



The Association between Vitamin D Level and Chronic Pain and Depression in Premenopausal Women

Premenopozal Erişkin Kadınlarda Vitamin D Düzeyi ile Kronik Ağrı ve Depresyon Arasındaki İlişki

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Abstract

Objective: To investigate the association between vitamin D level and non-specific musculoskeletal system pain and depression in premenopausal women.

Material and Methods: Two hundred eighteen premenopausal women with common musculoskeletal pain and unknown etiology were included into the study. Levels of pain and depression were respectively measured with 0-10 visual analog scale (VAS) and Beck Depression Inventory (BDI). Levels of serum 25(OH)D, parathormone, alkaline phosphatase, and calcium were also measured. The threshold value of vitamin D was accepted as 20 ng/mL. Patients with 25(OH)D<20 ng/mL were classified as the vitamin D deficiency group (group 1), and those with ≥20 ng/mL were accepted as the vitamin D group within normal limits (group 2).

Results: Of 218 participants, 174 (79.8%) were detected with vitamin D deficiency, while 44 (20.2%) were found with a normal level of vitamin D. A statistically significant difference was present between both groups as to VAS and BDI scores ($p<0.001$ and $p=0.001$, respectively), although both groups were similar as to age, body mass index (BMI), level of income, duration of complaints, educational status, family type, and profession ($p>0.05$). Whereas a negative correlation was present between level of vitamin D and VAS and BDI scores, no correlation was detected as to age, BMI, level of income, educational status ($p<0.001$); duration of complaints, and number of children ($p>0.05$).

Conclusion: Our study indicates that vitamin D deficiency is a frequent finding in premenopausal women with chronic, non-specific musculoskeletal pain and that the level of vitamin D is associated with levels of pain and depression.

Key Words: Vitamin D, pain, depression, women

Özet

Amaç: Premenopozal erişkin kadınlarda, D vitamini düzeyi ile nonspesifik kas-iskelet sistemi ağrısı ve depresyon arasındaki ilişkiyi araştırmak.

Gereç ve Yöntemler: Çalışmaya, nedeni belirlenemeyen yaygın kas-iskelet ağrısı bulunan 218 premenopozal kadın dahil edildi. Katılımcıların ağrı düzeyi 0-10 Vizüel Analog Skala (VAS) ile depresyon düzeyi ise Beck Depresyon Ölçeği (BDÖ) ile belirlendi. Katılımcıların serum 25(OH)D, parathormon, alkalen fosfataz ve kalsiyum düzeyleri belirlendi. D vitamini sınır değeri 20 ng/mL olarak kabul edildi. 25(OH)D<20 ng/mL olan hastalar D vitamini eksikliği (Grup 1), ≥20 ng/mL olan hastalar ise D vitamini normal (Grup 2) olarak kabul edildi.

Bulgular: İki yüz on sekiz katılımcının 174'ünde (%79,8) D vitamini eksikliği saptanırken, 44'ünde (%20,2) D vitamininin normal sınırlarda olduğu tespit edildi. Gruplar yaş, beden kitle indeksi (BKİ), gelir düzeyi, şikayet süresi, öğrenim durumu, aile tipi ve çalışma durumu yönünden benzer iken ($p>0,05$); VAS ve BDÖ skorları yönünden iki grup arasında istatistiksel olarak anlamlı fark mevcuttu ($p<0,001$ ve $p=0,001$, sırasıyla) D vitamini düzeyi ile VAS ve BDÖ skorları arasında negatif korelasyon saptanırken ($p<0,001$); yaş, BKİ, gelir düzeyi, öğrenim düzeyi, şikayet süresi ve çocuk sayısı arasında korelasyon tespit edilmedi ($p>0,05$).

Sonuç: Çalışmamız kronik, nonspesifik kas-iskelet ağrısı olan premenopozal kadınlarda D vitamini eksikliğinin sık bir bulgu olduğunu ve D vitamini düzeyinin ağrı ve depresyon düzeyi ile ilişkili olduğunu göstermektedir.

Anahtar Kelimeler: D vitamini, ağrı, depresyon, kadın

Introduction

One of the most significant symptoms decreasing the quality of life related to musculoskeletal disorders is pain. No underlying pathology is encountered in the majority of pains originating from disorders of the musculoskeletal system, and pains from the musculoskeletal system that are not based on a specific or underlying mechanical reason are called non-specific pains of the musculoskeletal system (1-4). Chronic non-specific musculoskeletal system pain and depression are serious public health problems, because the changes by chronic non-specific musculoskeletal system pain and depression affect not only the patient but also his/her family, employer, and related healthcare professionals. An interactive correlation is present between chronic pain and depression; chronic pain may lead to depression, or depressive patients may be encountered with the complaint of pain (5,6). Vitamin D is reported to have pro-apoptotic, anti-inflammatory, and immune-modulatory features and obtains calcium homeostasis. In addition to studies reporting the association between vitamin D deficiency and non-specific musculoskeletal system pain (7) and depression (8,9), there are also other studies reporting no association between non-specific musculoskeletal system pain (10) and depression (11,12). In our study, we aimed to investigate the association between vitamin D level and non-specific musculoskeletal system pain and depression in premenopausal women.

Material and Methods

The study was performed in the outpatient clinic of the Physical Medicine and Rehabilitation Department of Konya Training and Research Hospital between September 2012 and April 2013. Two hundred eighteen premenopausal women who were admitted to the clinic due to non-specific musculoskeletal pains (e.g., low back, back, knee, shoulder, extremities, arthralgia, and common body pain) within the last 6 months and without underlying specific medical challenges (e.g., arthritis, trauma, depression, lumbar disc hernia, infection, neoplasm, metastasis, osteoporosis, rheumatoid arthritis, fracture, neurological disorders, and serious spinal pathology) were consecutively included into the study. Approval was obtained from the local ethical board of Meram Medical School of Necmettin Erbakan University. Those accepting to participate were informed, and their consents were obtained.

With common musculoskeletal system pain for at least 6 months, 218 premenopausal women were included into the study. Those with systemic disorders, major psychiatric diseases, history of antidepressant and anxiolytic drug intake, fibromyalgia, polymyalgia rheumatica, ankylosing spondylitis, rheumatoid arthritis, diffuse idiopathic skeletal hyperostosis, multiple myeloma, metastatic and metabolic bone diseases, a disorder or history of disorder affecting vitamin D metabolism (such as gastric surgery, chronic liver disease, renal failure, intestinal malabsorption), and the use of drugs affecting the levels of vitamin D, parathormone, alkaline phosphatase, and calcium, cigarette smokers, those drinking alcohol regularly, within the menopausal cycle, and those with restricted mobility were excluded.

If necessary, laboratory and monitoring methods were used in order to have differential diagnostic criteria of chronic pain. Detailed history was obtained from each patient, and each participant was physically examined. Levels of pain severity and depression were respectively determined with the 0-10 visual analog scale (VAS) and Beck Depression Inventory (BDI), and levels of parathormone, alkaline phosphatase, and calcium were measured. In order to determine vitamin D levels, 25(OH)D was investigated in blood samples drawn in the morning. 25-OH-D3 is the best clinical marker to show the condition of vitamin D, because it indicates total vitamin D taken together with cutaneous synthesis and diet (13-15). The threshold value of vitamin D still remains controversial in the literature. For maximum calcium absorption and optimal health status, levels are suggested to be over 30 ng/mL. However, 20 ng/mL is described as the threshold value of serum 25(OH)D preventing secondary hyperparathyroidism, increased bone formation-resorption, and loss of bone mineral density (13).

In our study, the threshold value of serum 25(OH)D was accepted as 20 ng/mL, and all participants were categorized as group 1- the deficient group (<20 ng/mL), and group 2- the normal group (\geq 20 ng/mL). The Beck Depression Inventory (BDI), a valid and reliable method to measure depression level in society, is a 21-item survey evaluating items related to the symptoms of depression, such as hopelessness, irritability, cognitive problems, feelings of guilt or being punished, and physical symptoms, including fatigue, weight loss, and lack of sexual desire. A BDI score \geq 17 is consistent with the presence of depression (16). In our study, those with a BDI score of 17 and over were evaluated in favor of depression.

Statistical Analysis

All statistical analyses were performed using the IBM SPSS Release version 20. Appropriateness of variables to normal distribution rates was investigated with visual and analytical methods. Descriptive statistical data were presented as mean, standard deviation, numbers, and percentage. In the comparison of clinical features of participants with deficient and normal vitamin D levels, data appropriate for normal distribution rates were compared with student's t-test, and those inappropriate for normal distribution were compared with Mann Whitney U-test. In the comparison of frequencies, chi-square test was used. In order to define the linear association between independent variables and vitamin D level, Spearman's rho correlation coefficients were calculated. The statistical significance level was accepted as $p < 0.05$. As correlation coefficients, the correlations between 0-0.25 were assessed as "none," between 0.25-0.50 as "weak-moderate," between 0.50-0.75 as "severe," and between 0.75-1.00 as "much severe."

Results

Of 214 participants, 174 (79.8%) presented with vitamin D deficiency (group 1), while the level of vitamin D was within normal limits in 44 (20.2%) (group 2). The socio-demographic and clinical data of all participants are presented in Table 1. While a statistically significant difference was observed in both groups

as to VAS and BDI scores ($p < 0.001$ and $p = 0.001$, respectively), no statistically significant difference was found as to age, body mass index (BMI), level of income, duration of complaints, educational status, family type, and profession ($p > 0.05$) (Table 1). Depression level was 41.4% in group 1, whereas the rate was 20.5% in group 2 ($p < 0.001$). In terms of levels of serum parathormone, alkaline phosphatase, and calcium, no significant difference was detected between groups 1 and 2 ($p > 0.05$) (Table 2). While a negative correlation was found between the groups as to vitamin D level and VAS and BDI scores ($r = -0.601$, $p < 0.001$ and $r = -0.361$, $p < 0.001$, respectively), no correlation was determined between the groups as to age, BMI, level of income, duration of complaints, and number of children ($p > 0.05$). However, a positive correlation was present between VAS and BDI scores ($p < 0.001$ $r = -0.470$).

Discussion

Vitamin D deficiency is a common problem both in Turkey and across the world. The most significant source of vitamin D is sunlight. Vitamin D deficiency develops due to insufficient exposure to sunlight and poor absorption of vitamin D via dieting, and the most marked finding is pain. The pain generally starts in the low back and may extend to the pelvis, hip, back, and costas (17,18). It is reported that non-specific musculoskeletal pain due to vitamin D deficiency originates from insufficient Ca-P and from the fact that poorly organized bone matrix presses outward onto the periost (19). Although non-specific musculoskeletal pain is one of the most common complaints of admissions to physical medicine and rehabilitation departments in daily practice, vitamin D deficiency is not considered frequently in the differential diagnosis, and high cost-effective diagnostic and therapeutic modalities are applied. In studies, however, it is reported that a low level of vitamin D is a common symptom in those with non-specific and chronic musculoskeletal pain. Especially, the association between low level of vitamin D and pain in osteomalacia is well established (20-24). Moreover, there are also studies reporting that a definite improvement is seen at the level of pain after vitamin D supplementation in patients with non-specific and chronic musculoskeletal system pain and vitamin D deficiency (25-27). As consistent with the literature, our study indicates that vitamin D deficiency is a frequent finding in premenopausal women with non-specific musculoskeletal pain, and the level of pain is strongly associated with the level of vitamin D. Therefore, because its treatment is easy and pleasing when diagnosed, vitamin D deficiency as an underlying effect should be differentiated in musculoskeletal system pains with unknown etiology.

Depression is an important public health challenge due to its high prevalence and the loss of ability it causes (28). The prevalence of major depressive disorders was reported to be 21.3% in women (29). Lifelong prevalence of depression is higher in women, compared to men (30). It is emphasized that one of the reasons of depression leading to disorders in all fields of life is also vitamin D deficiency (8,9,19,31-35). In a systematic review and meta-analysis performed recently in 31,424 individuals, an association was reported between depression and low levels of

Table 1. Socio-demographic and clinical data of patients

	25(OH)D<20 (n=174)	25(OH)D≥20 (n=44)	p	
Age (year)	39.3±9.6	42.1±8.8	0.092	
BMI (kg/m ²)	27.8±5.9	26.6±4.7	0.205	
Level of income (dollar/month)	620.5±353.4	678.0±420.8	0.187	
Number of living children	2.5±1.5	2.2±1.0	0.109	
Duration of complaints (month)	18.5±17.5	18.0±22.4	0.298	
VAS scores	7.6±1.8	4.7±2.1	<0.001	
BDI scores	14.9±8.9	10.4±8.8	0.001	
Marital status	n (%)	n (%)	χ ²	
Married	158 (90.8%)	42 (95.5%)	1.002	0.539
Single	16 (9.2%)	2 (4.5%)		
Profession				
Employed	29 (16.3%)	9 (20.9%)	0.350	0.656
Unemployed	145 (83.7%)	35 (79.1%)		
Type of family				
Core family	107 (61.5%)	31 (70.5%)	1.214	0.298
Combined family	67 (38.5%)	13 (30.5%)		
Educational status			0.884	0.829
Illiterate	11 (6.3%)	3 (6.8%)		
Primary (8 years)	132 (75.9%)	29 (72.7%)		
High school (11 years)	15 (8.6%)	3 (6.8%)		
College (≥12yrs)	16 (9.2%)	6 (13.7%)		

BMI: body mass index; BDI: beck depression inventory; VAS: visual analog scale

Table 2. Laboratory findings of patients

	25(OH)D<20 (n=174)	25(OH)D ≥20 (n=44)	p
25-OH-D3 (ng/mL)	9.3±3.4	33.4±14.5	<0.001
Parathormone	63.9±28.7	58.2±28.7	0.351
Alkaline phosphatase	77.3±29.7	75.5±28.3	0.814
Calcium	9.3±0.4	9.4±0.4	0.073

vitamin D (33). In a study where the patients with vitamin D deficiency were included, Kaya et al. (27) treated the patients with vitamin D and calcium and reported that a significant alteration was observed in BDI scores 6 months after the follow-up. However, as well as studies reporting an association between depression and vitamin D deficiency, other studies reporting no correlation between depression and vitamin D deficiency are also present (12,13,36-38). Upon evaluating BDI≥17 in favor of depression, the rates of depression were 41.4% in group 1 and 20.5% in group 2 in our study. In a previous study performed by Yılmaz et al. (39), the rate of depression was 8.3% in healthy women. The fact that the depression rate was also higher in group 2 within normal limits in our study is considered to arise

from the fact that the patients with chronic non-specific musculoskeletal system pain constituted our study group and from the association between chronic pain and depression. It is reported that one of the disorders in which depression is commonly encountered is chronic pain syndrome, and at least 30% of such patients display major depression (6). Also, many neurons in the amygdala region of the brain and playing a key role in emotional status are reported to be associated with pain (40). In our study, vitamin D deficiency and level of depression seem to be associated at a moderate level. However, considering the association between chronic pain and depression, we consider that more comprehensive studies are needed to suggest an association between vitamin D deficiency and depression.

Our study also has various limitations. First, because only women patients were included into the study, our findings can not be generalized to the whole population. Also, levels of depression in our participants were not evaluated via structured psychiatric interviews. So, further studies of both genders, including more participants to reflect a major part of the population, are needed.

Conclusion

As a result, our study indicates that vitamin D deficiency is a widespread finding in premenopausal women with chronic non-specific musculoskeletal pain and that vitamin D level is associated with level of pain and depression. Thus, vitamin D deficiency should be taken into account in premenopausal women, and the deficiency should be corrected, if any.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Necmettin Erbakan University Faculty of Medicine.

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

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