Assessment of Bone Mineral Density in Psoriasis Patients without Arthritis

Artriti olmayan Psoriasis Hastalarinda Kemik Mineral Yoğunluğunun Değerlendirilmesi

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Abstract: In this study, we aimed to investigate the bone mineral density (BMD) of psoriasis patients, compare with healthy control group, and to evaluate whether topical corticosteroids and systemic treatments affect BMD in psoriasis patients. Forty psoriasis patients admitted to dermatology outpatient clinic and 36 healthy subjects were included in the study. Lumbar and femur BMD of patient and control groups were measured. No statistically significant difference was found with regard to BMD in psoriasis and healthy control groups. When we compare the L1-L4 scores, femur BMD, L1-L4 BMD, femur Z, spine Z, and values of the psoriasis patients who receiving topical and systemic treatments, we did not found statistically significant difference. Femur neck T score was significantly higher in the group receiving topical treatment than in the group receiving systemic treatment. There were not statistically significant difference between disease duration and severity. The L1-L4 scores, L1-L4 BMD, spine Z values did not differ significantly between nail involvement and non-nail involvement groups. But the femur neck, femur total and femur Z scores were significantly lower in the group with nail involvement than group without nail involvement. This study shows that BMD of psoriasis patients is not different from healthy control group.
Key Words: psoriasis, bone mineral density, osteoporosis, arthritis

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Özet: Çalışmamızda eklem tutulumu olmayan psoriasis hastalarında kemik mineral yoğunluğunu (KMY) değerlendirilerek sağlıklı kontrol grubu ile karşılaştırmayı ve topikal kortikosteroid ve sistemik tedavi kullanımının KMY üzerine etkisini göstermeyi amaçladık. Çalışmaya hastanemiz dermatoloji polikliniğine başvuran 40 psoriasis hastası ve 36 sağlıklı gönüllü dahil edildi. Hasta ve kontrol grubunun lomber ve femur KMY ölçüldü. Psoriazis ve sağlıklı kontrol gruplarında KMY açısından istatistiksel olarak anlamlı bir fark bulunmadı. Topikal ve sistemik tedavi alan psoriasisli hastaların L1-L4 skorları, femur KMY, L1-L4 BMD, femur Z, omurga Z ve kalsiyum değerleri karşılaştırıldığında, istatistiksel olarak anlamlı fark bulunmadı. Topikal tedavi alan grupta femur boynu T skoru, sistemik tedavi alan gruba göre anlamlı olarak daha yüksekti. Hastalık süresi ve şiddeti arasında istatistiksel olarak anlamlı fark yoktu. L1-L4 skorları, L1-L4 BMD, omurga Z, kalsiyum değerleri, tırnak tutulumu ve tırnak tutulumu olmayan gruplar arasında anlamlı farklılık göstermedi. Ancak femur boynu, femur total ve femur Z skorları tırnak tutulumu olan grupta tırnak tutulumu olmayan gruba göre anlamlı olarak düşüktü.Bu çalışma psoriasisli hastalarında, KMY'nin sağlıklı kontrol grubundan farklı olmadığını göstermektedir.
Anahtar Kelimeler: psoriasis, kemik mineral yoğunluğu, osteoporoz, artrit

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1. Introduction

Psoriasis is a common, chronic and inflammatory skin disease. Psoriasis can be seen in all age groups, affects men and women on an equal footing (1). Several inflammatory markers are responsible in the pathogenesis, while precise etiology is unknown (2). Psoriatic arthritis (PsA) is observed in 5-8% of the psoriasis patients and it generally affects women and men equally (3). Psoriasis and PsA is characterized by activated T cells in skin and inflammated synovial tissues due to increase in tumor necrosis factor (TNF)-alpha, interleukin (IL)-17 and IL-23 (4-8). It has been reported that psoriasis and PsA is associated with several comorbidities such as metabolic syndrome, cardiovascular diseases, osteoporosis and insulin resistance. These diseases may occur due to increased inflammation (1).

Osteoporosis is defined as reduced bone mass and changes in bone microarchitecture resulting in decreased bone strength and increased risk of fracture (9). The World Health Organization (WHO) defines osteoporosis as bone mineral density in postmenopausal women, $\leq$2.5 standard deviations of the mean of healthy young individuals of the same sex (T-score < -2.5) and low bone mass when the T-score is between -2.5 and -1 standard deviations (10,11). Bone mass is influenced by several factors such as nutritional factors including intake of calcium and vitamin D, hormonal profile and physical activity. Osteoporosis can affect overall phenotypes and many genes. In addition, 60 genes are well known to be related with BMD (12).

Others include smoking, alcohol consumption, chronic inflammatory diseases, malabsorption, endocrine disorders, severe liver disease, rheumatoid arthritis, ankylosing spondylitis, malignancies, sarcoidosis, amyloidosis, chronic obstructive pulmonary disease and multiple sclerosis. (13,14). It has also been demonstrated that drugs such as methotrexate, corticosteroids and retinoids changed BMD (15-18).

Psoriasis and PsA may be associated with decreases in BMD (19-21). In a study, it has been reported that there was no relationship between plaque psoriasis and decrease in BMD (22). Although many studies showed an association between psoriasis and osteoporosis, controversial results have also been reported (19,23-25).

In this study, we aimed to investigate the BMD of psoriasis patients, compare with healthy control group, and to evaluate whether topical corticosteroids and systemic drugs affect BMD in psoriasis patients.

2. Materials and Methods

A total of 40 consecutive patients diagnosed with psoriasis vulgaris without joint involvement, aged between 18 and 65, who have admitted to dermatology outpatient clinic; and 36 healthy volunteers were enrolled the study. The control subjects were recruited among volunteers from hospital staff with no dermatological and systemic diseases. Patients and healthy controls were enrolled the study by using file data.

Our study was approved by local ethics committee. The patients and volunteers were informed and written informed consents were obtained. All data were obtained from patients files. The study was designed as retrospectively.

Exclusion criteria were the presence of chronic medical disorders requiring medical treatments, fractures, infectious diseases, severe cardiovascular diseases, major hepatic and renal insufficiency, hemorrhagic diseases, serious anemia, pregnancy, psychiatric disorder, inflammatory diseases like rheumatoid arthritis, malabsorption syndromes, chronic obstructive pulmonary disease, metabolic bone disease, alcohol consumption, inflammatory bowel disease, malignancy, hyperthyroidism and hyperparathyroidism. Patients who received topical corticosteroid treatment less than three months, systemic corticosteroids, estrogen pills were also excluded.

All patients were questioned about smoking. PASI (Psoriasis Area Severity Index) scores were calculated.

We measured BMD of the lumbar spine and femur using dual-energy X-ray absorptiometry (DEXA) (Hologic QDR 2000, Waltham, MA, USA). Bone density was classified as normal (T score > 1), osteopenia (1 ≥ T score ≥ 2.5) or osteoporotic (T score < 2.5) based on DEXA findings according to the 1994 WHO criteria for osteoporosis (9, 10).

Statistical analyses were performed by using SPSS 22 program. Analysis of normality of the continuous variables was performed with Kolmogorov–Smirnov test. Comparison of categorical variables between the groups was analyzed via chi-square test or Fischer's exact test; and for continuous variables, independent sample t-test was used. One-way ANOVA was used for normally distributed parametric variables when comparing three groups. Pearson correlation test was used when analyzing correlation in parameters associated with osteoporosis and psoriasis. Mean, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of the variables was measured by the Kolmogorov Simirnov test. While Mann-whitney u test and independent sample t test were used for the analysis of quantitative data; chi-square test for qualitative data. Spearman correlation analysis was used for correlation analysis. A value of P <0.05 was considered statistically significant.

3. Results

Twenty-five (62.5%) of the 40 psoriasis patients were females and 15 (37.5%) were males. The ages of the patients ranged from 18 to 65 years with a mean of 43.8 ± 12.1 years. Duration of disease ranged from 1 to 40 years with a mean of 12.3 ± 10.9. Thirty-six healthy subjects were included in the control group, 22 (61%) females and 14 (39%) males. The age of the control group ranged from 20 to 65 years with a mean of 46.9 ± 11.3. The patient and control groups were similar in terms of age and sex (p> 0.05). 42.5% of the psoriasis patients were receiving topical treatment, 47.5% systemic treatment and 10% did not receive any treatment for psoriasis. In the group receiving systemic treatment, 78.9% were receiving methotrexate and 21.1% receiving cyclosporine. Nail involvement was 50 % (n=20) in patients with psoriasis.

The BMI values of the patients ranged from 18.4 to 42.2 with an average of 29.8 ± 6.0 kg / m2. There was no statistically significant difference between lumbar (L1-4), femur neck, femur total mean BMD values and mean BMD values of patients and healthy subjects in the control group (p> 0.05). In addition, the mean Z score for each bone density region was assessed and no statistically significant difference was found between the groups (p> 0.05). Demographic characteristics of psoriasis patients and control group are presented in Table 1.

When we compare the L1-L4 scores, femur BMD, L1-L4 BMD, femur Z, spine Z values of the psoriasis patients who receiving topical and systemic treatments, we did not found statistically significant difference. Femur neck T score was significantly higher in the group receiving topical treatment than in the group receiving systemic treatment (p < 0.05). Patients of 10% did not receive any treatment for psoriasis and they were excluded in the analyze. (Table 2).

Table 1.
Demographic data of psoriasis and control group

		Psoriasis (N=40)			Control (N=36)			
								P
Age		43,8	±	12,1	46,9	±	11,3	0,242
Sex	Female	25		63%	22		61%	0,901
	Male	15		38%	14		39%	
L1-L4 T Score		-0,4	±	1,4	-0,3	±	0,9	0,183
Femur Neck T Score		0,6	±	1,7	0,9	±	1,1	0,085
Femur Bmd T Score		1,1	±	0,2	1,2	±	0,2	0,165
L1-L4 Bmd		1,0	±	0,2	1,1	±	0,2	0,248
Femur Z Score		1,0	±	1,3	1,3	±	1,0	0,351
Spine Z Score		0,1	±	1,3	0,4	±	1,0	0,332

Independent sample t test / Mann-whitey u test / Chi-square test

Table 2.
Bone mineral densities of patients with psoriasis treated with topical and systemic treatment

	Topical treatment (N=17)			***Systemic treatment (N=19)***			
							P
L1-L4 T Score	-0,2	±	1,6	-0,6	±	1,2	0,547
Femur Neck T score	1,4	±	1,8	0,9	±	1, 4	0,030
Femur Total T score	1,2	±	0,2	1,1	±	0,1	0,075
L1-L4 T score	1,0	±	0,2	1,0	±	0,1	0,632
Femur Z score	1,4	±	1,4	0,7	±	1,1	0,080
Spine Z score	0,5	±	1,3	-0,1	±	1,2	0,125

Mann-whitey u test

There was not statistically significant difference between diasease duration and severity (Psoriasis area severity index values) in all psoriasis groups. The L1-L4 scores, L1-L4 BMD, spine Z scores did not differ significantly between nail involvement and non-nail involvement groups ($p>0.05$). But the femur neck, femur total and femur Z scores were significantly lower in the group with nail involvement than group without nail involvement ($p<0.05$) (Table 3).

Table 3.
Bone Mineral densities and association with nail involvement in patients with psoriasis

	Nail involvement (+) (N=20)	**Nail involvement (-) (N=20)**	
	Ort.±s.s.		***P***
L1-L4 T Score	-0,7 ± 1,2	-0,1 ± 1,5	0,250
Femur Neck T score	-0,2 ± 1,4	1,4 ± 1,7	***0,002***
Femur T Score	1,1 ± 0,1	1,2 ± 0,2	***0,012***
L1-L4 Z Score	1,0 ± 0,2	1,1 ± 0,2	0,317
Femur Z Score	0,5 ± 1,0	1,5 ± 1,3	***0,016***
Spine Z Score	-0,1 ± 1,2	0,4 ± 1,3	0,261

Mann-whitey u test

4. Discussion

Psoriasis is demonstrated to stimulate T cell activation by increasing T-helper (Th)1 and Th-17 cytokine secretion, leading to high IL-2, IL-6, IL-12, IL-23, IL-17, IFN (interferon)-γ, TNF-α, reseptor activator of nuclear factor kappa (RANKL) serum levels. Keratinocytes are shown to interact with T cells by producing these cytokines (26, 27). Since the etiopathogenesis of rheumatoid arthritis and psoriasis are linked with T cells; there are similarities in secreted cytokines, leading to changes in BMD. Cytokines such as IL-6, IFN-γ, TNF-α, which are responsible for osteoporosis, are also associated with psoriasis pathogenesis. It is well known that IL-6, IFN-γ, and TNF-α cause resorption of the bones (27). Inflammatory cytokines in psoriasis and rheumatoid arthritis are suggested to lead to osteoporosis. It has also been reported that long-term use of corticosteroids, retinoids and methotrexate changes BMD (27-35).

The mechanism of action of osteoporosis in PsA, palmoplantar psoriasis and rheumatoid arthritis is not fully known. Inflammatory cytokines released from inflamed tissue, increased vascularity and immobilization have been suggested (8,22). It has been reported that there is no decrease in BMD in plaque-type psoriasis, while BMD can decrease in patients with palmoplantar pustular psoriasis and PsA (1). However, no significant difference was found in the studies evaluating BMD in rheumatoid arthritis and PsA (27, 28). Similarly, Nolla et al, Borman et al, Dheda et al showed that there was no significant difference in patients with psoriasis and PsA compared to the control group in their studies (36-38). Solak et al suggested that there was no difference between psoriasis and BMD. It has been reported that longer disease duration in psoriasis patients leads to lower BMD (22). Chronic inflammation can induce the development of osteoporosis. There may be a relationship between osteoporosis and the duration of the disease. However, in our study, we did not find any relationship between disease duration and BMD. The results of our study were similar to the literature except disease duration.

In our study, there was not statistically significant difference between patients' lumbar (L1-4), femur neck, femur total mean BMD values, and mean BMD values of healthy subjects in the control group. L1-L4 score, femur BMD, L1-L4 BMD, femur Z, spine Z values did not differ significantly ($p > 0,05$) between the groups receiving and not receiving topical treatment. Femur neck T score was significantly higher in the group receiving topical treatment than the group without topical treatment.

It has been shown that the long-term use of low-dose methotrexate in patients with psoriasis and rheumatoid arthritis is associated with osteopenia and osteoporosis (39). We found that BMD was significantly lower in

the nail involvement group. We found that the femur neck T score was significantly lower than the control group in the group receiving systemic treatment. The higher femur neck T score in the group receiving topical treatment in our study may be due to the immunosuppressive treatment of the group not receiving topical treatment.

It is well known that psoriasis severity is higher in patients with nail involvement. Also, nail psoriasis is resistant to topical agents. In addition,systemic agents like methotrexate, cyclosporine and corticosteroids are common in the treatment of nail psoriasis (40). This result is consistent with the literature because the risk of joint involvement is high in people with nail involvement. The adverse effects of methotrexate on osteoblast-like cells have been shown to be reduced by folinic acid by Preston et al (41).

In our study, we could not determine how much of the patients' bodies were exposed to topical drugs, and they could not remember how long they have used these drugs or in which potency. Furthermore we could not measure the levels of phosphorus, alkaline phosphatase, parathormone and vitamin D in the psoriasis and healthy control group. This study also did not include patients that used short-term topical corticosteroids, shorter than 3 months.

There are no reports of osteoporosis associated with topical corticosteroids used in the treatment of skin diseases. However, inhaler corticosteroids used in asthma have been associated with a decrease in hip BMD values in relation to dose and duration (24,39,42). Systemic corticosteroid treatment may explain a faster decline in BMD than topical corticosteroid use. None of our patients included in the study received systemic and inhaled corticosteroid therapy. We found that topical corticosteroid administration did not affect BMD and also femur neck T score is higher in topical corticosteroid treatment comparing with systemic treatment. Köse et al reported that topical corticosteroids did not affect BMD values in patients with psoriasis (43). It has also been reported that UVB treatment in psoriatic patients affects bone density positively by stimulating vitamin D synthesis rather than reducing BMD (43,44). Furthermore we could not evaluate the effect of phototherapy on BMD and Vitamin D levels in our study.

In conclusion, our study shows that BMD of psoriasis patients is not different from healthy controls and topical corticosteroids did not decrease BMD values. However, physians should be aware of the risk of osteopenia and osteoporosis induced by topical and systemic drugs in patients with psoriasis.

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