ORIGINAL ARTICLE

Medical Journal of Western Black Sea
Batı Karadeniz Tıp Dergisi

Med J West Black Sea 2022;6(3): 317-322
DOI: 10.29058/mjwbs.1099523

Evaluation of Vitamin D Levels in Fibromyalgia Patients and the Relation to Functional Status

Fibromiyaljili Hastalarda D Vitamin Düzeylerinin Değerlendirilmesi ve Fonksiyonel Durum ile İlişkisi

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Cite this article as: Aktunç E et al. Evaluation of vitamin D levels in fibromyalgia patients and the relation to functional status. Med J West Black Sea. 2022;6(3):317-322.

Bu çalışma 11. Türk Romatoloji Sempozyumu'nda 250 kelimeden kısa bir özet şeklinde poster olarak sunulmuştur. (26-29 Mart 2015 Türkiye)

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Received
06.04.2022

Revision
12.09.2022

Accepted
03.10.2022

ABSTRACT

Aim: Fibromyalgia syndrome is a common musculoskeletal disorder, characterized by chronic widespread pain, multiple tender points, joint stiffness, and systemic symptoms without any underlying organic disease. The initial aim of the present study was to determine the vitamin D levels in patients with fibromyalgia and compare these values to those found in healthy subjects. Then, correlations between functional status, clinical severity of the disease, and vitamin D levels were assessed.

Material and Methods: This case-control study included 137 female fibromyalgia patients and 109 healthy female counterparts. The severity of pain was assessed by a visual analogue scale and the functional impact was evaluated through the Fibromyalgia Impact Questionnaire in the patient group. Vitamin D levels were compared between groups, and the correlation between vitamin D levels and questionnaire scores was determined.

Results: Vitamin D and parathormone levels did not differ significantly between groups (p=0.858, p=0.790 respectively). The mean Fibromyalgia Impact Questionnaire scores and the medians for the visual analogue scale did not differ significantly among vitamin D deficient, insufficient, and sufficient patients (p=0.548 , p=0.952 respectively). In addition, no significant correlation between vitamin D levels and the Fibromyalgia Impact Questionnaire score was found(Spearman's rho=0.056, p=0.513).

Conclusion: This study did not show any significant differences between the vitamin D levels of fibromyalgia patients and those of healthy subjects. Further, in fibromyalgia patients, there was no correlation between vitamin D levels and functional status or disease severity.

Keywords: Fibromyalgia, Vitamin D levels, Fibromyalgia impact questionnaire

ÖZ

Amaç: Fibromiyalji sendromu, yaygın ağrı, çok sayıda hassas nokta, eklemlerde katılık ve herhangi bir organik bozukluğa bağlanamayan sistemik semptomlarla karakterize, sık görülen bir kas iskelet sistemi bozukluğudur. Bu çalışmayı yapmaktaki başlangıç amacımız, fibromiyalji hastalarında D vitamini düzeylerini belirlemek ve sağlıklı bireylerdeki ile karşılaştırmaktı. Sonrasında fonksiyonel durum ve hastalık şiddeti ile D vitamin düzeyleri arasındaki bağıntıyı değerlendirdik.

Gereç ve Yöntemler: Bu vaka-kontrol çalışmasında, 137 kadın fibromiyalji hastası ve 109 sağlıklı kadın birey karşılaştırıldı. Hasta grubunda ağrı şiddetini değerlendirmek için görsel analog skala ve fonksiyonel durumu değerlendirmek için "Fibromiyalji etki anketi" kullanıldı. Her iki gruba ait D vitamini düzeyleri karşılaştırıldı. Fibromiyaljili hastalarda D vitamini düzeyleri ile "Fibromiyalji etki anketi" skoru arasındaki bağıntı değerlendirildi.

Bulgular: Gruplar arasında D vitamini ve parathormon düzeyleri bakımından anlamlı derecede fark yoktu(Sırasıyla p=0.858 , p=0.790). Hastalarda, ortalama "Fibromiyalji etki anketi" skoru ve ortanca görsel analog skala değeri, D vitamini düzeyinin eksik, yetersiz veya yeterli olması durumuna bağlı olarak anlamlı derecede bir değişim göstermedi(Sırasıyla p=0.548 , p=0.952). D vitamini düzeyleri ile "Fibromiyalji etki anketi" skoru arasında anlamlı bir ilişki izlenmedi(Spearman's rho=0.056, p=0.513).

Sonuç: Bu çalışmada fibromiyaljili hastalar ile sağlıklı bireyler arasında D vitamini düzeyleri bakımından anlamlı bir fark görülmedi. Fibromiyalji hastalarında D vitamini düzeyleri ile fonksiyonel durum ve hastalık şiddeti arasında anlamlı bir bağıntı yoktu.

Anahtar Sözcükler: Fibromiyalji, D vitamin düzeyi, Fibromiyalji etki anketi

INTRODUCTION

Fibromyalgia syndrome (FMS) is a common musculoskeletal disorder hallmarked by widespread pain, multiple tender points, joint stiffness, and systemic symptoms without any underlying disease (1). Mood disorders, fatigue, cognitive dysfunction, and insomnia are among the systemic symptoms associated with FMS (1). In the general population, the prevalence of FMS is estimated to be around 2% (2), with women nine times more prone to developing FMS than men (3). The etiology and pathogenesis of FMS, as well as the cause of the associated widespread pain, has not been determined (4). However, neuroendocrine and autonomic dysfunction, in addition to central pain and mechanisms of central sensitization, are among the factors thought to be linked to the emergence of pain in FMS (4). Environmental and genetic factors also play roles in the etiopathogenesis.

Vitamin D is an essential steroid prohormone, responsible for the utilization of dietary calcium (5). Deficiency of vitamin D negatively affects calcium and phosphorus metabolism, osteoblastic activity, ossification of bone matrix, bone turnover, and bone mineral density (5).

Inadequate vitamin D synthesis caused by inadequate sun expore as a result of, for example, working indoors, extensive clothing, and geographical disadvantages, is the principal reason for the worldwide pandemic of hypovitaminosis D. Many types of cancer, chronic pain, autoimmune diseases, hypertension, and growth and developmental delays in children have been shown to be related to hypovitaminosis D (6,7).

The association between low levels of vitamin D and nonspecific musculoskeletal pain, including FMS, is controversial. Several studies have reported a positive association, while others have found none (6,8-12). As indicated in various studies, patients with FMS are significantly and negatively affected by deterioration of functional status and quality of life (13,14). The latter reductions are generally attributed to fatigue, sleep disorders, and psychiatric signs that are frequently associated with widespread pain. These common signs and symptoms negatively affect the daily activities of patients. A review of the literature also supports relationships between vitamin D deficiency and quality of life, anxiety levels, sleep disorders, and depression-related issues in FMS patients (11,15,16).

The initial aim of the present study was to determine the vitamin D levels in patients with FMS and compare these values to those found in healthy subjects. Then, correlations between functional status, clinical severity of disease, and vitamin D levels were assessed.

MATERIAL and METHODS

This case-control study included a group of female FMS patients (n=137) diagnosed according to the 1990 American College of Rheumatology (ACR) critera (17) at the outpatient clinic of the Physical Therapy and Rehabilitation Department and an age matched female healthy control group (n=109). The study was approved by the local ethical committee for human research (Date: 02/05/2012, number: 2012/10-5), and all of the participants gave informed consent.

The demographic characteristics, past medical histories, and current use of medications in the subjects were questioned. Serum biochemistry values, including vitamin D and parathormone levels, were evaluated. Patients that had any diseases or that were on medications that affect vitamin D metabolism (e.g., metabolic bone diseases, chronic liver and kidney diseases, surgical interventions of the gastrointestinal tract, malabsorption syndromes, tuberculosis, and the use of antituberculosis or anticonvulsant drugs) were excluded from the study.

Information about age, body mass index [BMI = Weight (kg) / Height^2 (m)], marital status, child bearing status, level of education, occupation, and duration of daily sun exposure were recorded both for the case and control group subjects. A visual analogue scale (VAS) from 0 to 10 cm was utilized for assessment of the severity of pain in the FMS patients. The functional impact and severity of the FMS was evaluated through the Fibromyalgia Impact Questionnaire (FIQ), a tool that is valid and reliable for use in Turkish patients (18). The FIQ was developed by Burchardt et al. for assessment of the quality of life and functional status of FMS patients. The FIQ includes 10 questions with subheadings inquiring about physical functioning, the impact of pain on the patient's work status (e.g., missed days of work and difficulty in working), the severity of the pain, morning fatigue,

stiffness, anxiety, depression, and well-being over the past week. The maximum possible score, including all subheadings, is 100. Moderately affected FMS patients will score 50, whereas severely affected patients will score ≥70 (19).

Vitamin D levels were measured by high performance liquid chromatography using a Zivak HPLC system (Gebze, Turkey). Vitamin D levels are considered to be deficient if <20 ng/ml, insufficient if 20.1–29.9 ng/ml, and sufficient if ≥30 ng/ml (20). Parathormone levels were measured by a chemiluminescence technique using Immulite 2000 (Diagnostic Products Corp., LA, USA). The normal reference range for parathormone levels is 16–87 μg/L.

Statistical Analysis

Statistical analysis was performed using SPSS 20.0 (SPSS Inc.; Chicago, IL, USA). The continuous variables are presented as mean and standard deviation. The normality of the distribution for continuous variables was checked by Shapiro–Wilk's test. The normally distributed continuous variables among groups were compared by student t and ANOVA tests, otherwise Mann Whitney-U and Kruskall–Wallis analysis of variance were utilized. Categorical variables are presented as frequency and percent . Chi square test with yate's correction and Pearson's chi-square test were used to compare groups for categorical variables. As the parametric test assumptions are violated with FIQ scores and vitamin D levels, Spearman's test was used to determine correlations between these values. P values less than 0.05 were deemed to be statistically significant.

RESULTS

The present study consisted of a case group of 137 female patients with FMS and 109 healthy female control counterparts. The study and control groups were comparable with regards to mean age, BMI, child bearing status, marital status, educational status, occupation, and duration of sun exposure (Table 1).

The mean values for vitamin D and parathormone levels were not significantly different between the groups (Table 2) (p=0.858 , p=0.790 respectively). The study and control groups were also comparable with regards to having deficient, insufficient, or sufficient vitamin D levels (Table 3) (p=0.480). The mean FIQ scores and median VAS values were not significantly different among vitamin D deficient, insufficient, or sufficient subjects (Table 4) (p=0.548 ,

Table 1: Comparison of the demographical characteristics of the study and control group subjects.

		Study group (n=137)	Control group (n=109)	p
Age	(Mean±SD)	42.7±11.4	45.3±11.9	0.058*
	Median (Min-Max)	42 (16-72)	47 (19-69)	
Body mass index	(Mean±SD)	27.8±5.6	28.2±5.9	0.578*
	Median (Min-Max)	27.50 (18.10-55.47)	26.80 (16.80-44.10)	
Marital status n (%)	Married	118 (86.1)	96 (88.1)	0.400**
	Single	19 (13.9)	13 (11.9)	
Child bearing status	Median (Min-Max)	2 (0-7)	2 (0-6)	0.316**
Educational status n (%)	Primary school	66 (48.2)	59 (54.1)	0.626**
	College degree	48 (35.0)	35 (32.1)	
	Higher education	23 (16.8)	15 (13.8)	
Occupation n (%)	Employed	43 (31.4)	26 (23.9)	0.122**
	Unemployed	94 (68.6)	83 (76.1)	
Duration of sun exposure (minutes)	(Mean±SD)	117.3±99.0	103.8±94.1	0.163*
	Median (Min-Max)	120.00 (5.00-480.00)	60.00 (5.00-480.00)	

*Mann–Whitney U test, **Pearson's chi-square test

Table 2: Comparison of the study groups regarding vitamin D and parathormone levels.

	Study group (n=137)	Control group (n=109)	p *
Vitamin D (ng/ml) Median (Min-Max)	20.8 (4.6-59.0)	21.0 (4.0-44.6)	0.858
Parathormone (pg/ml) Median (Min-Max)	62.0 (12.8-141.0)	62.0 (12.8-198.0)	0.790

* Mann–Whitney U test

p=0.952 respectively). Variations in the FIQ score were not correlated with deficient, insufficient, or sufficient vitamin D levels in patients (Spearman's rho=0.056, p=0.513).

DISCUSSION

In the present study, we aimed to determine the vitamin D levels of patients diagnosed with FMS according to 1990 ACR criteria and to disclose any correlation between the degree of functional deterioration and the severity of the FMS in cases with lower vitamin D levels. This study failed to show significant differences between the vitamin D levels in FMS patients and healthy controls. We also failed to show correlations between vitamin D levels and the functional status and disease severity in FMS patients. In addition, the results of the two groups were similar in terms of parathormone levels.

FMS causes both physical and psychological impairment and affects the quality of life in patients (13). Quality of life is worsened by the frequently encountered concomitant problems in FMS, such as headaches, sleep disorders, anxiety, and depressive disorders, in addition to the widespread musculoskeletal pain itself. Likewise, defficiency of vitamin D has been acknowledged as a precipitator of both physical and psychological disorders and a contributor to deterioration of the quality of life of FMS patients in recent years. In some trials, the ameliorative effect of vitamin D supplementation on diffuse musculoskeletal pain and quality of life was evident, and those results were consistent with previous studies (21, 22).

Because there are vitamin D receptors in various body tissues apart from the musculoskeletal system, this vitamin is suggested to have an important role in the normal functioning of many organ systems (5). For this reason, various studies appraising the contribution of vitamin D deficiency to autoimmune disorders, cardiovascular disorders, depression, sleep disorders, diabetes, various types of cancers, and chronic nonspesific musculoskeletal pain have been carried out and are still under way (23, 24).

Although vitamin D has been suggested to cause pain through inflammatory cytokine synthesis, its exact role in the emergence of pain in many chronic painful conditions, other than osteomalasia, is yet to be explained in detail (10, 23). Vitamin D deficiency can cause chronic pain and can complicate diagnosis of widespread chronic painful conditions, including FMS. At the same time, chronic widespread pain has been shown to be more frequently associated with low levels of vitamin D than other rheumatologic conditions (6, 25, 26). Although there are a number of studies evaluating the relation between vitamin D levels and FMS, their results are contraversial. Some indicate a positive association (6,12,14,15,27,28), whereas others have found no relationship at all (8,11,29,30,31).

Okumuş et al. and Ulusoy et al. evaluated and compared the vitamin D status in FMS patients and healthy control subjects; neither reported a significant difference between the patients and controls (11, 32). Heidari et al. indicated a positive association of vitamin D deficiency with nonspecific skeletal pain, especially in female patients, but not in patients with FMS (33). Our results are in accordance with these findings as we did not observe significant differences between the vitamin D levels in FMS patients and their healthy counterparts. Likewise, we did not find a correlation between vitamin D levels and theseverity of pain in FMS patients. Moreover, the vitamin D sufficient, insufficient, and deficient subgroups among the FMS patients did not shown significant differences in the severity of pain as a function of the vitamin D level. Our results are also consistent with those of de Rezende et al. and Ozcan et al. (9, 12).

However, some studies in the literature suggest a significant corelation between the levels of vitamin D and the severity of pain in FMS patients (11, 15). In short, the findings in the literature regarding the relationship between vitamin D levels and the severity of pain are highly contraversial. The proposition of vitamin D deficiency or insufficiency causing or aggravating musculoskeletal pain requires proof,

Table 3: Comparison of the study groups regarding vitamin D levels.

Vitamin D	Study group n (%)	Control group n (%)	p*
Deficient	70 (51)	53 (49)	0.480
Insufficient	40 (29)	39 (36)	
Sufficient	27 (20)	17 (16)	
Total	137 (100)	109 (100)	

* Pearson's chi-square test

Table 4: Comparison of the mean Fibromyalgia Impact Questionnaire score and the median visual analogue scale value in fibromyalgia patients with respect to vitamin D levels.

Vitamin D		Deficient	Insufficient	Sufficient	p
FIQ†	(Mean±SD)	52.6±11.6	54.2±14.3	54.3±13.9	0.548*
	Median (Min-Max)	51.9 (33.7-87.3)	55.1 (14.4-89.4)	55.5 (15.4-76.3)	
VAS‡	Median (Min-Max)	7 (3-10)	7 (3-9)	6 (3-10)	0. 952**

†Fibromyalgia Impact Questionnaire score, ‡Visual analogue scale value, *Kruskall-Wallis analysis of variance, ** Pearson's chi-square test

such as an alleviation or elimination of musculoskeletal pain through vitamin D supplementation in patients. As the results vary greatly among studies, a presumed relation between the levels of vitamin D and musculoskeletal pain is hard to simply reject or accept. Some studies on patients with chronic pain suggest that lower vitamin D levels contribute to enhanced central sensitivity; pain processing was especially enhanced following mechanical stimulation (34). In a study comprising 174 patients with chronic pain by von Kanel et al., the lower vitamin D levels were found to be correlated with the severity, but not the extensiveness, of pain (34).

A report highlighting the positive effect s of vitamin D supplementation on pain and the quality of life in patients with diffuse musculoskeletal pain is consistently supported by previous studies (21, 22). In the present study of 137 patients with FMS, no correlation was observed between vitamin D levels and FIQ scores for disease severity and degree of functional impairment. Moreover, the FMS patients' FIQ scores did not differ significantly regardless of whether the patient was vitamin D deficient, insufficient, or sufficient.

Although Armstrong et al. showed a significant relationship between lower vitamin D levels and anxiety or depression, they failed to disclose any relation between vitamin D levels and FIQ scores in FMS patients (15). In a study investigating the relationship between serotonin and vitamin D levels and disease severity in patients with fibromiyalgia, no significant relationship was found between vitamin D and disease severity,but serotonin levels were found to be statistically significantly lower in the severe disease group(35). Okumuş et al., in their study on 40 FMS patients and 40 healthy controls, observed that the patient group was significantly overweight and physically more inactive than the control group. In addition, lower levels of vitamin D in the patient group were found to be associated with a negative effect on FIQ-ADL scores. Lower FIQ-ADL scores were suggested to reflect the level of impairment in daily activities and quality of life in the patient group (11). There was also a study on 42 patients of FMS that depicted the positive effect of oral vitamin D replacement therapy for 20 weeks on functional capacity (22). In the present study, the levels of vitamin D were not found to be significantly different in FMS patients compared to the control group, and vitamin D did not have any significant impact on the functional status or disease severity. Although there are plenty of studies in literature evaluating the relation between vitamin D levels and FMS, their results are highly contraversial. While numerous studies have reported vitamin D levels to be normal in FMS patients, there are also studies finding lower vitamin D levels. Lower levels of vitamin D may cause chronic pain, adding confusion to a definitive diagnosis in patients with chronic widespread painful conditions, including FMS.

In conclusion, vitamin D levels do not differ significantly between FMS patients and healthy control subjects. Moreover, there is not asignificant correlation between vitamin D levels and the intensity of pain or disease severity in FMS. Further studies are warranted in order to establish a firm bais for an evidence based approach to vitamin D defficiency in FMS patients.

Acknowledgment

None.

Author Contributions

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Conflicts of Interest

The authors declared that they had no conflict of interest.

Financial Support

No financial support was used for this study.

Ethical Approval

The study was approved by Bülent Ecevit University Ethics Committee (Date: 02/05/2012, number: 2012/10-5).

Review Process

Extremely reviewed and accepted for the publication.

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