

Evaluation of the effect of selective serotonin reuptake inhibitors on bone mineral density: an observational cross-sectional study

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Abstract

Summary Sixty patients diagnosed with generalized anxiety disorder and treated with either paroxetine, sertraline, or citalopram for at least 12 months were enrolled in this study, and the bone mineral density (BMD) of the patients was compared with that of 40 healthy volunteers. Selective serotonin reuptake inhibitor (SSRI) therapy in generalized anxiety disorder was found to be related with decreased BMD values.

Introduction The objectives of this study were to evaluate the effect of SSRI therapy on BMD in postmenopausal women diagnosed with generalized anxiety disorder (GAD) and to identify the effects of the duration of disease and treatment on risk factors for osteoporosis.

Methods Sixty patients diagnosed with GAD and treated with paroxetine, sertraline, or citalopram from the SSRI group for at least 12 months were enrolled. Social demographic features, the Hamilton Anxiety Scale (HAS) results, and the Hamilton Depression Scale (HDS) scores of all the patients were assessed. The BMD of the patients was measured by dual-

energy X-ray absorptiometry (DXA) at the femoral and lumbar regions. The patients were divided into three groups which are the paroxetine, sertraline, and citalopram groups. The BMD of the patients was compared with that of 40 healthy volunteers.

Results The L2–L4, total lumbar vertebrae, femoral intertrochanteric, total femoral Z-scores, and femoral Ward's region T-scores of the treatment group were lower than the median T- and Z-scores of the control group ($p < 0.05$). Of the treatment groups, the femoral neck, trochanteric and intertrochanteric T- and Z-scores, total femoral T- and Z-scores, and femoral Ward's T- and Z-scores of the sertraline group were significantly lower than the BMD values measured at the identical regions in the paroxetine and citalopram groups ($p < 0.05$). There was a significant negative correlation between the duration of treatment and the BMD values.

Conclusion SSRI therapy in GAD was found to be related with decreased BMD values. Further randomized controlled studies are warranted to determine whether SSRI use is a risk

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factor for osteoporosis; such studies should investigate these factors by performing BMD assessments before treatment.

Keywords BMD · GAD · Osteoporosis · SSRI

Introduction

Generalized anxiety disorder (GAD) is a chronic anxiety disorder with a lifetime incidence rate of 4–6 % that could be accompanied by other physical diseases. Selective serotonin reuptake inhibitors are the most commonly prescribed antidepressants for GAD. Generalized anxiety disorder and selective serotonin reuptake inhibitor therapy could be accompanied by various biological alterations throughout the systems of the body. In recent years, one of the most investigated biological alterations is osteoporosis. According to the World Health Organization (WHO), osteoporosis (OP) is a silent epidemic characterized by a predisposition to enhanced bone fragility and an increased risk of fracture [1]. Patterson-Buckendahl et al. showed that anxiety disorders influence bone metabolism by demonstrating that psychological stress causes a decrease in osteocalcin levels which increase during the construction of bone and concluded that chronic stress has a negative influence on growth [2]. In another study, concerning bone mineral density and anxiety-depression symptoms, it was shown that increased anxiety levels are correlated with decreased bone mineral density [3].

Although the studies investigating the effects of SSRIs on BMD are limited, these studies showed the negative effects of these drugs on BMD [4, 5]. In a study with bone cell culture, it was shown that the serotonergic pathway has a role in converting a mechanical stimulus into a chemical stimulus and that SSRI usage has negative effects on bone density, particularly in developing bones [6]. Richards et al. showed that SSRIs are clinically related to bone fragility, fall risk, a doubled risk of fracture, and decreasing BMD scores [7]. Functional serotonin receptors are present in osteoblasts and osteocytes. In *in vitro* media, these receptors stimulate the reproduction of osteoblasts in mice and facilitate differentiation in human osteoclasts. Serotonin receptors (5HT_{2B}) aid osteogenic differentiation in cell cultures [8]. A decrease in bone mass and strength and changes in bone structure are shown in mice with serotonin transporter gene defects. Mice exposed to fluoxetine hydrochloride are shown to have impaired bone mineral content and bone formation [9]. These studies support the hypothesis that the serotonin transporters in bone cells have an important role in defining bone mass, structure, and strength.

The objectives of our study are to evaluate the effect of selective serotonin reuptake inhibitor (SSRI) therapy on bone mineral density (BMD) in postmenopausal women who are diagnosed with generalized anxiety disorder, to identify the

effects on the risk factors for osteoporosis of the duration of illness and therapy, and to evaluate the effect of SSRIs on BMD.

Methods

Subjects

A total of 67 consecutive postmenopausal women between the ages of 50 and 65 years, who were admitted to the Ankara Numune Training and Research Hospital Psychiatry Department outpatient clinic, were enrolled in this study. All the patients were diagnosed with generalized anxiety disorder according to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-TR criteria by using Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and were treated with sertraline, paroxetine, or citalopram for at least 12 months. The SSRI dosage was in the therapeutic range although no dose limitation was set; the study is a naturalistic study. A score of more than seven points on the Hamilton Depression Scale; mental retardation; being diagnosed with another first-axis disorder; substance abuse including abuse of alcohol, the use of other drugs such as antipsychotics, thyroid hormone, steroids, and mood stabilizers; a disorder causing osteoporosis; a bone disease; or an endocrinological disease were the exclusion criteria for the study. A total of seven patients were excluded from the study including two patients with comorbid depression, two with hormone replacement therapy, one using steroids, one with rheumatoid arthritis, and one using antiepileptic drug.

The control group consisted of 40 healthy volunteers with no history of psychiatric disease who matched the criteria of the patients were enrolled in the study. The approval of the Ethics Committee was obtained. The patients were informed, and written informed consent forms were obtained from all of the participants.

Measurements

A sociodemographic data form was completed for all of the participants. Additionally, examination was administered to the patients, including a physical examination, height and weight measurements, and a body mass index (BMI) assessment, and a smoking history (never smokers or current/former smokers) was taken from each patient. The BMD measurements were performed in the Ankara Numune Training and Research Hospital Radiology Department. Bone mineral density assessment was performed by DXA in all of the patients at the right-hip femoral neck, trochanteric, intertrochanteric, and Ward's regions.

Structured clinical interview for DSM-IV axis I disorders

An interview form developed by Spitzer et al. was used, Turkish reliability and validity, for the DSM-IV Axis I diagnosis that was used in the study [10].

Hamilton depression scale

A form developed by Hamilton (1960) consisting of 17 questions was used, and a score of ≥ 14 indicates depression. The reliability and validity study of the Turkish version were conducted by Akdemir et al. [11] (It was used to exclude patients with major depressive disorder).

Hamilton anxiety scale

The form designed by Hamilton (1959) for determining the level of anxiety and distribution of symptoms in individuals was used in the study. The HAS consists of 14 questions that investigate physical and mental symptoms. The reliability and validity study of the Turkish version were conducted by Yazıcı et al. [12].

Bone mineral density

The BMD (g/cm^2) is performed by DXA in all of the patients at the right-hip femoral neck and in the trochanteric, intertrochanteric, and Ward's regions. The WHO criteria were used for osteoporosis and osteopenia. According to these criteria, a T-score < -1 or > -2.5 was defined as osteopenia, and a T-score ≤ -2.5 was defined as osteoporosis. The T-score is the number of standard deviations (SD) from the young adult mean, and the Z-score is the number of standard deviations above or below the average bone mineral density value for women of comparable age [13].

Statistical analysis

The statistical analyses were performed using SPSS for Windows Version 11.5. The normality of the constant variables was determined by the Shapiro-Wilk test. The descriptive statistics for the constant variables were defined as the mean \pm standard deviation, the median (the width between the quarters) or the median (as the minimum and maximum), whereas the categorical variables were defined by the case number as the percentage (%). The significance of the difference between the control and treatment groups for the mean BMI values and ages was evaluated by Student's *t* test. The significance of the difference between the control group and the individual drug groups for the mean BMI values and ages was evaluated by a one-way ANOVA test.

The significance of the differences between the case and control T- and Z-scores and the T- and Z-scores of the smoking

and non-smoking cases were determined by the Mann-Whitney *U* test. The significance of the T- and Z-scores' changes in the cases and controls was determined by the Kruskal-Wallis test. If significance were detected, multiple non-parametric comparison tests were performed to identify the groups in which significance was defined. The significance of the differences in smoking and bone loss between the groups was calculated by Pearson's chi-square test. The correlation between the BMD and other variables was determined by Spearman's correlation test. Statistical significance was defined as $p < 0.05$.

Results

The patients in the SSRI group (paroxetine, citalopram and sertraline) were postmenopausal and were between 50 and 65 years of age. There was no statistically significant difference between the control and the SSRI groups in terms of age and smoking history ($p > 0.05$) (Table 1).

The clinical and demographic characteristics of the control and drug groups are listed in Table 2. There was no statistical significance between the control and drug groups according to the BMI and smoking history (Table 2). There was no statistically significant difference between the drug groups in terms of the duration of disease and the duration of drug use (Table 1).

The Z-scores of L2, L3, and L4 vertebrae; the total lumbar vertebral region; the intertrochanteric region; and the total femoral region and the T-scores of the femoral Ward's region were lower in the patient group than those of the identical regions in the control group. The difference was statistically significant ($p < 0.05$) (Table 2).

The median Hamilton anxiety scores of the patients were 21 (5.00) in the paroxetine group, 16.5 (9.25) in the citalopram group, and 18.5 (7.50) in the sertraline group. There was no statistically significant difference between the groups ($p > 0.05$).

The Z-scores of L2, L3, and L4 vertebrae and the total lumbar vertebral region; the T-scores of the femoral neck and the femoral trochanteric region; and the T- and Z-scores of the femoral Ward's regions in the paroxetine group were lower than those of the identical regions in the control group ($p < 0.05$) (Table 3).

The Z-scores of L3 and L4 vertebrae and the total lumbar vertebral regions and the T-scores of the femoral neck, trochanteric region, and femoral Ward's region were lower in the citalopram group than those of the identical regions in the control group ($p < 0.05$) (Table 3).

The Z-scores of L2, L3, and L4 vertebrae; the total lumbar vertebral region; and the femoral Ward's region and the T- and Z-scores of femoral neck, trochanteric region, intertrochanteric region, and the total femoral region were

Table 1 Demographic characteristics of control and SSRI groups

Variables	Control (n=40)	Paroxetine (n=20)	Citalopram (n=20)	Sertraline (n=20)	p
Age (year)	56.5±4.2	55.0±0.6	56.9±3.2	56.2±2.6	0.261 ^a
Body Mass Index	28.8±3.7	27.2±4.6	28.7±3.2	26.3±3.5	0.069 ^a
Smoking history (current/former users)	12 (30.0 %)	8 (40.0 %)	7 (35.0 %)	8 (40.0 %)	0.830 ^b
Duration of disease (month)	–	42 (24–96)	36 (18–120)	48 (24–108)	0.230 ^c
Duration of drug use (month)	–	24 (12–36)	24 (12–60)	30 (12–36)	0.182 ^c
Mean drug dose (mg/day)	–	30 (20–40)	20 (10–20)	62.5(50–100)	

^a One-way ANOVA test^b Pearson's chi-square test^c Kruskal-Wallis test

lower in the sertraline group than those of the identical regions in the control group, which were all statistically significant (Table 3).

A comparison of the treatment groups and the T- and Z-scores of the femoral neck, trochanteric region, total femur, and femoral Ward's region of the sertraline group were shown to be lower than those areas of the citalopram and the paroxetine groups ($p<0.05$) (Table 3).

There was a medium correlation between the BMI and the Z-score of the L1 vertebra ($r=0.096$, $p<0.05$), a low correlation between the BMI and the Z-score of the L2 vertebra ($r=0.226$, $p<0.05$), a low correlation between the BMI and the Z-score of the L4 vertebra ($r=0.210$, $p<0.05$), a medium correlation between the BMI and the Z-score of the femoral neck ($r=0.347$, $p<0.05$), a medium correlation between the BMI and the T- and Z-scores of the trochanteric region ($r=0.244$, $p<0.05$; $r=0.307$, $p<0.05$), a medium correlation between the BMI and the T- and Z-scores of intertrochanteric region ($r=0.334$, $p<0.05$; $r=0.387$, $p<0.05$), a medium correlation between the BMI and the T- and Z-scores of the total femoral region ($r=0.277$, $p<0.05$; $r=0.336$, $p<0.05$), and a low correlation between the BMI and the Z-score of the femoral Ward's region ($r=0.241$, $p<0.05$). All of the correlations were statistically significant.

In the patient group, smokers had lower femoral trochanteric T-scores, femoral intertrochanteric T- and Z-scores, total femoral T- and Z-scores, and femoral Ward's region Z-scores, which were statistically significant.

Of all the patients, there was no statistically significant correlation between the duration of disease and the T- and Z-scores measured at L1–L4, the total lumbar, femoral neck, femoral trochanteric, femoral intertrochanteric, total femoral, and femoral Ward's regions ($p>0.05$).

Of all the patients, there was a medium negative correlation between the duration of treatment and the L1 vertebral T- and Z-scores ($r=-0.537$, $p<0.05$; $r=-0.547$, $p<0.05$), a medium negative correlation with the L2 vertebral T- and Z-scores ($r=-0.508$, $p<0.05$; $r=-0.608$, $p<0.05$), a weak negative correlation with the L3 vertebral T- and Z-scores ($r=0.424$,

$p<0.05$; $r=-0.459$, $p<0.05$), a weak negative correlation with the L4 vertebral T- and Z-scores ($r=-0.396$, $p<0.05$; $r=-0.310$, $p<0.05$), a weak negative correlation with the total lumbar vertebral T- and Z-scores ($r=-0.420$, $p<0.05$; $r=-0.405$, $p<0.05$), a weak negative correlation between the femoral neck trochanteric region T- and Z-scores ($r=-0.406$, $p<0.05$; $r=-0.419$, $p<0.05$), a weak negative correlation with the intertrochanteric Z-scores ($r=-0.28$, $p<0.05$), a weak negative correlation with the total femoral T- and Z-scores ($r=-0.328$, $p<0.05$; $r=-0.339$, $p<0.05$), and a weak negative correlation with the femoral Ward's region T- and Z-scores ($r=-0.401$, $p<0.05$; $r=-0.333$, $p<0.05$).

Table 2 T- and Z-scores for the control and SSRI Groups

Variables	Control group	SSRI group	p^a
L1 T	-0.95 (1.95)	-0.60 (1.38)	0.622
L1 Z	0.05 (1.48)	-0.20 (1.10)	0.059
L2 T	-1.40 (2.33)	-1.00 (1.98)	0.773
L2 Z	-0.15 (1.63)	-0.55 (1.38)	0.003
L3 T	-0.95 (2.15)	-1.10 (0.80)	0.303
L3 Z	0.05 (1.68)	-0.50 (0.60)	<0.001
L4 T	-1.45 (1.45)	-1.20 (1.10)	0.927
L4 Z	-0.40 (1.45)	-0.80 (0.80)	<0.001
Total L T	-1.40 (1.70)	-0.80 (1.30)	0.344
Total L Z	-0.20 (1.30)	-0.70 (1.20)	<0.001
Neck T	-0.50 (1.28)	-0.10 (1.25)	0.126
Neck Z	0.45 (1.38)	0.35 (1.68)	0.057
Troch T	-0.30 (1.65)	0.00 (1.28)	0.359
Troch Z	0.15 (1.48)	0.05 (1.30)	0.118
Inter T	0.00 (1.30)	-0.20 (1.10)	0.053
Inter Z	0.30 (1.13)	-0.10 (1.10)	<0.001
Total F T	-0.30 (1.45)	-0.40 (0.98)	0.772
Total F Z	0.20 (1.20)	-0.10 (1.20)	0.002
Ward's F T	-0.75 (1.68)	-0.40 (1.58)	0.009
Ward's F Z	0.75 (1.23)	0.65 (1.68)	0.677

^a Mann-Whitney U test

Table 3 T- and Z-scores for the control and drug groups

Variables	Control	Paroxetine	Citalopram	Sertraline	<i>p</i> ^a
L1 T	−0.95 (1.95)	−0.60 (0.80)	−0.65 (2.28)	−0.75 (2.03)	0.326
L1 Z	0.05 (1.48)	−0.40 (0.60)	−0.10 (1.10)	−0.40 (2.10)	0.075
L2 T	−1.40 (2.33)	−0.50 (1.90)	−1.50 (2.98)	−1.00 (1.28)	0.992
L2 Z	−0.15 (1.63) ^{b,c}	−0.40 (1.40) ^b	−0.30 (1.80)	−0.95 (0.88) ^c	0.021
L3 T	−0.95 (2.15)	−1.00 (0.80)	−1.00 (1.40)	−1.20 (0.75)	0.622
L3 Z	0.05 (1.68) ^{b,c,d}	−0.50 (0.60) ^b	−0.50 (1.50) ^d	−0.60 (0.90) ^c	0.002
L4 T	−1.45 (1.45)	−1.20 (0.60)	−1.20 (1.05)	−1.20 (1.35)	0.847
L4 Z	−0.40 (1.45) ^{b,c,d}	−0.80 (0.50) ^b	−0.80 (0.65) ^d	−0.85 (1.48) ^c	0.004
Total L T	−1.40 (1.70)	−0.80 (1.20)	−0.80 (1.28)	−1.30 (1.15)	0.756
Total L Z	−0.20 (1.30) ^{b,c,d}	−0.70 (0.68) ^b	−0.70 (1.18) ^d	−0.70 (1.48) ^c	0.004
Neck T	−0.50 (1.28) ^{b,c,d}	0.30 (0.50) ^{b,e}	0.30 (0.80) ^{d,f}	−0.95 (0.38) ^{c,e,f}	<0.001
Neck Z	0.45 (1.38) ^c	0.40 (0.50) ^e	0.40 (0.90) ^f	−0.80 (0.55) ^{c,e,f}	<0.001
Troch T	−0.30 (1.65) ^{b,c,d}	0.10 (0.50) ^{b,e}	0.05 (0.90) ^{d,f}	−0.95 (1.40) ^{c,e,f}	<0.001
Troch Z	0.15 (1.48) ^c	0.50 (0.30) ^e	0.50 (1.18) ^f	−0.70 (0.93) ^{c,e,f}	<0.001
Inter T	0.00 (1.30) ^c	−0.20 (0.40) ^e	−0.20 (1.48) ^f	−0.95 (0.55) ^{c,e,f}	<0.001
Inter Z	0.30 (1.13) ^c	0.30 (0.40) ^e	0.30 (1.10) ^f	−0.90 (0.55) ^{c,e,f}	<0.001
Total F T	−0.30 (1.45) ^c	−0.30 (0.60) ^e	−0.30 (1.33) ^f	−0.90 (0.50) ^{c,e,f}	<0.001
Total F Z	0.20 (1.20) ^c	0.20 (0.20) ^e	0.20 (1.53) ^f	−1.00 (0.20) ^{c,e,f}	<0.001
Ward's F T	−0.75 (1.68) ^{b,d}	0.50 (1.00) ^{b,e}	0.50 (1.30) ^{d,f}	−1.10 (0.88) ^{e,f}	<0.001
Ward's F Z	0.75 (1.23) ^{b,c}	1.30 (0.60) ^{b,e}	1.10 (0.90) ^f	−0.50 (0.30) ^{c,e,f}	<0.001

^a Kruskal-Wallis testBonferroni-corrected Mann-Whitney *U* test^b The difference between the control group and the paroxetine group was statistically significant^c The difference between the control group and the sertraline group was statistically significant^d The difference between the control group and the citalopram group was statistically significant^e The difference between the sertraline group and the paroxetine group was statistically significant^f The difference between the sertraline group and the citalopram group was statistically significant

There was no statistically significant correlation between the Hamilton anxiety scores and the T- and Z-scores of L1–L4, the total lumbar, the femoral neck, the femoral trochanteric, femoral intertrochanteric, total femoral, and femoral Ward's regions of the patients ($p > 0.05$).

Discussion

The most frequent psychiatric comorbidities observed in patients with generalized anxiety disorder are major depression and dysthymia. The comorbidity is 62.4 % with depression and 40 % with dysthymia [14].

Whereas some studies that investigated the relationship between depression and osteoporosis reported a decrease in BMD, others reported that there was no significant difference in BMD between the patient and control groups [15–21]. Depression has effects on bone density by changing the hypothalamic-pituitary-adrenal axis and increasing proinflammatory cytokines such as interleukin-6 and TNF- α [22]. The non-inclusion of patients with a score lower than seven on the HDS is important to exclude the confounding effects of depression on BMD.

The median Hamilton anxiety scores were 21.0 in the paroxetine group, 16.5 in the citalopram group, and 18.5 in the sertraline group, which were not significantly correlated with the BMD scores. No study was found in the literature regarding this topic in older patients. Dorn et al. investigated the BMD scores in adolescent girls with anxiety and

depressive symptoms and found that lower BMD scores were associated with higher anxiety levels [3]. This result might be a consequence of not excluding depression in this study.

Nicotine addiction is found in 25.8 % of the occurrence of anxiety disorders in the literature. It has been reported that nicotine helps in coping with stress by increasing the ACTH and cortisol levels and that tobacco consumption increases the risk of osteoporosis, hip fracture, and early menopause [23, 24]. In our study, the T-scores of the femoral trochanteric region, the T- and Z-scores of the intertrochanteric region, the total femoral T- and Z-scores, and the femoral Ward's Z-scores were lower in smoking individuals than in non-smoking individuals.

Osteoporosis is more prevalent in obese individuals [25]. In our study, the medium BMI scores were over 25 kg/m² in the SSRI and control groups. Because there was no significant statistical difference in the BMI between the groups, it is important to equalize the effects of the BMI on BMD. Studies have shown a positive correlation between BMD scores and the BMI [26]. Our study is consistent with previous studies showing a positive correlation between the BMI and BMD scores. The results support the hypothesis that a higher BMI is a protective factor for osteoporosis.

The results of studies investigating the effects of SSRI use on BMD vary. Richards et al. evaluated the association between SSRI use and BMD and fractures; they reported that SSRI use was associated with decreased BMD, an increased risk of falling, and a 2-fold increased risk of a clinical fragility fracture [7]. In a prospective cohort study by Diem et al. of

2,722 elderly women, including SSRI users, TCA users, and non-user healthy controls, the hip BMD was measured at the beginning of treatment and at the end of 4 years, and an increased rate of bone loss at the hip was shown in the SSRI users compared to the TCA users and the non-user control group [5]. The finding in our study that the BMD scores of L2, L3, and L4 vertebrae, the total lumbar vertebra, the total femoral neck, femoral trochanteric, and femoral Ward's regions in patients using SSRIs were significantly lower than those of the identical regions in the control group was consistent with results in the studies mentioned [4, 5, 7, 27, 28].

Additionally, studies have shown no significant difference in the BMD scores during SSRI treatment. In these studies, the effects of SSRIs and TCAs on BMD were usually assessed together [29]. In a study by Spangler et al., involving 50–79-year-old postmenopausal women, the bone mineral density of the hip, spine, and whole body was measured at baseline and three years, and no statistically significant associations were observed between depressive symptoms or antidepressant (SSRI or TCA) therapy and 3-year changes in BMD or fracture risk [30]. In another study by Cummings et al., the effects of antidepressant use on BMD were evaluated in women over 65 years of age. The BMD values of antidepressant users were reported to be similar to those of non-antidepressant users [31]. The results obtained in these studies and the result of our study might differ because the effects of SSRIs and TCAs on the BMD have not been evaluated separately. In a study by Halbreich et al., involving patients on psychotropic therapy (antidepressants or antipsychotics) for schizophrenia and affective disorders, the lumbar vertebral (L2–L4) BMD values of the patients were compared with the age- and gender-expected values, and their BMD values were found to be lower than the expected values, a finding that was particularly more pronounced in males [32]. Because untreated patients were not included in this study, it is not clear whether the results are diagnosis related, and/or treatment related [33].

The different results obtained from the studies examining the effects of antidepressant use on BMD might have many causes. The first of these reasons might be the different methods used in the studies. In some studies, the BMD scores were compared with those of healthy subjects, whereas in other studies, the BMD results were evaluated at the beginning of the study and then during the study. Another factor could be the different number of subjects enrolled in the studies. The other element that is difficult to control might be that the BMD could be affected by hormone levels, nutrition, physical activity, smoking, and alcohol. The most important fact might be that the medication used by the subjects for other medical reasons should be detected for the BMD scores which is a long process [34–36].

In our study, the T- and Z-scores of the sertraline group at the femoral neck region, the femoral trochanteric region and the intertrochanteric region, the total femoral scores, and the

scores in the femoral Ward's region were lower than those of the citalopram and paroxetine groups. This difference could be explained by the longer duration of disease and the longer treatment period in the sertraline group. No studies have performed subgroup analyses of the drugs used in the treatment.

We did not find a statistically significant correlation between the duration of disease and the T- and Z-scores of L1–L4, femoral neck, intertrochanteric region, trochanteric region, total femur, and femoral Ward's region. We did not find any study in the literature that investigated the effects of the duration of disease and the duration of treatment on the BMD scores. Not finding a correlation between the duration of disease, disease severity and BMD scores and discovering a negative correlation between the duration of treatment and BMD scores are hypothesized to be related to low BMD scores resulting from SSRI treatment.

Our study is the first study to perform a subgroup analysis of SSRI effects on BMD scores. The strengths of our study are as follows: there are no statistically significant differences between the groups in terms of factors that might affect BMD scores such as the BMI and smoking. To equalize the effects on the BMD scores, the hormone levels were not detected because all of the subjects in the study were postmenopausal women.

The limitations of our study are as follows: being unable to document the BMD changes related to postmenopausal osteoporosis because sufficient data regarding the menopause duration of the women were not obtained, not enlisting the antidepressant treatment, and not knowing the BMD scores before the study. BMD might be decreased with various lifestyle variables. Our study design did not include nutrition factors, physical activity, family history of bone loss, calcium and vitamin D deficiency, and hormonal parameters. Therefore, it is difficult to test SSRI treatment as a single variable. Additional prospective and randomized, placebo controlled studies that include these factors should be performed. This study contained a small number of subjects, and a particular group of subjects were enrolled in the study; therefore, these results could not be generalized to the general population, which is another reason for more comprehensive studies to be performed.

Conflicts of interest None.

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