Düşünen Adam The Journal of Psychiatry and Neurological Sciences 2011;24:314-320
DOI: 10.5350/DAJPN2011240407

Brief Report

Comparison of Bone Mineral Density Levels in Young-adult Patients with Schizophrenia and Healthy Controls

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ABSTRACT

Comparison of bone mineral density levels in young-adult patients with schizophrenia and healthy controls

Objective: The aim of this study was to assess bone mineral density levels of patients with schizophrenia and to compare the results with healthy controls.

Methods: Fourteen patients with schizophrenia and 31 healthy controls, between 22 and 44 years of age, were enrolled in this cross-sectional study. Bone mineral density (BMD) levels of each group were measured by Dual Energy X-ray Absorbiometry (DEXA). The patients were assessed using the Positive and Negative Symptom Scale (PANSS). All patients had been receiving antipsychotic treatment for at least 2 years. Patients' sociodemographic caharacteristics and risk factors for osteoporosis (antipsychotic use, sunlight exposure, physical activity, etc.) were documented.

Results: As compared with the healthy controls, the patients with schizophrenia had significantly lower BMD at the lumbar spine and at all sites of the proximal femur. Correlation analysis showed that the only factor related with the femoral BMD only in patients with schizophrenia was the age. No association between BMD and gender, PANSS score, type of antipsychotic medications, and other risk factors for osteoporosis were observed.

Conclusions: In this study, we found that BMD in schizophrenia patients was lower than that of healthy controls and this finding suggest that osteoporotic changes may be seen in younger ages. Further prospective studies are needed to better clarify the relationship between osteoporosis and schizophrenia.

Key words: Schizophrenia, antipsychotics, osteoporosis, bone mineral density, young patient

ÖZET

Genç-erişkin şizofreni hastalarında kemik mineral yoğunluğu düzeyinin sağlıklı kontrollerle karşılaştırılması

Amaç: Bu çalışmanın amacı, genç-erişkin şizofreni hastalarında kemik mineral yoğunluğunun değerlendirilmesi ve sağlıklı kontrollerle karşılaştırılmasıdır.

Yöntem: Bu kesitsel çalışmaya, yaşları 22 ve 44 arasında değişen 14 şizofreni hastası ve kontrol grubu olarak, 31 sağlıklı birey dahil edildi. Her iki grubun kemik mineral yoğunluğu ölçümü Dual Energy X-ray Absorbiometry (DEXA) ile yapıldı. Hastalar, Pozitif ve Negatif Semptom Ölçeği (PANSS) ile değerlendirildi. Hastaların tamamı, en az 2 yıldır şizofreni tanısı ile antipsikotik kullanmaktaydı. Hastaların sosyodemografik özellikleri ve osteoporoz için risk faktörleri (antipsikotik kullanımı, güneş ışınlarına maruziyet, fiziksel aktivite, vs.) sorgulanarak kemik mineral yoğunluğu ile ilişkisi araştırıldı.

Bulgular: Sağlıklı kontrollerle karşılaştırıldığında, şizofreni hastalarında, hem lomber omurgada hem de proksimal femurun tüm bölgelerinde kemik mineral yoğunluğu daha düşüktü. Bağıntı analizi sonucunda, şizofreni hastalarında, yalnızca femur bölgesindeki kemik mineral yoğunluğu ile ilişkili tek faktör olarak yaş bulundu. Kemik mineral yoğunluğu ile cinsiyetin, PANSS skorlarının, kullanılan antipsikotik türünün ve osteoporoz için risk faktörü olan diğer etkenlerin ilişkisi olmadığı tespit edildi.

Sonuç: Bu çalışmada şizofreni hastalarının kemik mineral yoğunluğunun, sağlıklı bireylere göre daha düşük bulunması, şizofreni olgularında genç yaşta osteoporotik değişikliklerin olabileceğini düşündürmektedir. Şizofreni ve osteoporoz arasındaki ilişkiyi daha iyi açığa çıkaracak prospektif çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Şizofreni, antipsikotik, osteoporoz, kemik mineral yoğunluğu, genç hasta

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Date of receipt:
March 09, 2011

Date of acceptance:
May 03, 2011

INTRODUCTION

Osteoporosis is a disease characterized with reduced bone mass and strength and increased fracture risk (1). It may cause substantial physical, psychological and financial problems for patients and their relatives (2). The most prevalent types of osteoporosis are postmenopausal osteoporosis and age-related osteoporosis (3). The most important risk factor for development of osteoporosis is reduction of gonadal

hormone levels. Reduction of gonadal hormone levels is generally related with menopause in women and hypogonadism in men (4,5). Osteoporosis may develop due to medication use or alcohol consumption (3). Chronic alcoholics and patients taking glucocorticoid treatment are also under risk of osteoporosis (6,7). Several psychiatric diseases and psychotropic drugs may cause or accelerate osteoporosis due to evident chronic or repetitive neuroendocrin changes (8). It is also known that many psychotropic drugs cause reduction in levels of gonadotropins and gonadal hormones (9). Classical antipsychotics block D2 receptors in hypothalamo-pituitary axis in schizophrenia patients and this leads to elevation of prolactin levels and hypogonadism in both men and women. Conditions such as alcohol and substance abuse and excessive smoking observed in schizophrenia patients are among other factors which may cause osteoporosis (10-13). Factors such as immobility, malnutrition and vitamin D deficiency due to decreased sunlight exposure may also increase osteoporosis risk (14). In a cross-sectional study, osteoporosis-related non-traumatic fracture prevalence in chronic schizophrenia patients was reported nearly 25% (15). Osteoporosis risk may substantially increase for schizophrenia patients due to both disease itself and cumulative effect of a series of processes related with medications used (16).

Although several studies were done about bone mineral density of schizophrenia patients, most of them were done in other countries. Geographical location is an important factor among other factors affecting bone mineral density (17); bone mineral densities of schizophrenia patients were not investigated adequately in Turkey. In a recent study by Altındağ et. al. (18), bone mineral density of schizophrenia patients taking antipsychotic medications were reported to be lower than controls. Authors observed reduction of bone mineral density of patients they followed-up and although they did not made a specific comment related with medication due to lack of their information about previous antipsychotic use and short-term follow-up, they emphasized the relationship between schizophrenia and osteoporosis. Aim of this study is to compare bone mineral density of schizophrenia patients to healthy controls by considering factors such as exposure to sunlight and breast milk which may affect bone mineral density and investigating these factors.

METHODS

Cases admitted to Psychiatry Outpatient Clinic of Düzce University Faculty of Medicine Hospital between July and December 2005 and diagnosed as schizophrenia according to DSM IV criteria were included in the study Exclusion criteria were alcohol abuse, malnutrition, co-morbid somatic disease and use of medications known to affect bone mineral density (i.e., glucocorticoids, anticonvulsants, heparin, oral contraceptives etc.). Patients were being followed-up for at least 2 years by schizophrenia diagnosis and were taking antipsychotic medications. In order to exclude effect of age-related osteoporosis, schizophrenia patients under the age of 45 were recruited and compared to healthy controls. Fourteen schizophrenia patients who gave consent to participate in the study were evaluated after these exclusion and inclusion criteria.

A socio-demographic form asking their marital status, exposure to sunlight (LOW=duration of daily sunlight exposure <1 hour; NORMAL=between 1 and 2 hours; HIGH= >2 hours), daily mobility status (NORMAL=at least 3 times weekly exercise, walking or running; LOW=less than the time previously stated; HIGH=>2 hours), duration of breast-feeding and type of antipsychotic (atypical or conventional) and Positive and Negative Symptom Scale (PANSS) was administered. PANSS is one of the most frequently used scale to assess positive and negative symptoms. It is a semi-structured interview scale consisting of severity evaluation by 30 items and 7 scores. It was adapted to Turkish by Kostakoğlu et al. (20). Thirty-one healthy volunteers with similar age and gender characteristics were also recruited as control group. Written consent was also taken after informing patients and their relatives were informed about the study. Local ethical committee approval of Düzce University Faculty of Medicine was also taken before the beginning of the study.

Bone mineral densities of patients recruited were

measured by Ge-Lunar Dpx-Nt Pro (Lunar Corp, Adison, WI, USA) device. Assessments were done at femur neck and lumbar spine (L1-L4). Patienst were defined by using t-scores and according to World Health Organization criteria. According to these criteria, patients having T-score under -1 SD are normal, T-score between -1 SD and -2.5 SD are osteopenic and T-score under -2.5 SD and lower are osteoporotic (21).

Statistical Methods

SPSS 10.0 for Windows software was used for analyzing data. Data were assessed by Kolmogorov-Smirnov test for normal distribution. Due to normal distribution of our study data, mean values were compared by Student's t-test in double groups and by one-way ANOVA in groups over two. Pearson correlation method was used for correlation analysis and chi-square method was used for comparison of categorical variables.

RESULTS

Nine men and 5 women were recruited in the study. Mean age of patients was 33.07±8.92 (range: 24-42) and controls was 34.35±7.04 (range: 22-44). Socio-demographic characteristics and bone mineral density measurements of patients and controls were compared

Table 1: Comparison of socio-demographic data and densitometry findings of patients and controls

	Patient	Control	Statistical Test	p
Gender (number)				
Men	9	15	χ^2= 0.15	0.36
Women	5	16		
Age (year)	33.07±8.92	34.35±7.04	t= -0.52	0.64
Height (cm)	167.43±7.54	165.23±9.36	t= 0.78	0.41
Weight (kg)	74.64±11.11	73.35±11.70	t= 0.35	0.73
Marital status(n)				
Single	10	5		
Married	2	17	χ^2= 0.25	0.002
Divorced	2	9		
Educational level (year)	8.71±3.19	12.53±4.69	t= -2.58	0.01
Bone mineral density-Femur	-0.66±0.99	0.16±1.08	t= -2.41	0.02
Bone mineral density -Spine	-0.60±1.40	0.20±1.15	t= -2.02	0.04

χ^2: Chi-square Test, t= Student's T test

Table 2: Evaluation of factors which may affect femoral bone mineral density in schizophrenia patients

	Bone mineral density -Femur	Range	95% confidence interval for mean		Statistical test	p value
			Lower limit	Upper limit		
Exposure to sunlight						
Low	-0.73±1.07	-1.7 – 0.8	-2.43	0.98		
Normal	-0.93±1.03	-2.7 – 0.2	-1.88	0.02	F= 0.52	0.61
High	0.2	0.2				
Mobility						
Low	-0.80±0.67	1.8 – 0.2	-1.28	-0.32	t= 0.84	0.41
Normal	-0.30±1.63	-2.7 – 0.8	-2.89	2.29		
Breast milk						
Adequate	-1.27±0.47				t= -1.00	0.34
Inadequate	-0.60±1.09		-2.14	0.81		
Symptom severity						
Positive symptom	-0.28±1.64				t= 0.91	0.38
Negative symptom	-0.81±0.65		-0.75	1.82		
Antipsychotic type						
Conventional	-0.98±1.23				t= 0.90	0.39
Atypical	-0.48±0.85		-1.71	0.71		

F: One-way analysis of variance, t: Student's T test

Table 3: Evaluation of factors which may affect bone mineral density of lumbar spine in schizophrenia patients

	Bone mineral density -Lumbar spine	Range	95% confidence interval for mean		Statistical test	P value
			Lower limit	Upper limit		
Exposure to sunlight						
Low	-1.18±1.97	-3.2 – 1.4	-4.29	1.94		
Normal	-0.43±1.27	-2.7 – 1.2	-1.61	0.75	F= 0.58	0.58
High	0.5	0.5				
Mobility						
Low	-0.49±1.34	-3.2 – 1.2	-1.45	0.47	t = -0.45	0.66
Normal	-0.88±1.73	-2.7 – 1.4	-3.62	1.87		
Breast milk						
Adequate	-0.60±1.52		-2.29	2.29	t = 0.01	0.98
Inadequate	-0.60±1.64					
Symptom severity						
Positive symptom	-0.85±1.72		-2.21	1.52	t =-0.41	0.69
Negative symptom	-0.51±1.34					
Antipsychotic type						
Conventional	-0.64±1.34		-1.84	1.71	t = 0.07	0.94
Atypical	-0.58±1.52					

F: One-way analysis of variance, t: Student's T test

in Table 1. No significant difference of bone mineral density was found between groups according to gender. Bone mineral density at femur and lumbar spine was not correlated with marital status in both patients and controls. Eight patients were taking atypical and 6 patients were taking conventional antipsychotics. No significant difference was found for femoral (Table 2) and lumbar spine (Table 3) bone mineral density when compared according to duration of sunlight exposure, mobility level, duration of breast-feeding, severity of negative or positive symptoms according to PANSS and duration of atypical antipsychotic use.

No statistical difference was found between bone mineral density measurements of patients and alcohol use, smoking, positive and negative symptom scores, educational levels and marital status ($p<0.05$). The only factor correlated with bone mineral density was age (only at femoral area) ($r=0.35$, $p=0.02$).

DISCUSSION

In this study, bone mineral density was found significantly lower than healthy controls in young adult schizophrenia patients without risk factors for osteoporosis excluding antipsychotic use.

There are several studies showing low bone mineral density in chronic schizophrenia patients (14,16,22). Polydypsia (23), neuroleptic use and related hyperprolactinemia (8,24-29), excessive smoking (11), substance and alcohol dependence (6) and lack of mobility (30) are among risk factors of higher osteoporosis prevalence among psychiatric patients. Schizophrenia generally starts in adolescence and young adulthood. Thus, antipsychotic use and consequent metabolic changes also start at these ages. Life styles of patients also change (going out less, less mobility etc.) at this period of time. Each of these factors or their common effect may cause peak bone mineral density remain at a lower level (30). This may explain lower bone mineral density of our patients although they are less than 45 years old. No difference was found between bone mineral density values of men and women. Bergemann et al. (31) examined women with schizophrenia and found that bone turnover is increased but bone mineral density is normal in these patients. It is thought that time of onset of schizophrenia can be 5 years earlier in men than women (32). For this reason, exposure to factors related with schizophrenia and which may affect bone mineral density is longer for male patients (16). In our study, although it was found that gender has no effect on bone mineral density, low number of patients and not exactly knowing ages of disease onset in our patient

group can be interpreted as limitations of our study.

Hyperprolactinemia is one of the most frequent side effects of conventional antipsychotics and of risperidone among atypical antipsychotics (33). Classical antipsychotics cause more hyperprolactinemia and osteoporosis than atypical neuroleptics (14,34). Hyperprolactinemia may have acute and chronic effects at both women and men (35). Among these, there are reduction of bone mineral density and osteoporosis (36). In our study, type of antipsychotic used (conventional or atypical) does not found to make any difference for bone mineral density. Our findings showed that atypical antipsychotics may cause osteoporosis as well as conventional antipsychotics in contrast to previous findings.

Effect of psychopathology on bone mineral density may be due to both positive and negative symptoms. Patients with negative symptoms are less mobile and reluctant to go outside. This may cause reduction in 25-hydroxy-vitamin D3 levels. Positive symptoms such as paranoid delusions may negatively affect bone mineral density by malnutrition (14). In a recent study by Lee et al. (37), it was reported that negative symptoms are related with osteoporosis rather than antipsychotic use. In our study, schizophrenia patients were evaluated according to symptom severity (negative or positive) and daily mobility level and risk factors of osteoporosis such as immobility, exposure to sunlight and duration of breast-feeding which were not mentioned in previous studies were also assessed. None of these factors are found to affect bone mineral density. A factor within the nature of the disease but not known yet can negatively affect bone turnover of schizophrenia patients according to these findings.

Bone density is negatively affected in schizophrenia patients in our study like in previous studies. There may be several factors for this. It will be useful to evaluate the effects of each of these factors on bone mineral density of schizophrenia patients separately. Vitamin D supplementation is recommended to patients with low bone mineral density in clinical practice (38). Investigating whether prophylactic vitamin D supplementation to schizophrenia patients will prevent this reduction may be an interesting area for new studies. Regular nutrition with adequate calcium intake, regular exercise and adequate exposure to sunlight as a preventive measure can be recommended for schizophrenia patients.

Our study has several limitations. First of all, our relatively smaller sample size may hinder generalizability of our findings. Due to cross-sectional nature of our study, it is impossible to explain the deterministic relationship between our findings. Moreover, not assessing hormone levels related with gonadal and bone metabolism and indicators of bone turnover are among other limitations of our study.

In conclusion, there is reduction of bone mineral density even among young patients with schizophrenia and this reduction is seen in not only cases using conventional antipsychotics but using atypical antipsychotics as well. Relationship between development of osteoporosis and breast-feeding, mobility and exposure to sunlight was not found to be statistically significant. Findings of our study which also showed that negative symptoms are not correlated with reduced bone mineral density should be supported by longitudinal follow-up studies which evaluate first episode patients and all factors known to affect osteoporosis.

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