VITAMIN D LEVELS IN WOMEN WITH FIBROMYALGIA AND RELATIONSHIP BETWEEN PAIN, TENDER POINT COUNT AND DISEASE ACTIVITY

RAMAZANAZIM OKYAY[1], BURHANFATIH KOÇYIĞIT[2], SAVAŞ GÜRSOY[2]
[1]Ceyhan Community Health Center, Adana, Turkey, [2]Gaziantep University Medical Faculty, Department of Physical Medicine and Rehabilitation, Gaziantep, Turkey

ABSTRACT

Introduction*: Fibromyalgia syndrome (FMS) is a chronic syndrome characterized by widespread musculoskeletal pain, tender points and fatigue. There are several studies suggesting a possible relationship between musculoskeletal pain and vitamin D deficiency. In this study, we aimed to compare serum vitamin D levels between fibromyalgia patients and control groups and investigate the relationship between vitamin D and clinical findings on patients with fibromyalgia syndrome.*

Materials and methods*: This case control study enrolled 79 women with fibromyalgia who fulfilled the American College of Rheumatology 1990 criteria and 80 healthy women. All subjects were evaluated with vitamin D and other biochemical markers. The patients were divided into three groups based on their serum vitamin D levels (normal, insufficient, deficient). Visual analogue scale and fibromyalgia impact questionnaire were used to evaluate the patients with FMS.*

Results*: Mean serum vitamin D levels were lower in the FMS group than in the controls (12.99±8.37 ng/ml vs.16.05±9.42 ng/ml, p=0.037). Vitamin D level was significantly negative correlated with visual analogue scale, tender point count and fibromyalgia impact questionnaire (p=0.000, r=-0.578; p=0.001, r=-0.361; p=0.000, r=-0.621).*

Conclusion*: It was concluded that vitamin D deficiency may be related to the clinical findings in patients with FMS.*

Key words*: Fibromyalgia, vitamin D, pain, Turkey.*

DOI:10.19193/0393-6384_2016_1_38

Received *May 30, 2015;* ***Accepted*** *January 02, 2016*

Introduction

Fibromyalgia syndrome (FMS) is a rheumatic disease characterized by chronic widespread musculoskeletal pain which is accompanied by sleep disorder, fatigue, morning stiffness, cognitive disturbance, depression and anxiety[1, 2]. FMS affects 3-4% of the population and most of the patients are female[3]. Pathophysiology of widespread pain developed in patients with FMS has not been fully understood yet. Peripheral and central mechanisms as well as genetic and environmental factors are likely to play a major role in FMS etiopathogenesis.

Vitamin D is an essential dietary component that has achieved an increasing prominence in the public health arena. Vitamin D may be more appropriately defined as a prohormone since its active form functions as a hormone. Vitamin D deficiency appears to be a widespread global problem prevalent in all age groups. Estimates suggest that up to 1 billion people around the world may have vitamin D deficiency or insufficiency[4].

Studies state vitamin D deficiency risk factors; breastfeeding without supplementation, dark skin pigmentation, female gender, lack of direct sun exposure, winter season, chronic gastrointestinal disease[5]. The most important impact of vitamin D is on calcium, phosphorus metabolism and bone mineralization. Lack of vitamin D leads to proximal muscle weakness, defects in skeletal mineralization, increased risk of falling and widespread body pain[6].

Some studies suggest an association between low vitamin D levels and non-specific musculoskeletal pain[7, 8]. The relationship between low levels of vitamin D and FMS is controversial. While some studies reported a correlation between low serum vitamin D levels and higher rates of musculoskeletal pain in FMS patients[9, 10, 11], others reported no relationship[12, 13, 14].

The purpose of our study is to determine serum vitamin D level in patients with FMS and compare them to the control group, with specific aims to investigate the correlations between vitamin D level and visual analogue scale (VAS), tender points count (TPC) and Fibromyalgia Impact Questionnaire (FIQ).

Materials and methods

The study is a consecutive case control study. 79 women aged between 18-55 who applied to Gaziantep University Faculty of Medicine Sahinbey Research and Application Hospital Department of Physical Medicine and Rehabilitation policlinic between May-September 2014 and diagnosed with FMS according to American College of Rheumatology (ACR) 1990 criteria were included in the study as the patient group. The control group included 80 volunteer healthy women who did not have any systemic diseases and showed similarities with the patient group in terms of age and demographic characteristics.

The study was carried out on premenopausal women. The following patients were excluded from the study: those with systemic metabolic disease, malignancy, pregnancy, endocrine disorders, drug therapy such as calcium, oral contraceptives, vitamin D or some other drugs.

At the same day of loco-motor examination, blood samples were obtained from all subjects after over-night fast. Complete blood count, c reactive protein, erythrocyte sedimentation rate, liver, kidney, thyroid-parathyroid function tests, serum phosphorus, calcium, alkaline phosphatase were measured with routine laboratory methods in sera of all patients and controls.

Serum 25-hydroxyvitamin D (25-OHD) level was measured by enzyme-linked immunosorbent assay (ELISA) method and results were reported in units of ng/ml. Vitamin D levels were measured during the summer period. The reference range for 25-OHD ≥ 30 ng/ml was considered as normal, vitamin D deficiency was defined as serum 25-OHD levels lower than 20 ng/ml while a level between 20 and 30ng/ml was defined as insufficiency[4].

Each member of both groups filled in and signed a detailed survey form that queries age, marital status, height, weight, body mass index (BMI), educational status, VAS and FIQ.

Tender points were determined by digital pressure from eighteen points indicated according to the ACR classification criteria[15].

VAS was used for evaluation of pain severity. The scale is 10 cm long and the patient marks the point (0= no pain, 10=the most severe pain) on a vertical or horizontal line corresponding to severity of the pain felt.

FIQ measures 10 different factors namely physical function, feeling well, not being able to go to work, having challenges at work, fatigue, morning fatigue, stiffness, anxiety and depression. Higher scores indicated greater impairment. Total maximum score is 100[16].

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) statistical software package (SPSS, v.11.5for Windows, SPSS Inc. Chicago). All results are expressed as mean ± standard deviation, number and percentage. Normal distribution of data was tested using Shapiro-Wilk test. Chi-squared test and Mann-Whitney U test was performed in order to identify differences in categorical and continuous variables between groups. Spearman correlation analysis was used to determine the correlations between findings. Kruskal-Wallis test was used to compare between subgroups of vitamin D and clinical scales. P values less than 0.05 were considered significant, at 95% confidence interval.

Results

The mean age was 36.97±8.95 and 35.75±10.67 years for the patient and control groups, respectively (p=0.325). The mean values of BMI were 27.70±3.82 in patients and 26.74±5.40 in controls (p=0.059). The demographic characteristics of the patient and control subjects are presented in Table 1.

The patient and control groups were compared in terms of vitamin D levels. In the patient group, vitamin D levels were normal in 10.1%; 79.7% were suffering insufficiency, 10.1% were suffering deficiency of vitamin D.

	Patients	Controls	p value
Age (Mean±SD)	36.97±8.95	35.75±10.67	0.325
BMI (Mean±SD)	27.70±3.82	26.74±5.40	0.059
Marital status, n (%)			
Married	60 (75.9)	51 (63.8)	0.130
Single	13 (16.5)	24 (30.0)	
Widowed/divorced	6 (7.6)	5 (6.3)	
Education			
Primary education or less	47 (59.5)	39 (48.8)	0.379
High school	16 (20.3)	19 (23.8)	
University of higher	16 (20.3)	22 (27.5)	

Table 1: Socio-demographic characteristics of patients and control groups.
SD: Standard deviation
BMI: Body mass index

In the control group 10.0% of individuals had normal vitamin D levels. The rates of insufficiency and deficiency were found to be as 63.8% and 26.3%, respectively. There was a significant difference between groups (p=0.029). The average serum vitamin D levels were lower in the patient group (p=0.037) (Table 2).

When patients were classified according to their vitamin D levels (normal, insufficient, deficient) significant difference was found between clinical scale values between groups (Table 3).

Vitamin D level was significantly negative correlated with VAS, TPC and FIQ (p=0.000, r=-0.578; p=0.001, r=-0.361; p=0.000, r=-0.621, respectively) (Table 4).

	Patients (n=79)		Controls (n=80)		p value
Vitamin D	**n**	**%***	**n**	**%***	
Deficient	63	79.8	51	63.7	**0,029**
Insufficient	8	10.1	21	26.3	
Normal	8	10.1	8	10.0	
Mean±SD	12,99±8,37 ng/ml		16,05±9,42 ng/ml		**0,037**

Table 2: Vitamin D levels in FMS patients and control group.
SD: Standard deviation

	Vitamin D deficiency	Vitamin D insufficiency	Normal Vitamin D levels	p
VAS	7.38±1.40	6.37±0.51	5.12±0.99	0.000
TPC	13.80±1.38	12.25±0.88	11.75±0.88	0.000
FIQ	56.58±8.87	48.75±2.76	41.37±8.15	0.000

Table 3: The relationship between vitamin D subgroups of FMS patients and the clinical scales.
VAS: Visual analogue scale
TPC: Tender points count
FIQ: Fibromyalgia Impact Questionnaire

	VAS		TPC		FIQ	
	r	p	r	p	r	p
Vitamin D	-0,578	0.000	-0.361	0.001	-0.621	0.000

Table 4: The correlation analysis between vitamin D levels and clinical scales.
VAS: Visual analogue scale
TPC: Tender points count
FIQ: Fibromyalgia Impact Questionnaire

Discussion

In recent years, interest on vitamin D has increased and several studies investigating the relationship between vitamin D and various diseases were performed. Serum 25 (OH) vitamin D measurement is an adopted method to determine patients' vitamin D status. Compared 1-25 (OH) vitamin D it has a longer half-life and additionally it shows the body reserves. Thus it is a more preferable measurement for clinicians[17].

The aims of our study are to identify serum vitamin D levels, and to investigate the relationship between vitamin D and clinical findings on patients with fibromyalgia.

It has been widely accepted that vitamin D is an essential nutrient for human body and is involved in various biological processes. It takes part in the regulation of more than 200 genes (18). Vitamin D deficiency is prevalent all over the world especially among children, women and the elderly. Vitamin D regulates neuromuscular functioning, reduces inflammation, and decreases the risk of some cancer types, autoimmune diseases, and cardiovascular diseases[19]. Hypovitaminosis D induces osteoarthritis, chronic pain and muscle pain[10].

Many studies examining vitamin D levels in FMS patients reported low or insufficient levels[9, 10, 11]. Armstrong et al[9] included 75 FMF patients in their study. All patients had serum vitamin D levels measured and completed the FIQ, Hospital Anxiety and Depression Score. Deficient levels of vitamin D was found in 13.3% of the patients, while 56.0% had insufficient levels and 30.7% had normal levels. Patients with vitamin D deficiency had higher Hospital Anxiety and Depression Score than patients with insufficient levels or than patients with normal levels. However, there was no relationship between vitamin D levels and Hospital Anxiety and Depression Scores. Bhatty et al.[10] forty female patients were included in their study.

Thirty two (80%) patients had Vitamin D deficiency and 8 (20%) patients had Vitamin D insufficiency. Olama et al.[11] were included 50 FMS patients and 50 healthy controls in their study. FMS patients had significantly lower serum vitamin D than controls. Serum level of the vitamin D is inversely correlated with VAS of pain, Beck score for depression and bone mineral density at lumbar spine. On the other hand, some studies did not report differences in serum levels of vitamin D between FMS patients and healthy control[12, 13, 14].

In our study vitamin D levels in patients with FMS were found to be lower than the control group. Our study showed significant negative correlation between vitamin D levels and VAS, TPC and FIQ.

It is not still known whether hypovitaminosis D contributes to FMS symptoms or it is a result of the disease. In the first theory, vitamin D affects neuronal excitability, activates signal transduction systems, inhibits COX–2expression and degrades prostaglandins. Furthermore vitamin D decreases the levels of TNF alpha and inhibits nitric oxide synthase. Nitric oxide is an important neurotransmitter to the development of central sensitization (19). In the second theory, patients with FMS are less exposed to sunlight due to reduced functional ability[18]. In addition, vitamin D deficiency may become more apparent among FMS patients due to the negative effects of the disease on patient diet.

Our study indicated that patients with fibromyalgia had severe vitamin D deficiency. Additionally, this study demonstrated significant correlation between lower vitamin D levels and VAS, TPC and FIQ. Results from this study revealed that FMS patients with 25-(OH) vitamin D lower than 20 ng/ml have higher scores in VAS, TPC and FIQ. We thought that pain severity, disease activity and quality of life may be related with low vitamin D level in FMS patients.

In conclusion, our study revealed that the majority of FMS patients referred to our clinic had insufficient levels of vitamin D. We found a clear relationship between low vitamin D levels and high levels of pain, disease activity. Although there are several studies evaluating vitamin D levels in FMS and other chronic musculoskeletal diseases, the results are contradictory. It is necessary to educate health professionals regarding the optimization of vitamin D status in the management of such patients. Vitamin D deficiency should be kept in mind in patients with chronic widespread musculoskeletal pain.

Small sample size is the limitation of our study. Large scale follow-up studies should design the effect of vitamin D supplementation in the patients with FMS.

References

1) Rooks DS. *Fibromyalgia treatment update*. Curr Opin Rheumatol 2007; 19: *111-7*.
2) Thompson ME, Barkhuizen A. *Fibromyalgia, hepatitis C infection and the cytokine connection*. Curr Pain Headache Rep 2003; 7: *342-7*.
3) Sarzi-Puttini P, Rizzi M, Andreoli A, Panni B, Pecis M, et al. *Hypersomnolence in fibromyalgia syndrome*. Clin Exp Rheumatol 2002; 20: *69-72*.
4) Holick MF. *Vitamin D deficiency*. N Engl J Med 2007; 357: 266-81.
5) Hickey L, Gordon CM. *Vitamin D deficiency: new perspectives on an old disease*. Curr Opin Endocrinol Diabetes 2004; 11: *18-25*.
6) Holick MF. *Resurrection of vitamin D deficiency and rickets*. J Clin Invest 2006; 116: *2062-72*.
7) Atherton K, Berry DJ, Parsons T, Macfarlane GJ, Power C, et al. *Vitamin D and chronic widespread pain in a white middle-age. British population: evidence from a cross-sectional population survey*. Ann Rheum Dis 2009; 68: *817-22*.
8) Plotnikoff GA, Quigley JM. *Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain*. Mayo Clin Proc 2003; 78: *1463-70*.
9) Armstrong DJ, Meenagh GK, Bickle I, Lee AS, Curran ES, et al. *Vitamin D deficiency is associated with anxiety and depression in fibromyalgia*. Clin Rheumatol 2007; 26: *551-4*.
10) Bhatty SA, Shaikn NA, Irfan M, Kashif SM, Vaswani AS, et al. *Vitamin D deficiency in fibromyalgia*. J Pak Med Assoc 2010; 60: *949-51*.
11) Olama SM, Senna MK, Elarman MM, Elhawary G. *Serum vitamin D level and bone mineral density in premenopausal Egyptian women with fibromyalgia*. Rheumatol Int 2013; 33: *185-92*.
12) Ulusoy H, Sarica N, Arslan S, Ozyurt H, Cetin I, et al. *Serum vitamin D status and bone mineral density in fibromyalgia*. Bratisl Lek Listy 2010; 111: *604-9*.
13) Huisman AM, White KP, Algra A, Harth M, Vieth R, et al. *Vitamin D levels in women with systemic lupus erythematosus and fibromyalgia*. J Rheumatol 2001; 28: *2535-9*.
14) Tandeter H, Grynbaum M, Zuili I, Shany S, Shvartzman P. Serum 25-OH vitamin D levels in patients with fibromyalgia. Isr Med Assoc J 2009; 11: 339-42.
15) Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, et al. *The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee*. Arthritis Rheum 1990; 33: *160-72*.
16) Sarmer S, Ergin S, Yavuzer G. *The validity and reliability of the Turkish version of the Fibromyalgia Impact Questionnaire*. Rheumatol Int 2000; 20: *9-12*.
17) Binkley N, Ramamurthy R, Krueger D. *Low vitamin D status: definition, prevalence, consequences, and correction*. Endocrinol Metab Clin North Am 2010; 39: *287-301*.
18) Olama SM, Senna MK, Elarman MM, Elhawary G. *Serum vitamin D level and bone mineral density in premenopausal Egyptian women with fibromyalgia*. Rheumatol Int 2013; 33: *185-92*.
19) Shipton EA, Shipton EE. *Vitamin D and Pain: Vitamin D and Its Role in the Aetiology and Maintenance of Chronic Pain States and Associated Comorbidities*. Pain Research and Treatment, vol. 2015.

Ethical consideration
The study protocol was approved by the Gaziantep University local ethical committee.

Corresponding author
Dr. BURHAN FATIH KOÇYIĞIT (M.D.)
Gaziantep University Medical Faculty, Department of Physical Medicine and Rehabilitation
Gaziantep University Medical Faculty, Department of Physical Medicine and Rehabilitation
Gaziantep
(Turkey)