pain Questionnaire used to determine the affective dimensions of pain (as 0=no headache, 1=low headache, 2=mild headache, 3=severe headache) [18].

Since neuroendocrine abnormalities have role in FMS etiopathogenesis, premenopausal women were included into the study. All subjects were asked to complete a general questionnaire including questions about detailed personal medical history, vitamin D usage, age, location, menstruation cycle, smoking and alcohol consumption. Participants who had neurological, inflammatory, endocrine, chronic disease, osteoporosis, pregnancy previously existing psychiatric illness and taking vitamin D supplementation were excluded from the study. Since serum 25-OH vitamin D levels show seasonal variations and summer sunshine is an important source of vitamin D, blood samples were taken from the patients in July and August.

Serum 25-OH vitamin D levels were measured in Roche E170 hormone analyzer by electrochemiluminescence method and results were reported in units of ng/ml.

Descriptive statistical methods (mean, standard deviation) were used to evaluate the data. All results are expressed as mean plus minus standard deviation and percentage. The unpaired Student's t test was used to evaluate the significance of differences between groups. Spearman correlation analysis was used to determine the correlations between findings. P values less than 0.05 were considered significant, at 95%confidence interval. Data were analyzed using the SPSS/PC statistical software package (SPSS, v.20.0 for Windows, SPSS Inc. Chicago).

This study was approved by the ethics committee of Ataturk University Faculty of Medicine, and informed consent was obtained from each subject.

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 1983.The authors declare that there is no conflict of interest.

RESULTS

The mean age of patients was 35±7.45 years for the FMS group and 36±8.29 years for the control group. There were no significant differences between groups in terms of age (p>0.05). The mean duration of symptoms in the FMS group was 4.35±1.20 years. The mean tender point score in the FMS group was 15.3±1.8 points.

25-OH vitamin D levels of FMS patients and control group are shown in Table 1. Serum 25-OH vitamin D levels were significantly lower in patient group compared with control group (p=0.04). There was no significant correlation between age and 25-OH vitamin D levels. Mean, standard deviation and percentage values of clinical findings are given in Table 2.

The correlations of 25-OH vitamin D levels and clinical findings in FMS patients were analyzed (Table 3). There were significantly negative correlations between 25-OH vitamin D levels and widespread body pain (r=-0.731, p<0.01), Beck depression scores (-0.777, p<0.01), headache (-0.629, p<0.01), and sleep disorder (r=-0.767, p<0.01) in FMS patients.

Table 1. 25-OH vitamin D levels of FMS patients and the control group

	FMS group	Control group	p
25-OH vitamin D (ng/ml)	13.92±6.19	20.49±7.63	0.04

Table 2. Mean, standard deviation and percentage values of clinical findings in FMS patients

Clinical finding	Mean ± SD	%
WBP	3.97±2.65	
Fatique	2.83±2.45	
FIQ	19.27±21.52	
NTP	5.95±5.45	
Beck DS	23.46±21.22	
Morning Stiffness (minutes)	12.36±4.74	
Headache		73.70
Sleep Disorder		63.20

SD: Standard deviation, WBP: Widespread Body Pain, FIQ: Fibromyalgia Impact Questionnaire, NTP: Number of Tender Points, Beck DS: Beck Depression Scores

Table 3. Correlation coefficients (r) of 25-OH vitamin D levels with clinical findings in FMS patients

	WBP	Fatigue	FIQ	NTP	Beck DS	Morning Stiffness	Headache	Sleep Disorder
25-OH Vitamin D	-0.731*	0.196	0.231	-0.250	-0.777*	0.683	-0.629*	-0.767*

WBP: Widespread Body Pain, FIQ: Fibromyalgia Impact Questionnaire, NTP: Number of Tender Points, Beck DS: Beck Depression Scores, * :p<0.01

DISCUSSION

The main aim of the study is to identify serum 25-OH vitamin D levels and to investigate the relationship between 25-OH vitamin D and clinical findings on patients with fibromyalgia syndrome (FMS), which is a chronic pain syndrome.

In literature, findings on vitamin D levels in FMS patients show varying scores. Many studies examining vitamin D levels in FMS patients in different countries of the world have reported low or insufficient levels. Low levels have been reported in studies which were conducted in Europe [19,20], the United States [21], in S. Arabia and Pakistan with a high percentage of as 74 % of FMS patients [22]. Low levels of vitamin D were also reported in a recent study conducted on 141 FMS patients in Turkey. Vitamin D deficiency was detected in 76 % of patients and it was concluded that vitamin D treatment in FMS patients might cause regression of disease symptoms [23].

On the contrary there are studies which have not reported differences in serum levels of vitamin D levels between FMS patients and healthy controls [24]. Similar with most studies in the literature, in our study vitamin D levels in patients with FMS

were found to be lower than the level in the control group.

The relation of vitamin D deficiency and chronic pain is also focused in literature. In many studies vitamin D deficiency is pointed to play a role in chronic widespread pain syndromes including fibromyalgia [25,26]. Although the basic function of vitamin D is to regulate bone metabolism, muscle and nervous system are two of the target organs of vitamin D [27].

Even though it is not exactly known how vitamin D deficiency creates pain and how vitamin D therapy reduces pain, there is strong evidence for abnormal central pain processing in FMS in vitamin D insufficiency. There are several theories on how vitamin D level affects pain. One of these theories suggests that insufficient vitamin D causes impairment on bone metabolism by a series of reactions. Insufficient vitamin D levels impair bone mineralization by causing formation of a spongy matrix below the periosteal membrane. This gelatin-like matrix can expand by liquid absorption and can cause formation of an outward pressure from periosteum. As a result, it causes pain generation in these tissues, which are highly innerved by nerve fibers [28,29]. Another theory suggests that infections activate inflammatory cytokines, which modulates central and peripheral pain sensation in FMS [30]. Since 1,25(OH)2 vitamin D takes part in immune system regulation, a relationship can be set between vitamin D deficiency and muscle pains [31].

In a recent study conducted with a large population of 3495 women and 3365 men FMS patients, relationship between 25-OH vitamin D levels and increased pain level in female patients were reported [31].

On the other hand, in many studies conducted with FMS patients, negative correlations were also found between vitamin D levels and widespread body pain [25], and skeletal pain [26]. In our study, negative correlations were found between vitamin D levels and widespread body pain and headache in FMS patients. Our results point additional evidence on the fact that vitamin D deficiency might create pain.

Since FMS patients have various symptoms and no significant disorder could be found by physical examination and laboratory findings, symptoms are thought to be psychological. Many studies showed negative correlation between 25-OH vitamin D levels and Beck depression scores on FMS patients [32,33]. Besides there are many reasons for abnormal pain sensation and other symptoms of FMS patients, psychological disorders are accepted to have a role in improvement of severity of pain sensation.

Another noteworthy finding of our study is, the significant negative correlation ($r=-0.777$, $p<0.01$) found between vitamin D levels and Beck depression scores in FMS patients supports the data that increased prevalence of depression might be observed in FMS patients.

In a study determining 25-OH vitamin D levels in FMS patients and healthy controls, much sleep disturbance was reported to be seen in patients who had lower 25-OH vitamin D levels [33]. Similarly, a relationship between 25-OH vitamin D levels and sleep disturbance was found in our study.

As a result of our study, we determined that vitamin D levels are lower in patients with FMS than those in control group, and we concluded that vitamin D levels are effective on FMS symptoms. Since etiopathogenesis of FMS is not well known, treatment of FMS should be planned according to existence and severity of prominent symptoms.

Small sample size is the limitation of our study. Since determination and, if necessary, replacement of 25-OH vitamin D levels can play a key role in treatment of FMS symptoms; we consider that, relation between 25-OH vitamin D and fibromyalgia symptoms should be supported by follow-up studies conducted in large number of patients, including study groups with and without vitamin D supplementation.

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