Effects of Vitamin D on Pain Severity, Quality of Life, Depression and Sleep in Patients with Fibromyalgia

Fibromiyaljili Hastalarda Vitamin D'nin Ağrı Şiddeti, Yaşam Kalitesi, Depresyon ve Uyku Üzerine Etkileri

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ABSTRACT

Objective: The aim of this study was to investigate the role of 25-hydroxyvitamin D (25OHD) concentrations on symptoms in the Fibromyalgia Syndrome (FMS).

Material and Methods: 80 female patients diagnosed with FMS were divided into 2 groups according to serum 25OHD concentration: 25OHD <20 ng/ml and 25OHD ≥20 ng/ml. We evaluated all patients with the Visual Analogue Scale (VAS), Fibromyalgia Impact Questionnaire (FIQ), Short Form-36 (SF-36), Beck Depression Inventory (BDI), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Arizona Sexual Experience Scale (ASES).

Results: The VAS, FIQ, PSQI, ESS, and physical role components of the SF-36 scores were significantly higher in patients with 25OHD <20 ng/ml than those with 25OHD ≥20 ng/ml (p value 0.01; 0.037; 0.016; 0.031, respectively). No significant difference was found between the groups for the BDI and ASES scores (p>0.05). Spearman correlation analysis showed a significant negative correlation between the serum 25OHD concentration and the VAS, FIQ, PSQI and ESS scores (p values 0.01, 0.02, 0.02, 0.03, respectively).

Conclusion: Vitamin D deficiency may be a factor associated with symptom severity, sleep and wakefulness problems, and physical function in FMS. Therefore, serum 25OHD status should be evaluated in patients with FMS and its importance in treatment management should not be ignored.

Keywords: Depression, Fibromyalgia, Serum 25-hydroxyvitamin D, Sleep, Symptom severity

ÖZ

Amaç: Bu çalışmanın amacı, serum 25 hidroksivitamin D konsantrasyonlarının Fibromiyalji Sendromu'ndaki (FMS) semptomlar üzerindeki rolünü araştırmaktır.

Gereç ve Yöntemler: FMS tanısı almış 80 kadın hasta serum 25-hidroksivitamin D (25OHD) konsantrasyonuna göre 2 gruba ayrıldı: 25OHD <20 ng/ml ve 25OHD≥20 ng/ml. Tüm hastalar Görsel Analog Skala (VAS), Fibromiyalji Etki Anketi (FIQ), Kısa Form-36 (SF-36), Beck Depresyon Envanteri (BDI), Pittsburgh Uyku Kalitesi İndeksi (PSQI), Epworth Uykululuk Skalası (ESS) ve Arizona Cinsel Deneyim Ölçeği (ASES) ile değerlendirildi.

Bulgular: VAS, FIQ, PSQI, ESS ve SF-36'nın fiziksel rol komponenti skorları 25OHD <20 ng/ml olan hastalarda 25OHD ≥20 ng/ml olan hastalara göre anlamlı olarak daha yüksekti (p değeri, sırasıyla 0.01; 0.037; 0.016; 0.031). BDI ve ASES skorlarında gruplar arasında anlamlı farklılık saptanmadı (p>0.05). Spearman korelasyon analizinde serum 25OHD düzeyleri ve VAS, FIQ, PSQI and ESS skorları arasında anlamlı negatif korelasyon saptandı (p değeri, sırasıyla 0.01, 0.02, 0.02, 0.03).

Sonuç: Vitamin D eksikliği FMS'de semptom şiddeti, uyku ve uyanıklık problemleri ve fiziksel fonksiyon ile ilişkili bir faktör olabilir. Bu nedenle FMS'li hastalarda serum 25OHD düzeyleri değerlendirilmeli ve bunun tedavi yönetimindeki önemi göz ardı edilmemelidir.

Anahtar Sözcükler: Depresyon, Fibromiyalji, Serum 25 hidroksivitamin D, Uyku, Semptom şiddeti

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INTRODUCTION

Fibromyalgia syndrome (FMS) is a chronic noninflammatory disease characterized by widespread musculoskeletal pain, sensitive spots, sleep disturbance, morning stiffness, and fatigue (1). It affects 2-3% of the population and is most commonly seen in the 25-55 years age range (2). It has been reported that it is 10 times more frequent in women than in men (2). Although the pathogenesis of FMS is not fully understood yet, the role of neuroendocrine, metabolic, and immunologic factors has been suggested in many studies (3,4). FMS may be associated with symptoms related to many systems. In this respect, it is an important health problem that can reduce the quality of life and cause loss of the labor force. It may lead to serious health expenses due to difficulties in treatment management.

Vitamin D is a hormone that has become increasingly important in recent years and has been shown to play a role in inflammatory processes and pain pathways in addition to the calcium and phosphorus metabolism (2). A serum 25 hydroxyvitamin D (25OHD) concentration below 20 ng/ml is defined as vitamin D deficiency (5). In vitamin D deficiency, widespread body pain and fatigue may be seen, similar to FMS symptoms (6-8). In this respect, vitamin D has been the focus of attention in FMS. Gendelman et al. have shown that vitamin D has a healing effect on pain thanks to its anti-inflammatory effects (9). In addition, recent studies have shown that vitamin D is involved in the sleep process, and vitamin D status is associated with sleep disorders (10,11). It is suggested that vitamin D accomplishes this role by providing neural expression of vitamin D receptors (VDR) in the brain, especially in the hypothalamus (12). Although some studies have suggested that vitamin D deficiency may be associated with chronic pain and FMS symptoms (6,8), other studies report no relationship (13,14). Therefore, there is still no consensus on the relationship between vitamin D and FMS.

This study aims to evaluate the effects of vitamin D concentration on pain, disease severity, quality of life, depression, sleep, and sexual function in FMS, which is a very important health problem due to the difficulties in treatment management.

MATERIAL and METHODS

This cross-sectional descriptive study included 80 women (mean age: 37,9 ±8,6) who presented to the Physical Medicine and Rehabilitation Outpatient Clinic between December 2018 and May 2019. Patients diagnosed with FMS according to the diagnostic criteria of the American College of Rheumatology and were aged 18-65 years were included in the study (1). Kafkas Medical Faculty Ethical Committee approved the study (date: 28.11.2018/ decision no:17). Patients who participated in the study were informed about the study and their written informed consent was obtained. The principles of the Declaration of Helsinki were complied with at all stages of the study. The patients were excluded if they had myofascial pain syndrome; rheumatologic, endocrine or neurological diseases; hepatic or chronic renal disease; cardiovascular diseases, malabsorption, malignancy; neurological or psychiatric disease; cognitive impairments or osteoporosis; a history of menopause, and pregnancy or lactation. Patients who had received vitamin D supplementation for the last 3 months or systemic corticosteroid treatment for any reason were excluded from the study. Sociodemographic characteristics, the body mass index (BMI) values, and duration of symptoms of all participants were recorded.

Blood samples of all patients were taken in the same period for the measurement of vitamin D concentrations. Serum 25OHD concentrations measurement were made using the enzyme-linked immunosorbent assay (ELISA) method (Beckman Coulter, UniCel DxI 600, US and Canada). Vitamin D deficiency was considered to be 25OHD below 20 ng/ml and patients were divided into 2 groups according to the serum 25OHD concentration: 25OHD <20 ng/ml and 25OHD ≥20 ng/ml. All the patients were evaluated with the following scales.

The Visual Analogue Scale (VAS)

Pain and numbness for daytime and night were evaluated by a visual analogue scale (VAS). The patient was asked to mark the severity of pain on a 100 mm line with "no pain" on one end and "most unbearable pain" on the other end. The distance from the starting point to the point marked by the patient was recorded.

The Fibromyalgia Impact Questionnaire (FIQ)

This scale, for which the Turkish validity and reliability was shown by Ediz et al., was used to evaluate the current health status of patients with FMS (15). FIQ is a self-rating scale composed of physical functioning, work status, depression, anxiety, morning tiredness, stiffness, pain, fatigue, and well-being over the past week. The total score is evaluated over 100 points and high scores are associated with low functionality levels.

The Short Form Health Survey (SF-36)

This scale was developed to assess the quality of life associated with the general health status, and the Turkish validity and reliability study was conducted by Koçyiğit et al. (16). The SF-36 measures the health domains of physical functioning, physical role, body pain, general health, vitality, social function, emotional role, and mental health. The subscales evaluate health between 0 and 100. As each health field score increases in SF-36, the health-related quality of life also increases.

The Beck Depression Inventory (BDI)

The Beck Depression Inventory (BDI) was used to assess the severity of depression. It is a Likert-type questionnaire, which is composed of 21 items, each of which is scored between 0 and 3. The questionnaire measures the affective, cognitive and somatic symptoms. The score range is 0 to 63. High scores indicate increased severity of depression. The Turkish version was validated by Hisli (17).

The Pittsburgh Sleep Quality Index (PSQI)

This scale has been adapted to Turkish by Agargun et al. (18). PSQI assesses sleep quality and related disorders, and consists of seven sub-components (sleep quality, latency, duration, efficiency, disturbance, drug use, and daytime functions) and 19 items. Each component is evaluated on a score of 0 to 3 and is evaluated with a total sleep score ranging from 0 to 21. High scores represent low sleep quality. A PSQI total score <5 points is considered "good" sleep quality and > 5 points is "bad" sleep quality (18).

The Epworth Sleepiness Scale (ESS)

This scale was developed to evaluate the general level of sleepiness, and its Turkish validity and reliability has been conducted by Izci et al. (19). It is a self-report questionnaire that evaluates the tendency of falling asleep in eight different daily life situations (while reading books, watching television, sitting in public, sitting in the car, lying in the afternoon, talking to someone else, sitting quietly without alcohol after lunch, while in a car stopped in traffic for a few minutes). The ESS score ranged from 0 to 24, and a score of ≥10 indicates excessive daytime sleepiness.

The Arizona Sexual Experience Scale (ASES)

The Arizona Sexual Experience Scale (ASES) was used to identify sexual dysfunction, and its Turkish validity and reliability study has been conducted by Soykan (20). This scale has a different form for men and women. It is a self-rating Likert-type questionnaire, which is composed of 5 items, each of which is scored between 0 and 6, and the score range is 5 to 30. The cutoff value for sexual dysfunction was reported to be 11 points (20).

Statistical Analysis

For descriptive statistics of the data, the mean, standard deviation, median, minimum, maximum, frequency and percentage values were used. The distribution of variables was checked with the Kolmogorov-Smirnov test. The independent sample t test or Mann-Whitney U test were used in the analysis of quantitative independent data. The Chi-Square test was used for the comparison of qualitative data. Spearman correlation analysis was used for correlation analysis. SPSS 22.0 was used for statistical analyses. Statistical significance was defined as a p value <0.05.

RESULTS

The median age of the 80 women with fibromyalgia was 36 years (min 20-max 63). The sociodemographic characteristics of the included patients are summarized in Table I.

Table I: Demographic characteristics of the patients.

		Min-Max	Median	Mean±sd
Age (years)		20.0 - 63.0	36.0	37.9 ± 8.6
Height (cm)		150.0 - 174.0	160.0	161.3 ± 5.6
Weight (kg)		50.0 - 94.0	70.0	69.9 ± 10.1
BMI (kg/cm^2)		19.9 - 36.1	26.3	26.4 ± 3.5
Education (n-%)	Primary School			10 12.5
	Middle School			22 27.5
	High School			11 13.8
	University			37 46.3
Occupation (n-%)	Working			37 46.3
	Nonworking			43 53.8
Socio-Economic Status (n-%)	Low			24 30.0
	Middle			33 41.3
	High			23 28.8
Marital Status (n-%)	Married			63 78.8
	Single			17 21.3
Symptom Duration (months)		1.0 - 120.0	11.5	17.8 ± 23.9

Min, minimum; max, maximum; sd, standard deviation; BMI, body mass index.

The serum vitamin D concentration was below 20 ng/ml in 57.5% of the patients and 42.5% had a value of 20 ng/ml or more. The mean serum 25OHD concentration of all patients was 19.8 ± 11.6 ng/ml. There was no statistically significant difference between the groups with and without vitamin D deficiency in terms of sociodemographic characteristics (p>0.05) (Table II).

The median value of the symptom duration associated with fibromyalgia was 11.5 months (min 1- max 120) and no significant difference was found between the groups (p>0.05). The VAS, FIQ, PSQI, and ESS scores were significantly higher in patients with 25OHD <20 ng/ml than those with 25OHD ≥20 ng/ml (p value 0.01; 0.037; 0.016; 0.031, respectively). There was no significant difference in BDI and ASES scores between the groups (p>0.05). There was a significant difference between the groups in SF-36's physical role component only (p<0.05) (Table II). SF-36's physical role component score was significantly higher in patients with 25OHD ≥20 ng/ml than those with 25OHD <20 ng/ml (p=0.044).

Table II: Comparison of groups according to vitamin D concentration.

		25(OH)D < 20 (n=46)		25(OH)D ≥ 20 (n=34)		p
Age (years) (median (min-max))		34 (20-63)		39.5 (22-59)		***0.018***
Height (cm) (median (min-max))		160 (150-174)		160 (155-168)		0.276
Weight (kg) (median (min-max))		70 (50-90)		70 (54-90)		0.988
BMI (kg/cm^2) (median (min-max))		26.3 (19.9-35.4)		26.0 (21.0-36.1)		0.774
Education (n-%)	Primary School	6	13.0	4	11.8	0.795
	Middle School	14	30.4	8	23.5	
	High School	5	10.9	6	17.6	
	University	21	45.7	16	47.1	
Work status (n-%)	Working	19	41.3	18	52.9	0.302
	Not working	27	58.7	16	47.1	
Socio-Economic Status (n-%)	Low	15	32.6	9	26.5	0.774
	Middle	19	41.3	14	41.2	
	High	12	26.1	11	32.4	
Marital Status (n=%)	Married	35	76.1	28	82.4	0.793
	Single	11	23.9	6	17.6	
Symptom Duration (months) (median (min-max))		12.0 (1.0-96.0)		9.5 (1.0-120.0)		0.727
Visual Analogue Scale (median (min-max))		8 (4-10)		6 (2-9)		**0.001**
Fibromyalgia Impact Questionnaire (mean±sd)		59.2 ± 18.5		49.7 ± 21.6		***0.037***
Beck Depression Inventory (median (min-max))		14.5 (5.0-35.0)		13.5 (2.0-46.0)		0.399
Pittsburgh Sleep Quality Index (mean±sd)		8.4 ± 3,5		6.3 ± 4.2		***0.016***
Epworth Sleepiness Scale (median (min-max))		7.0 (1.0-19.0)		5.0 (0-16.0)		***0.031***
Arizona Sexual Experience Scale (median (min-max))		15.0 (6.0-27.0)		14.5 (2.0-26.0)		0.394
Short form 36 (median (min-max))						
Physical Function		57.5 (20-100)		60.0 (10.0-100.0)		0.845
Physical Role		25.0 (0-100)		50.0 (0-100)		***0.044***
Pain		45.0 (0-100)		42.5 (0-100)		0.574
General Health		42.5 (0-90.0)		47.5 (10.0-100)		0.513
Vitality, Energy or Fatigue		40.0 (0-80.0)		42.5 (5.0-100)		0.830
Social Function		62.5 (12.5-100)		50.0 (12.5-100)		0.700
Emotional Role		33.3 (0-100)		33.3 (0-100)		0.383
Mental Health		52.0 (24.0-92.0)		52.0 (8.0-100)		0.722

Min, minimum; max, maximum; sd, standard deviation; BMI, body mass index

Spearman correlation analysis showed a significant negative correlation between serum 25OHD concentrations and VAS, FIQ, PSQI, and ESS scores (Table III; p values were 0.01, 0.02, 0.02, 0.03, respectively). Serum 25OHD concentrations were not correlated with SF-36 scores (p>0.05) (Table IV).

DISCUSSION

In this cross-sectional study, in which 80 women with FMS were included, it was concluded that serum 25OHD had a positive effect on the pain level, disease activity, sleep, and physical role in patients with FMS. However, in patients with vitamin D deficiency in BDI, ASES and other components of SF-36, no significant difference was found between the other groups. In many studies on this subject, a significant correlation has been reported between the serum vitamin D concentrations and pain and FMS-related quality of life, similar to our results (6, 8, 21). In contrast, some other studies have suggested that there is no statistically significant difference between these two groups, with and without vitamin D deficiency (3, 7, 22).

It is a well-known fact in recent years that vitamin D has an important role in many systems in the human body, and its popularity is increasing. It plays a role in musculoskeletal system function with its effects at the cell nucleus or cell membrane level. Vitamin D deficiency has become the focus of attention in FMS due to the similarity of its symptoms with FMS. It has been reported that vitamin D concentration is lower in patients with FMS than in normal controls (6, 23, 24). In FMS, as can be vitamin D deficiency may develop due to depression, immobilization, functional capacity limitation and consequently decreased sun exposure, its contrast may be possible (24). Therefore, the question of whether vitamin D deficiency is a cause or result in FMS is still controversial. In the study performed by Dogru et al. in order to clarify this issue, it was reported that FMS symptoms, the depression index, and the quality of life were improved after vitamin D treatment but there was no relationship between these parameters and the vitamin D levels at baseline (7). These results are not compatible with the results of our study. The difference in our inclusion criteria and grouping according to vitamin D concentrations may be the cause of this condition. In our study, we found that there was a significant negative correlation between serum 25OHD concentrations and the intensity of pain as measured by the VAS. This result is compatible with the results of some other studies (8, 25). In contrast, Ulusoy et al. found no relationship between 25OHD concentrations and the pain as measured by VAS (13). Another finding of this study was the significant negative correlation between the 25OHD concentration and the FIQ score. While there are studies supporting these findings (8), there are also incompatible studies (3, 12).

A study by McCarty et al. concluded that vitamin D deficiency was significantly associated with sleep disorders and chronic widespread pain (11). It was suggested that daytime sleepiness could be healed with vitamin D treatment and that vitamin D deficiency may lead to sleep disorder due to chronic pain (11). Olama et al. reported that sleep disorders were more common in patients with FMS who had 25OHD ≤20 ng/ml compared to those with 25OHD >20 ng/ml (24). Consistent with the results of these studies, PSQI and ESS scores were significantly higher in patients with FMS who had vitamin D deficiency in our study. Also, serum 25OHD concentration and PSQI and ESS scores were significantly correlated in the correlation analysis.

Table III: Association of serum 25OHD concentration with clinical parameters.

		VAS	Fibromyalgia Impact Questionnaire	Beck Depression Inventory	Pittsburgh Sleep Quality Index	Epworth Sleepiness Scale	Arizona Sexual Experience Scale
25OHD	r	-0.506	-0.334	-0.173	-0.345	-0.325	-0.095
	p	***0.001***	***0.002***	0.125	***0.002***	***0.003***	0.402

VAS, Visual Analogue Scale; 25OHD, 25 hydroxyvitamin D

Table IV: Association of serum 25OHD concentration with quality of life.

		Physical Function	Physical Role	Pain	General Health	Vitality, Energy or Fatigue	Social Function	Emotion Role	General Health
25OHD	r	0.022	-0.204	0.129	0.054	0.079	0.012	-0.049	0.044
	p	*0.845*	*0.070*	0.254	*0.636*	*0.486*	*0.917*	0.668	0.697

25OHD, 25 hydroxyvitamin D

In patients with and without vitamin D deficiency, there was no significant difference in SF-36 scores except for the physical role component. Similarly, no correlation was found between serum 25OHD and SF 36 components in the correlation analysis. These results are consistent with the results of Dogru et al. (7). However, in the same study, it was suggested that SF-36 scores showed a significant improvement in all sub-components except body pain after vitamin D treatment in patients with FMS who also had vitamin D deficiency. While this improvement was consistent with the results of Yılmaz et al. (25), no significant correlation was found between vitamin D and health status in another study (26).

Depressive symptoms are frequently seen in FMS. In studies conducted on the subject, it was reported that the rate of depression was 60-70% in women with FMS (27). Consistent with these results, the depression rate was 73% in our study. Depressed women with FMS exhibited higher symptom severity and reported worse symptoms than their non-depressed controls (28). Depression is therefore a subject that should be considered in patients with FMS. In contrast to our study, vitamin D concentrations were correlated with the Beck depression score in a study that investigated the relationship between vitamin D and depression (24). There are studies showing that there may be some improvement in the depression level with vitamin D treatment (7, 25). These discrepancies in the results can be explained by the fact that the scales are patient dependent and may be affected by some environmental factors and the patient's current mood.

The prevalence of sexual problems in FMS is known to be high. It has been suggested that sexual function is significantly associated with disease severity, quality of life, and depression in FMS (29). In addition, Krysiak R et al. have reported that low vitamin D concentrations were associated with sexual dysfunction in women (30). Therefore, we have also included evaluation of sexual function in our study. We have detected the sexual dysfunction rate of women with FMS as 30%, in harmony with other studies. No significant difference was found in the comparison of women with and without vitamin D deficiency in terms of the ASES score. In addition, Dogru et al., who reported similar results, suggested that there was no improvement in ASES scores after vitamin D treatment (7). Even if no relationship was found between vitamin D and the ASES score, we think that sexual dysfunction should be investigated in women with FMS.

Meta-analyses in recent years suggest that vitamin D may be a determining factor in FMS (23). However, heterogeneity in study strategies hampers any consensus on this issue. Also, the inclusion and exclusion criteria, the number of patients, and the region where the study was can vary and seasonal heterogeneity can be present. The lack of quantitative assessment methods in FMS causes the results of the evaluation to be dependent on the patient. Another limitation of our study is the lack of a control group. However, the exclusion of all patients with vitamin D concentrations and other factors that may affect the assessment criteria used, and performing the serum 25OHD measurements in the same season strengthen our study.

CONCLUSION

In conclusion, vitamin D deficiency may be a factor associated with symptom severity, sleep and wakefulness problems, and physical function in FMS. Therefore, serum vitamin D concentrations should be evaluated in patients with FMS and its importance in treatment management should not be ignored. Relevant studies that take other factors that could be effective on FMS into account and include larger patient populations are needed.

Ethics Committee Approval: This research complies with all the relevant national regulations, institutional policies and is in accordance the tenets of the Helsinki Declaration, and has been approved by the Kafkas Medical Faculty Ethical Committee, Kafkas University (approval number: 28.11.2018/ decision no:17).

Author Contributions: **ÜY:** Concept, **ÜY, SBG:** Design, **SBG:** Supervision, **ÜY, SBG:** Resources, **ÜY, SBG:** Materials, **ÜY, SBG:** Data Collection and/or Processing, **ÜY, SBG:** Analysis and/ or Interpretation, **ÜY, SBG:** Literature Search, **SBG:** Writing Manuscript, **ÜY:** Critical Review.

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