

Is There Any Alteration in Bone Mineral Density in Patients with Depression?

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SUMMARY: Is There Any Alteration in Bone Mineral Density in Patients with Depression?

Objective: Depression is associated with some alterations in behavior and hypothalamic-pituitary-adrenal axis function that may be risk factors for decreased bone mineral density (BMD). There is considerable inconsistency as to whether depressed patients really have decreased BMD or not. Decreased BMD has been reported in patients suffering from major depression in some studies, but not in some others. Moreover, few studies have investigated BMD in male depressed patients. The aim of this study was to investigate BMD in patients with major depression, including male ones.

Method: BMD was investigated in forty-two inpatients that fully met the DSM-IV criteria for major depressive disorder (21 women, 21 men; mean age $\pm$ SD: 37.57 $\pm$ 8.70) and compared with that in twenty-three healthy controls (12 women, 11 men; mean age $\pm$ SD: 33.73 $\pm$ 7.16). The severity of clinical symptomatology was assessed by the Montgomery-Asberg Depression Rating Scale (MADRS). BMDs of lumbar vertebrae (L1-L4) and femur neck were measured using dual energy X-ray absorptiometry.

Results: We found no difference in the values of BMDs of lumbar vertebra (L1-L4) and femur neck between depressive patients and controls among women or men. However, BMDs of the males in the control group were higher than those of the healthy females for both regions investigated; this gender difference was not observed in the depressive patients.

Conclusion: Major depression is not associated with any alteration in BMD either in women or in men.

Key Words: Depression, bone mineral density, gender

INTRODUCTION

Osteoporosis is a widespread disease of bone metabolism, which affects whole skeleton. It is an important cause of morbidity especially in elderly people. In osteoporosis, there is a mass decrease in the unit of bone volume. This mass decrease is a consequence of the increase in the ratio of bone resorption to bone formation. Its etiology is unknown, but there are many risk factors reported; advanced age, female gender, menopause, smoking, alcohol consumption, decreased calcium intake, sedentary life, etc. Osteoporosis is diagnosed by detecting the decrease in Bone Mineral Density (BMD) (Krane and Holick 1994).

Following reports about pathological fractures related to osteoporosis in patients with major depression (Van Vort et al. 1990), many studies have been performed on this issue. BMD has been reported to decrease in psychiatric diseases such as schizophrenia, anorexia nervosa or major depression (Halbreich and Palter 1996). The decrease in BMD is considered to be due to hypercortisolemia which is common in psychiatric disorders and especially in depression. In some studies on depressive patients, BMD has been reported to decrease (Schweiger et al. 1994, Michelson et al. 1996, Schweiger et al. 2000, Özdemir et al. 2002, Yazıcı et al. 2003), while in some others no difference has been found between patients and controls (Amsterdam and Hooper 1998, Whooley et al. 1999, Reginster et al. 1999, Kavuncu et al. 2002).

In this study, we aimed to investigate if BMD of patients with major depressive disorder was different from controls. Moreover, taking the fact that previous studies were in general performed on

women into consideration, we included men in the study population.

METHOD

Subjects

Totally 42 patients with major depressive disorder (21 men and 21 women; mean age $\pm$ SD: 37.57 $\pm$ 8.70; age range: 18-55) and 23 healthy controls (11 men and 12 women; mean age $\pm$ SD: 33.73 $\pm$ 7.16; age range: 18-55) were included in the study. Major depressive disorder diagnosis was determined according to DSM-IV criteria (American Association of Psychiatry 1994). Clinical and laboratory evaluations were performed in order to exclude the patients with concomitant diseases (endocrine or metabolic disorders such as diabetes, hyperthyroidism, Cushing's disease, rheumatic diseases, chronic obstructive pulmonary diseases, and liver and kidney diseases) or with drug history (corticosteroids, oral contraceptives, etc.) or with substance and alcohol abuse, which might affect BMD, from the study. All of the women were in premenopausal period. Patients with a history of previous or current psychiatric diseases other than depression were excluded. Routine laboratory evaluations for parameters, which could affect bone mineral density, were performed. Renal functions (Blood urine nitrogen (BUN), creatinine), hepatic functions (ALT, AST), calcium, phosphorus, ALP levels and thyroid functions (T_3 , T_4 , TSH) were within normal limits. Subjects with abnormal measurements were excluded as well. Severity of clinical symptomatology was assessed with Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979). Patients who did not begin to receive antidepressant treatment or whose MADRS scores were above 25 despite antidepressant treatment for 1-2 weeks were included in the study. During the study, 26 patients had been receiving antidepressants for 1-2 weeks at standard doses (13 patients venlafaxin, 4 patients fluoxetine, 3 patients fluvoxamin, 4 patients sertraline, 2 patients amitriptyline). The remaining 16 patients had not been on antidepressant treatment yet. Out of the 42 patients, fifteen were at their first depressive attack and 27 had one or more previous episodes. Mean number of episodes was 2.78 $\pm$ 2.75. Mean duration of the last episode was 5.94 $\pm$ 9.03 months and of the disease was 63.60 $\pm$ 82.95 months. Control subjects were from the hospital staff. Physical and psychiatric examinations and laboratory eval-

uation of control subjects were performed in order to be sure that they were without any physical or psychiatric disease and did not have any previous problem which might affect bone mineral density.

The study was performed on inpatients of Erciyes University Psychiatric Clinics. All patients who did not have any of the exclusion criteria and who gave consent for participation were included in the study. All patients were informed about the study and written consents were obtained before their participation. Approval from Ethics Committee of Erciyes University was obtained before the study.

Procedure

Bone mineral densities of L1-L4 vertebrae and femur neck of all subjects were measured with DEXA (dual energy X-ray absorptiometry) method. Hologic QDR-4500 DXA instrument was used for the measurement. Mean BMD values of both regions, their differences from mean BMD values of individuals in the same age group (Z-score) and of young adults (T-score) with standard deviation were separately calculated. Body mass indexes (BMI, kg/m²) of the subjects were also calculated.

Statistical analyses

Ages and BMI measurements of patients and controls were compared with t-test for independent groups. Mean BMD values, Z- and T-scores of patients and controls were compared with two-way ANCOVA test, taking disease status and gender as independent factors and age and BMI as covariates. Moreover, male and female patients were separately compared with ANCOVA test. Correlations between BMD values and some variables like age, BMI, number of episodes and MADRS scores were evaluated with Pearson's correlation test. Results were expressed as mean $\pm$ standard deviation and level of significance was accepted as $p < 0.05$.

RESULTS

There was not any statistically significant difference between patients and controls in terms of mean age and BMI (Table 1).

There was not any statistically significant difference between patients and controls in BMD values, T- or Z-scores. There was not any significant difference in any region between patients and controls even after men and women were taken

TABLE 1. Clinical and Demographic Characteristics of Patients and Controls

	Patients (n=42)	Controls (n=23)	Comparison
Age (years)	37.57±8.70	33.73±7.16	t=1.80;p>0.05
Gender (M/F)	21/21	11/12	-
BMI (kg/m ²)	27.06±3.46	25.25±3.56	t=1.99;p>0.05
MADRS score	34.97±5.71	-	-
Total duration of the disease (months)	63.60±82.95	-	-
Number of episodes	2.78±2.75	-	-
Duration of the last episode (months)	5.94±9.03	-	-

M: Male, F: Female, BMI: Body Mass Index

into consideration separately, either (Table 2, Figure 1).

In control group, BMD in both regions and Z- and T-scores in femur neck of men were higher than those of women, although this gender difference was not detected in the patient group (BMD of lumbar vertebrae; $F=4.82$, $df=1,20$, $p<0.05$, BMD, Z- and T-scores of femur neck; $F=14.51$, $df=1,20$, $p<0.05$, $F=8.61$, $df=1,20$, $p<0.05$, $F=7.32$, $df=1,20$, $p<0.05$, respectively; Table 2).

MADRS scores of the patients were positively correlated with Z- and T-scores of lumbar vertebrae ($r=0.510$ and $r=0.507$; $p<0.05$). Total duration of the disease and the last episode were not correlated with BMD, Z- or T-scores of both regions. When patients with only one episode were evaluated separately, total duration of the disease was not found to correlate with BMD. Number of episodes was positively correlated with Z- and T-scores of femur neck ($r=0.534$ and $r=0.328$; $p<0.05$).

DISCUSSION

The mean finding of the present study is that there is no significant difference between bone mineral density values of patients with major depressive disorder and those of healthy controls. This finding is consistent with those of some other recent studies. Kavuncu and colleagues performed a study on 42 depressive patients and 42 controls who were all pre-menopausal women and found that their BMD measurements were similar (2002). In their study on fewer patients, Amsterdam and Hooper showed that BMDs of depressive patients with or without hypercortisoluria were not different from controls (1998). In another study with a greater number of subjects (Whooley et al.

1999), falling down and fracture risk was considerably higher in elderly depressive women, but their BMD measurements were not different from controls. There are some studies that have reported that depressive symptoms are more frequent in women with osteoporosis (Coelho et al. 1999), but some other studies have not revealed any relationship between depressive symptomatology and BMD in postmenopausal women (Reginster et al. 1999). The superiority of our study to the previous ones is the inclusion of male patients.

On the other hand, there are some other studies have shown that BMD values of depressive patients were lower. Michelson and colleagues found that BMD measurement was lower, urinary cortisol excretion was higher and serum osteocalcin concentration was lower in depressive women (1996). They concluded that decreased values of BMD were related to high cortisol levels, hyperestrogenism and low levels of growth hormone. In another study, BMD measurements of premenopausal women with depressive disorder were found to be lower, but levels of serum cortisol and indicators of bone turnover like osteocalcin were similar (Yazıcı et al. 2003). As a result, it was proposed that the decrease of BMD in depressive disorder might be a consequence of the increase in bone resorption and the decrease in bone formation together. In another study that evaluated indicators of bone remodeling in women who were in their first depressive episode, osteoporosis was thought to be due to calcium secretion from the bones and the inhibitor effect of parathormone on remodeling (Herran et al. 2000). The studies that have been performed on male depressives and that have investigated the BMD are scarce. Schweiger and colleagues repeated BMD measurements of

TABLE 2. BMD Measurements, Z- and T-scores of Patients and Controls.

		Patients (n=42)			Controls (n=23)		
		Men (n=21)	Women (n=21)	Total (n=43)	Men (n=11)	Women (n=12)	Total (n=23)
	BMD (g/cm ²)	0.97±0.15	0.96±0.11	0.96±0.13	1.03*±0.07	0.95±0.09	0.99±0.09
Lumbar vertebrae	Z-score	-0.94±1.42	-0.53±1.07	-0.73±1.24	-0.11±0.71	-0.65±0.66	-0.39±0.73
	T-score	-1.10±1.43	-0.74±1.04	-0.90±1.23	-0.29±0.71	-0.81±0.83	-0.56±0.80
	BMD (g/cm ²)	0.87±0.13	0.85±0.24	0.86±0.20	0.90*±0.11	0.75±0.08	0.82±0.12
Femur neck	Z-score	-0.32±1.06	-0.50±1.08	-0.42±1.06	0.23*±1.02	-1.12±0.96	-0.47±1.19
	T-score	-0.97±1.22	-0.90±1.06	-0.93±1.12	-0.30*±1.24	-1.40±0.82	-0.87±1.16

*: Significantly higher than female controls

depressive patients approximately two years later and found BMD levels lower especially in males (2000). Possible reasons for the decrease in

BMD were proposed as hormonal alterations (hypercortisolemia, changes in growth hormone levels, subclinical hypogonadism, subclinical thyroid anomalies), increase in inflammatory mediators (increase in interleukin activity), decreased physical activity, loss of weight, nutritional disorders and electrolyte disturbances.

In our study BMD levels of depressive men and women were similar to those of controls. This finding does not exclude the presumptive effect of aforementioned mechanisms like hormonal alterations on osteoporosis, but emphasizes the questions whether these alterations are present in depression and, if they are, what the extent of this presence is. For example, in some recent studies basal cortisol levels have been reported not to increase prominently in depressive patients (Assies et al. 2004, Kartalcı 2004). The findings of Yazıcı and colleagues are in the same direction (2003). Michelson and colleagues did not find secretion of growth hormone different from controls (1996).

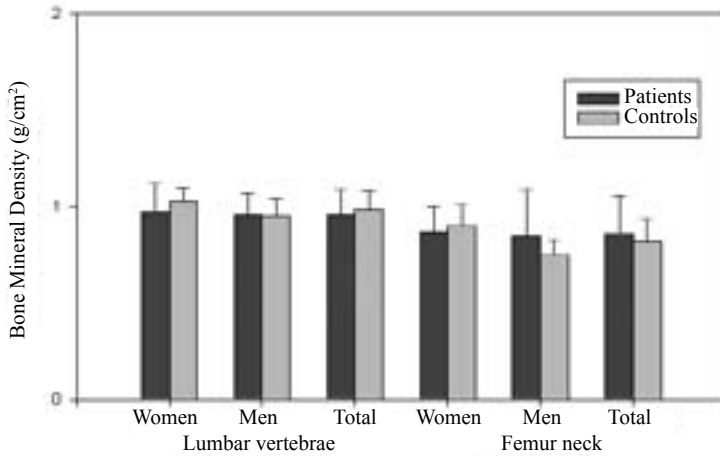
Mean age of our study population was lower than many other studies, which found decreased BMD levels, and the inconsistency between these studies and ours might be due to this difference in age. Furthermore, current use of antidepressants might be a confounding factor in our study, since it was reported that as antidepressants relieved depressive symptoms, CRH (Corticotrophin Releasing Hormone) and consequently, cortisol levels

began to decrease as well (Pariante et al. 2004). The thought that antidepressants could lead to improvement in BMD as a consequence of cortisol decrease seems reasonable, but as our patients were still in depressive condition during the study, this factor should not be as important as previously proposed.

Our finding that BMD values in men were slightly higher than in controls, while similar in depressive group may be commented in such a way that if depression had a lessening effect on BMD, this effect should be more prominent in men. However, as there was not any statistically significant difference between depressive and healthy men, our comment may not be so valid.

Another finding of our study is the relation between the severity of depression and Z- and T-scores of lumbar vertebrae. As the severity of depression increased, bone mineral density was found to decrease, but the difference from the controls did not reach a statistical significance. In our study, we did not take hypothalamic-pituitary-adrenal (HPA) axis into consideration, but the reason for this decrease might be the prominent increase in the activity of HPA axis in severe depression. Cortisol levels were reported to be inadequately suppressed in dexamethasone suppression test in patients with severe depression (Rush et al. 1997, Esel et al. 2004). Nevertheless, we found that depression did not cause BMD levels to decrease. Moreover, there was not any significant relationship between the severity of depression and BMD. Our findings revealed that the relationship between the severity

FIGURE 1. BMD of Lumbar Vertebrae and Femur Neck in Men and Women From Patient and Control Groups



of depression and deviation in BMD was weak and limited.

Limitations of our study are that there is no measurement of related hormones and indicators of bone turnover besides BMD and that we do not exclude the effect of antidepressants on BMD by measuring pre- and post-treatment levels.

As a conclusion, our findings revealed that bone mineral density did not differ in depression.

Moreover, our study included male patients who were not adequately evaluated in previous studies and showed that there was no change in BMD in male patients in contrast to previous presumptions. Further studies with greater patient population especially focused on gender difference are needed.

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