Effects of Vitamin D Therapy on Quality of Life in Patients with Fibromyalgia

Fibromiyalji Hastalarında D Vitamini Tedavisinin Yaşam Kalitesi Üzerinde Etkisi

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ABSTRACT

Objective: The role of vitamin D in the etiopathogenesis of fibromyalgia and non-specific musculoskeletal pain is controversial. In our study, we aimed to investigate the effect of vitamin D therapy on quality of life in patients with fibromyalgia.

Materials and Methods: Seventy patients diagnosed with fibromyalgia and 65 age- and sex-matched controls were included in the study. Patients were grouped as deficient (<20 ng/mL), inadequate (20-30 ng/mL), and sufficient (>30 ng/mL) according to the levels of vitamin D. Vitamin D replacement was performed for patients with deficiencies and inadequacies. Before and after vitamin D therapy, patients filled in the assessment tools, fibromyalgia impact questionnaire (FIQ), Arizona sexual experience scale (ASEX), Beck depression inventory (BDI), visual analog scale (VAS), and short form-36 (SF-36).

Results: Vitamin D deficiencies and inadequacies were observed in 60% of the patients (n=42). Among patients with low and normal levels of vitamin D, no statistically significant difference was observed in their values. In scales examined after vitamin D replacement therapy, statistically significant differences were observed in the FIQ, BDI, VAS, and SF-36 compared with pre-treatment.

Conclusion: Vitamin D deficiency seems to be linked to the pathogenesis of fibromyalgia. Vitamin D supplementation may improve the quality of life in patients with fibromyalgia.

Keywords: Depression, fibromyalgia, quality of life, vitamin D, widespread pain

ÖZ

Amaç: D vitamininin fibromiyalji ve nonspesifik kas-iskelet sistemi ağrılarının etyopatogenezindeki rolü tartışmalıdır. Çalışmamızda fibromiyalji hastalarında D vitamini tedavisinin yaşam kalitesi üzerine etkisini araştırmayı amaçladık.

Gereç ve Yöntem: Çalışmaya fibromiyalji tanısı konulan 70 hasta ve yaş-cinsiyet olarak benzer 65 kişi kontrol grubu olarak dahil edildi. D vitamini düzeylerine göre hastalar, eksiklik (<20 ng/mL), yetersizlik (20-30 ng/mL) ve yeterli (> 30 ng/mL) olarak gruplandırıldı. Eksiklik ve yetersizlik saptanan hastalar için D vitamini replasmanı yapıldı. D vitamini tedavisinden önce ve sonra, hastalar yaşam kalitesi formları olan fibromiyalji etkilenme anketi (FEA), Arizona cinsel yaşantılar ölçeği (ACYÖ), Beck depresyon ölçeği (BDÖ), Vizüel Analog skala (VAS) and Kısa form-36 (KF-36) ile değerlendirildi.

Bulgular: D vitamini eksikliği ve yetersizliği hastaların % 60'ında (n=42) gözlendi. D vitamini düşük ve normal hastalar arasında yaşam kalitesi açısından istatistiksel fark saptanmadı. D vitamini replasman tedavisinden sonra yapılan incelemelerde FEA, BDÖ, VAS 'ya göre ağrı skoru ve KF-36' da tedavi öncesi ile karşılaştırıldığında istatistiksel olarak anlamlı farklılıklar gözlendi.

Sonuç: D vitamini eksikliği fibromyalji patogeneziyle bağlantılı görünmektedir. Fibromyalji hastalarında D vitamin replasmanı yapmak hayat kalitesini yükseltebilir.

Anahtar Kelimeler: Depresyon, fibromyalji, hayat kalitesi, D vitamini, yaygın ağrı

Introduction

Fibromyalgia syndrome (FMS) is a non-inflammatory disease with widespread musculoskeletal pains, fatigue, and susceptibilities, the cause of which is not fully understood [1]. It is a syndrome accompanied by many systemic disorders and is observed in all ages, genders, and races. It is 10 times more frequent in women [2]. Its prevalence increases with age but is most commonly seen between the ages of 20 and 55 years [3]. Although symptoms concerning many systems may be observed, the most disturbing symptom is widespread pain. This is an important issue not only for the patient but also for the physician. Unfortunately, there is no known effective therapy of FMS. FMS is not a life-threatening disease; however, it can lead to serious health expenses owing to the difficulties encountered in its therapy [4].

The symptoms of FMS are similar to symptoms observed in vitamin D deficiency. Recently, researchers have been curious about this issue and have conducted a number of studies [5-9]. While there were factors that could cause confusion such as methodological differences and heterogeneous patient populations in these studies, vitamin D deficiency was reported in a considerable proportion of patients with FMS in almost every study. Despite this fact, the relationship between FMS and serum vitamin D levels is controversial, an important finding. Patients' pains can be reduced and thus the quality of life increased with an inexpensive therapeutic method such as vitamin D replacement. In a placebo-controlled study carried out on this topic, vitamin D replacement was found to be ineffective [9]. However, the number of patients was insufficient in this study. Additionally, all of the participants did not continue with the aforementioned study. In this prospective study, the aim was to assess the effect of vitamin D replacement on clinical symptoms and disease associated scores in patients with FMS who were observed to have vitamin D deficiency.

Materials and Methods

Patients and assessment

Seventy female premenopausal patients who were diagnosed with FMS according to the 2010 FMS classification criteria set and who volunteered to participate in the study and 65 healthy age- and sex-matched controls were included in this prospective study [10]. Patients who had additional diseases and conditions including obesity, smoking, alcohol use history, osteoporosis, and osteoarthritis as well as those with a history of drug use that may affect the calcium metabolism currently or prior were excluded from the study. Blood samples were taken from patients in the month of August during which the level of vitamin D is the highest. The serum 25-OH vitamin D level was measured by using an enzyme-linked immunosorbent assay (ELISA) method. A serum vitamin D level of ≤20 ng/mL was identified as vitamin D deficiency, a serum level of 21-29 ng/mL was identified as vitamin D inadequacy, and a serum level of ≥30 ng/mL was identified as normal.

Female patients in the postmenopausal or climacteric period were not included in the study. The aim here was to reduce the effect of hormonal changes and the effect of osteoporosis which frequently accompanies the postmenopausal period and thus may affect pain. All patients and healthy volunteers were informed about the study and informed consent was obtained. Before vitamin D replacement, the patients were assessed using the following scales: fibromyalgia impact questionnaire (FIQ), short form-36 (SF-36), visual analog scale (VAS), Arizona sexual life questionnaire (ASEX), and Beck depression scale. Patients with vitamin D deficiency and inadequacy were given a weekly dose 50,000 IU vitamin D (Devit-3; Deva) for 12 weeks orally. At the beginning of the fourth month after the initiation of therapy, control serum vitamin D levels were measured. It was observed that the vitamin D levels of all patients returned to normal (≥30 ng/mL). After therapy, scoring that was performed before therapy was repeated. Vitamin D levels of the patients before and after replacement were compared. The local ethics committee approval was obtained for the study.

Assessment tools

Sociodemographic Information Form

This was developed by researchers and it recorded the patient's age, gender, educational level, socioeconomic status, place of residence, marital status, and duration of illness.

Fibromyalgia impact questionnaire

This was used to assess the current health status of patients with fibromyalgia. Physical functioning, work status, depression, anxiety, morning tiredness, stiffness, pain, fatigue, and well-being over the past week were measured [11]. Its adaptation, reliability, and validity studies were performed by Ediz et al. [12] for Turkey.

Beck depression inventory (BDI)

It was used to determine the risk of depression in the test subject and to measure the level of depressive symptoms and the change in severity. It was developed by Beck et al. [13]. Its adaptation, reliability, and validity studies were performed by Hisli [14] for Turkey.

Arizona sexual life

ASEX, which was developed by McGahuey et al. [15] and the validity and reliability studies of which were carried out by Soykan [16] in Turkey, was used. In the validity and reliability study in Turkey, it was observed that the internal consistency and reliability of the scale was high with 0.89-0.90 Cronbach's values and as such valid in establishing the sexual dysfunction. The scale with separate forms for females and males was filled in by the patients, and there was no need for special training for its interpretation. The score range of the six-point Likert-type scale consisting of five items was 5-30, an increase in the total score indicates sexual dysfunction. According to Soykan, scale score of ≥11 is the breaking point for sexual dysfunction.

Visual Analog Scale

This is a scale that measures the severity of pain. VAS is a continuous scale, usually 10 cm (100 mm) in length, and the score is determined by measuring the distance and consists of 3 parts (0-30 mm: mild, 40-60 mm: moderate, 70-100 mm: severe). The scale is adapted to Turkish norms and is used in numerous studies measuring pain [17].

SF-36

This is a developed scale for the measurement of quality of life. Its Turkish validity and reliability studies were performed [18].

Statistical analysis

The statistical analysis of the study data was conducted using the Statistical Package for Social Sciences version 13.0 (SPSS Inc.; Chicago, IL, USA). Descriptive statistics are presented as frequency, percentage, mean, and standard deviation. A non-parametric test, one-sample Kolmogorov-Smirnov test was used to determine whether results from study groups conformed to normal distribution. For the analysis of differences in continuous variables between two groups, the Mann-Whitney U test was used in cases where the data distribution was abnormal and Student's *t*-test was used in cases where the data distribution resembled normal distribution. A p value less than 0.05 was considered statistically significant.

Results

In the study, the average age of the patients with fibromyalgia was 38.7±5.2 years. Among these patients, 95.7 % of them (n=67) were married, and 94.3% of them (n=66) had at least one child. The level of vitamin D was observed to be below 30 ng/mL in 60% of the patients (n=42) and in 50.7% of controls (n=33). Biochemical and demographic parameters of patients with FMS and controls are listed in Table 1.

Among patients with low and normal levels of vitamin D, no statistically significant difference was observed in their values in the FIQ, BDI, VAS, and ASEX (Table 2). In scales examined after vitamin D replacement therapy for patients, statistically significant differences were observed in the FIQ, BDI, and pain scale (VAS) compared to pre-treatment (p values, respectively, 0.001, 0.001, 0.001). After vitamin D therapy, no significant difference was observed in the fields of ASEX and sleep scores (VAS) (p values, respectively, 0.176, 0.317) (Table 3).

There were no significant difference in patients' quality of life forms between the normal vitamin D group compared and the low vitamin

Table 1. Demographic and laboratory data of study groups

Parameter	Patient (n=70)	Control (n=65)
Age (y)	38.74±5.2	38.03±4.8
Disease duration (y)	5.96±4.6	
Number of births	2.01±0.9	1.93±0.5
Number of children	1.97±0.8	1.85±0.6
Hemoglobin (g/dL) (12-16 g/dL)	12.9±0.7	12.6±0.6
Calcium (mg/dL) (8.8-10.6 mg/dL)	9.3±0.4	9.4±0.3
Phosphorus (mg/dL) (2.5-4.5 mg/dL)	3.4±0.4	3.4±0.4
Alkaline phosphatase (U/L) (30-120 U/L)	72.5±19.8	74.04±13.6
Parathyroid hormone (ng/L) (12-65 ng/L)	53.4±18.4	41.8±12.2
Vitamin D, n (%) >30 ng/mL	28 (40%)	32 (49.3%)

Values are presented as mean±standard deviation.

Table 2. Scores of FIQ, BDI, VAS, ASEX, sleep VAS, and SF-36 according to vitamin D levels

Parameter	Patients with low vit. D (n=42)	Patients with normal vit. D (n=28)	p
FIQ	61.2±13.5	61.9±15	NS
BDI	15.6±10	18.3±11	NS
VAS	84.4±12.3	85±13	NS
ASEX	18.2±5.2	18.7±6	NS
Sleep scale (VAS)	4.9±2	5.1±1.6	NS
SF-36			
1. Physical function	19.7±3.9	20.5±4.4	NS
2. Role physical	5±1.3	4.9±1.1	NS
3. Role emotional	3.7±1	3.6±0.9	NS
4. Bodily pain	5.2±1.3	5.3±1.3	NS
5. Social function	6.7±2.2	5.9±1.5	NS
6. Mental health	19.2±5	17.7±4.8	NS
7. Vitality	13.1±3.2	12.4±3.9	NS
8. General health	11.3±4	11.2±4.1	NS

FIQ: fibromyalgia impact questionnaire; BDI: Beck depression inventory; VAS: visual analog scale; ASEX: Arizona sexual experience scale

VAS: 0-30: mild, 40-60: moderate, 70-100: severe; BDI: 0-9: normal, 10-16: mild, 17-29: moderate, 30-63: severe; FIQ: 0-39: mild, 39-59: moderate, 59-100: severe.

Values are presented as mean±standard deviation.

$p<0.05$ is significant, NS: nonsignificant

D group (Table 2). After vitamin D therapy, statistically significant improvements were observed in physical function, physical role limitations, emotional role limitations, social function, mental health, vitality, and general health fields in patients' quality of life forms (SF-36). No significant difference was observed in bodily pain levels before and after therapy (Table 3).

Discussion

Fibromyalgia syndrome has gained more importance in recent years due to the fact that its etiology has not been illuminated and that patients are not totally satisfied with the current therapeutic approaches [19]. Although the pain observed in FMS is generally described by being burning, gnawing, throbbing, and sharp, sometimes patients cannot describe the character of the pain. The pain and the perception of pain observed in FMS have several features [20]. The severity of the pain may indicate variability and fluctuations. The pain threshold is low and normally pain may occur even against a non-painful stimulus. The level of pain experienced is greater than is expected from the painful stimulus. The pain lasts longer than expected, and it is commonly felt without indicating anatomical spread. The pain threshold value of patients with FMS is lower compared to healthy people [21]. Patients' quality of life is severely impaired because of the widespread pain, and as a result, they lead isolated lives. The time that the patient keeps for himself/herself and his/her family decreases. This causes unhappiness within the family. They become apathetic and anhedonic and enter into a vicious circle. Considering that the prevalence in adult society is 2%-4%, it should be considered as a major health problem for people and society.

There are many studies carried out to describe the etiopathogenesis of FMS. The aim of these studies is to open the door to targeted therapies for FMS's etiopathogenesis. More than one cause plays a role in FMS's possible etiopathogenesis. One of them may also be the deficiency in serum vitamin D. Likewise 1.25(OH)D (active vitamin D) functions in around 30 tissues and organs in the cell nucleus and cell membrane; the musculoskeletal system being one of them [22]. Therefore, vitamin D is important for the normal development and function of the musculoskeletal system. Bone and muscle pains are the well-known symptoms of vitamin D deficiency, and it is documented to be seen without osteomalacia's biochemical changes [23].

In the study, it was observed that vitamin D replacement had positive effects on scores associated with quality of life in patients with FMS. However, no significant improvement was observed in bodily pain levels after therapy. There are also some studies that have not found changes in body pain [24, 25]. Even though vitamin D deficiency does not play a role in the etiopathogenesis of FMS, the positive effect seen with vitamin D replacement is important in terms of increasing a patient's quality of life and providing an increase in mobilization. Increasing vitamin D deficiency along with the increased immobilization, depression, and consequently reduced exposure to the sun in FMS is the result of a vicious circle. We believe that vitamin D replacement will contribute to the breaking of this vicious circle in patients with vitamin D deficiency.

The relationship between FMS and serum vitamin D levels has yet to be clearly illuminated. Is vitamin D deficiency the cause or the result of FMS? This subject is the point of concern among researchers. In analogy to our study,

Table 3. Baseline and post-treatment scores of FIQ, BDI, VAS, ASEX, sleep VAS, and SF-36

Parameter	Patients with low vit. D (n=42)	After vit. D treatment (n=42)	p
FIQ	61.2±13.5	59.1±13.6	0.001*
BDI	15.6±10	14.8±9.9	0.001*
VAS	84.4±12.3	79.9±12.7	0.001*
ASEX	18.2±5.2	17.9±5.2	NS
Sleep scale (VAS)	4.9±2	4.7±2	NS
SF-36			
1. Physical function	19.7±3.9	20.8±4	0.001*
2. Role physical	5±1.3	5.5±1.4	0.001*
3. Role emotional	3.7±1	4.2±1.1	0.001*
4. Bodily pain	5.2±1.3	6±1.4	NS
5. Social function	6.7±2.2	7.4±2.5	0.01*
6. Mental health	19.2±5	20.2±4.9	0.001*
7. Vitality	13.1±3.2	13.6±3.8	0.003*
8. General health	11.3±4	12.5±4.5	0.001*

FIQ: fibromyalgia impact questionnaire; BDI: Beck depression inventory; VAS: visual analog scale; ASEX: Arizona sexual experience scale

VAS: 0-30: mild, 40-60: moderate, 70-100: severe; BDI: 0-9: normal, 10-16: mild, 17-29: moderate, 30-63: severe; FIQ: 0-39: mild, 39-59: moderate, 59-100: severe

Values are presented as mean±standard deviation.

$p<0.05$ is significant, NS: nonsignificant

the number of studies in the literature is limited in which patients are assessed before and after vitamin D replacement. In a randomized controlled study carried out by Warner et al. [9], it was reported that vitamin D was not associated with the pain in patients with widespread pain syndrome and that no response was received with vitamin D replacement. Vitamin D replacement was performed in a study in which 30 patients with FMS whose vitamin D levels were below 32 ng/mL were included. A significant improvement was observed in patients' VAS pain values when the therapy was given. It was emphasized that optimizing the vitamin D level in patients with FMS would make positive contributions to the perception of pain [26]. In a meta-analysis consisting of 12 studies and 1,854 patients, it was stated that vitamin D and chronic widespread pain syndrome were associated. In this meta-analysis, the use of low values such as 8-10 ng/m: as a diagnostic threshold value in widespread pain syndrome instead of 20 ng/mL of hypovitaminosis physiological value was emphasized to be better [27].

As a result, in the study done, it was observed that vitamin D deficiency was frequently observed in patients with FMS, and an improvement was observed with vitamin D therapy. However, a higher reduction rates in the FIQ score and BDI score have been suggested as clinically significant by some authors [28]. In a recent study by Yilmaz et al. [29] including patients with chronic nonspecific widespread musculoskeletal pain, it was reported that replacement of vitamin D improved the quality of life (SF-36). In another study, there were no correlations found between vitamin D and health status [30]. Assessment tools for determining the fibromyalgia are patient-dependent, and some environmental factors and personal mood at that time may affect the questionnaire. There is no quantitative method. The fact that it was not placebo-controlled is another shortcoming of this study. However, the fact that patients with factors that would affect the vitamin D level and the situations that caused chronic pain were excluded strengthens the study.

Vitamin D deficiency may be a factor involved in the pathogenesis of FMS. It seems to be associated with the pathogenesis in these patients. In addition, serum vitamin D levels should be checked as a general health problem and patients should be supported where necessary. Long-term randomized, placebo-controlled prospective studies with larger populations are required for the clarification of the relationship between FMS and vitamin D.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Pamukkale University (Decision Date: 28.06.2012/ Decision No: 136).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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