The Effects of Prolactin-Raising and Prolactin-Sparing Antipsychotics on Prolactin Levels and Bone Mineral Density in Schizophrenic Patients

Şizofreni Tanılı Hastalarda Prolaktini Yükselten ve Az Etkileyen Antipsikotiklerin Prolaktin Seviyesi ve Kemik Mineral Yoğunluğu Üzerine Etkileri

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ABSTRACT

Introduction: We aimed to investigate the effects of antipsychotics on prolactin levels in patients diagnosed with schizophrenia and the effects of hyperprolactinemia on bone mineral density (BMD) in patients on long-term antipsychotics.

Method: In this study, we included eighty consecutive patients who were diagnosed with schizophrenia according to DSM-IV, had been using the same antipsychotic for the last ten months, and fulfilled the inclusion criteria. Data on sociodemographic characteristics of the patients were collected through an information sheet. The Scale for the Assessment of Negative Symptoms (SANS) and the Scale for the Assessment of Positive Symptoms (SAPS) were used to rate positive and negative symptoms of the patients. In addition, their body mass indices (BMI) were calculated. Prolactin levels were measured through luminescence immune assay and BMD measurements were made at lumbar and femoral sites using dual-energy x-ray absorptiometry. Haloperidol (n=20) and risperidone (n=20) were assigned to prolactin-raising antipsychotic group, and olanzapine (n=20) and quetiapine (n=20) were assigned to prolactin-sparing antipsychotic group for this study. The effects of antipsychotics on BMD were compared among these groups.

Results: Hyperprolactinemia was determined in 60% of haloperidol using patients, 90% of risperidone using patients, 25% of olanzapine using patients and 10% of quetiapine using patients. Mean prolactin levels were found to be significantly higher in prolactin-raising antipsychotic using group (p<0.001). There were no statistically significant differences in BMD values between the two groups, for the sites where the measurement was done. Lumbar spine and femoral neck T-scores and Z-scores in the prolactin-raising group significantly negatively correlated with the treatment durations and chlorpromazineequivalent doses (p<0.05). BMI and BMD values of both groups also displayed statistically significant positive correlations (p<0.05).

Conclusion: The statistically significant differences in mean prolactin levels and numbers of patients with hyperprolactinemia between the treatment groups support the validity of classifying the antipsychotics as prolactin-raising and prolactin-sparing. The relationship of BMD with the treatment duration and doses in the prolactin-raising antipsychotic using group was deemed to be important, since it indicated that a decrease in BMD was to be expected in long-term antipsychotic treatment. (Archives of Neuropsychiatry 2014; 51: 205-210)

Key words: Schizophrenia, antipsychotic, prolactin-raising, bone mineral density

Conflict of Interest: The authors reported no conflict of interest related to this article.

ÖZET

Giriş: Bu çalışmada şizofreni tanısı alan hastalarda antipsikotiklerin prolaktin seviyeleri üzerine etkisinin ve uzun süre antipsikotik kullanan hastalarda hiperprolaktinemiyenin kemik mineral yoğunluğu (KMY) üzerine etkilerinin araştırılması amaçlandı.

Yöntem: Çalışmaya DSM-IV'e göre şizofreni tanısı konulan, en az on iki aydır aynı antipsikotigi kullanan ve çalışmaya alınma kriterlerini karşılayan ardışık 80 hasta alındı. Hastaların sosyodemografik özelliklerini içeren bilgi formu dolduruldu. Klinik durumlarını değerlendirmek için pozitif ve negatif semptomları değerlendirme ölçekleri (SAPS ve SANS) uygulandı, beden kitle indeksleri (BKİ) belirlendi. Prolaktin düzeyleri Luminesan İmmün Assay (LIA) ile ölçüldü. KMY ölçümleri ise Dual Enerji Xray Absorbsiyometri (DEXA) yöntemi ile femoral ve lumbar bölgeden yapıldı. Çalışmada haloperidol (n=20) ve risperidon (n=20) prolaktini yükselten, olanzapin (n=20) ve ketiapin (n=20) ise prolaktini az etkileyen antipsikotik olarak kabul edildi. Antipsikotiklerin KMY üzerine olan etkileri bu gruplar arasında karşılaştırıldı.

Bulgular: Haloperidol kullanan hastaların %60'ında, risperidon kullanan hastaların %90'ında, olanzapin kullanan hastaların %25'inde ve ketiapin kullanan hastaların %10'unda hiperprolaktinemi saptandı. Ortalama prolaktin seviyesi prolaktini yükselten antipsikotik kullanan grupta anlamlı ölçüde yüksek bulundu (p<0.001). Ölçüm yapılan bölgelerde KMY açısından gruplar arasında istatistiksel olarak anlamlı bir farklılık yoktu. Prolaktini yükselten grupta, tedavi süresi ve klorpromazin eşdeğer dozları ile lumbar vertebra ve femur KMY, t ve z skorları arasında istatistiksel olarak anlamlı negatif korelasyon vardı (p<0.05). Her iki grubun BKİ ve KMY değerleri arasında istatistiksel olarak anlamlı pozitif korelasyon bulundu (p<0.05).

Sonuç: Çalışmamızda gruplar arasında ortalama prolaktin seviyeleri ve hiperprolaktinemi hastası sayısı yönünden istatistiksel olarak anlamlı farklılığın bulunması "prolaktin yükselten" ve "prolaktini az etkileyen" antipsikotikler tarzında bir sınıflamanın doğruluğunu güçlendirmektedir. Prolaktini yükselten antipsikotik kullanan grupta tedavi süresi ve tedavi dozları ile KMY arasında bir ilişkinin bulunmuş olması, KMY'deki azalmanın uzun süreli tedavi ile beklenebilecek bir durum olmasına işaret etmesi açısından önemli olduğu değerlendirilmiştir. (Nöropsikiyatri Arşivi 2014; 51: 205-210)

Anahtar kelimeler: Şizofreni, antipsikotik, prolaktin, kemik mineral yoğunluğu

Çıkar Çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

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Introduction

Hyperprolactinemia is a common and important side effect of treatment with antipsychotics. Release of prolactin, which is an anterior pituitary hormone, is tonically inhibited by dopamine, which is released from the hypothalamus to the tuberoinfundibular system. Antipsychotics eliminate the inhibitory effect of dopamine on prolactin by inhibiting dopamine D2 receptors in the tuberoinfundibular system and lead to hyperprolactinemia (1,2).

In clinical hyperprolactinemia, prolactin level is above 18.00 ng/mL in men and above 30 ng/mL in women. In particular, compared with male patients, women in the postnatal period, adolescents, and children carry a higher risk in terms of developing hyperprolactinemia caused by antipsychotic treatment (3).

In studies investigating antipsychotics, development of hyperprolactinemia has been reported with a rate of 60%–75% in women and 34%–43% in men (1,2). Even with low-dose antipsychotics (200 mg chlorpromazine/day or .5–1.5 mg haloperidol daily), prolactin may increase, and as the drug dose is increased, prolactin levels also increase in proportion (4,5).

The effects of antipsychotics on prolactin levels demonstrate variance. Among atypical antipsychotics, risperidone, paliperidone, amisulpride, and sulpiride are the ones that lead to an increase in the prolactin level with the highest rate. Classical antipsychotics and zotepine lead to a marked increase in prolactin levels, whereas clozapine, olanzapine, quetiapine, ziprasidone, sertindol, and asenapine lead to slight or transient increases (6).

Currently, it is a generally accepted approach to categorize antipsychotics according to their effects on prolactin levels as prolactin-raising and -sparing antipsychotics (7,8).

Increased prolactin level results in hypogonadism by inhibiting pulsatile release of gonadotropin releasing hormone from the hypothalamus. It is known that hypogonadism negatively affects bone resorption and remodeling in men and women. Studies have reported that long-term use of antipsychotics may lead to a decrease in BMD and osteoporosis in relation with hyperprolactinemia (9,10,11).

The World Health Organization (WHO) accepts osteoporosis as a silent epidemic disease that is characterized with a tendency to bone fracture and increase in fracture risk because of disruption in the bone mass and bone tissue (12). WHO bases the diagnosis of osteoporosis on BMD measurements obtained using the Dual Energy X-Ray Absorptiometer (DEXA) method and presence of fracture (12).

In this study, it was aimed to (1) examine the effects of haloperidol and risperidone, which are typical antipsychotic drugs increasing prolactin levels, and quetiapine and olanzapine, which slightly increase prolactin levels on prolactin levels, (2) examine the effects of hyperprolactinemia on BMD, and (3) determine the relationship of the antipsychotic drug dose used and drug usage time with the risk of osteoporosis development.

Methods

Eighty consecutive patients who presented to the Ankara Numune Education and Research Hospital (ANERH) Psychiatry Out-patient Clinic and who were diagnosed with schizophrenia according to the DSM-IV diagnostic criteria and who had been using the same antipsychotic drug for at least 12 months were examined in terms of prolactin levels and BMD.

Patients who were aged below 18 years and above 55 years, who were diagnosed with metabolic bone disease that was known to lead to osteoporosis, who exhibited findings of any endocrinological disease on physical examination or who had abnormal menstruation because of any endocrinological disease, who had menopause, mental retardation, Axis I diagnosis, malnutrition, and who used an additional psychotropic drug other than biperiden and who used medications that are known to affect BMD, such as glucocorticoids, heparin, lithium, anticonvulsant agents, oral contraceptives, and anti-thyroid drugs, were not included in the study.

All patients used one type of the antipsychotic treatment and were in partial or full remission. Although the antipsychotic drugs were within the therapeutic dose range, no dose limitation was made.

The study was approved by the ethics committee of our hospital, and informed consent was obtained from all patients.

In the study, haloperidol (n=20) and risperidone (n=20) were accepted as antipsychotics that increased prolactin levels and olanzapine (n=20) and quetiapine (n=20) were accepted as antipsychotics that slightly affected prolactin levels, and the effects of antipsychotics on BMD were compared between these groups.

Physical examination was performed, and BMI was calculated by measuring the height and weight in patients who met the inclusion criteria. The information form containing the sociodemographic properties was filled in. SANS and SAPS scales were used to evaluate the clinical states of patients. The antipsychotic doses used by patients were recorded and equivalent doses were calculated.

BMD values of patients included in the study were measured in the L1-L4 vertebrae and femoral neck, trochanteric and interthorcanteric regions, and Ward's area (the triangular area in the femoral neck where the trabeculae are thin and sparse normally) of the right hip using the DEXA method.

In our study, patients who had osteoporosis or osteopenia were defined as patients with bone loss, and the others were defined as patients without bone loss (normal) in addition to BMD measurement. Osteoporosis assessments are performed by T and Z scores. The T score defines the comparison of the measured BMD with the mean BMD of the young adult reference population as standard deviation. The Z score defines the comparison of the measured BMI with the reference value by age and gender as standard deviation (13). According to the criteria of WHO, a T score below –1 SD is considered normal, a T score between –1 SD and –2.5 SD is considered to be osteopenia, and a T score of –2.5 SD and above is considered to be osteoporosis. The criteria of WHO were used in this study.

Venous blood samples of patients included in the study were obtained between 08.00 and 10.00 am in the morning and placed in anticoagulase-coated tubes and their sera were separated by centrifuging at 3000 rpm for 10 min. The sera were kept at -70°C . When the planned patient number was completed, the sera were collectively examined in the ANERH Hormone Laboratory. The prolactin level was measured by luminescence immunoassay method using the Architect kit. A prolactin level above 18.00 ng/mL in women and above 30.00 ng/mL in men was considered as hyperprolactinemia.

In this study, SPSS 11.0 (Statistical Package for Social Sciences 11.0 for Windows) was used for statistical assessments. Frequency distributions were calculated for descriptive statistics, and arithmetic mean and standard deviation values were calculated for continuous variables. In comparison of dual groups, Student's t-test was used for the groups that demonstrated a parametrical distribution, Mann-Whitney U test and chi-square test were used for the groups that demonstrated non-parametrical distribution. Pearson's correlation analysis was used in the assessment of the correlations between the variables. The predictability of the variables related with bone mineral density was tested with multiple regression analysis. A p value of <0.05 was considered statistically significant.

Results

Demographic and clinical properties

In this study, 38 female and 42 male patients were included. The mean age of the patients was 36.59 ± 10.00 years. The mean age of the female patients was 35.13 ± 9.42 years, and the mean age of the male patients was 37.90 ± 10.38 years. The mean disease time was 8.40 ± 7.77 years. The mean BMI of patients was 27.46 ± 5.08 kg/m². The mean SANS score of all the patients was 36.14 ± 20.19 . The mean SAPS score of all patients was 18.75 ± 13.92 . Forty-eight (60.0%) patients were smokers, and the mean number of cigarettes consumed daily was 26.10 ± 15.29 .

Endocrine properties

The mean prolactin level of all patients was 35.10 ± 40 ng/mL. Hyperprolactinemia was found in 12 (60%) patients who used haloperidol, 18 (90%) who used risperidon, five (25%) who used olanzapine, and two (10%) who used quetiapine.

When antipsychotic agents are classified as prolactin-raising and prolactin-sparing antipsychotics, the prolactin levels of the groups who used antipsychotics that increased prolactin levels and that slightly affected prolactin levels are shown in Table 1.

It was determined that the mean prolactin level in the group who used prolactin-raising antipsychotics was higher compared with the group who used antipsychotics (Group 1) that slightly affected prolactin levels (Group 2) ($p < .001$) (Table 1). In the group, in which prolactin-raising antipsychotics were used, the number of patients with an increased prolactin level was higher compared with the group in which antipsychotics that slightly affected prolactin levels were used ($p < .001$) (Table 1).

Clinical properties

Clinical variables in the groups in which prolactin-raising antipsychotics and antipsychotics that slightly affected prolactin levels were used are shown in Table 2.

The time of usage of antipsychotic agents is longer in the group in which prolactin-raising antipsychotics were used compared with the group in which antipsychotics that slightly affected prolactin levels were used ($<.001$). There is no significant difference between the groups in terms of the disease time, mean chlorpromazine equivalent dose, SAPS and SANS scores, and mean BMI value. The daily cigarette consumption is higher in the group in which prolactin-raising antipsychotics were used compared with the group in which antipsychotics that slightly affected prolactin levels were used ($p < .05$) (Table 2).

Bone Mineral Density Data

There was no statistically significant difference between the group in which prolactin-raising antipsychotics were used and the group in which antipsychotics that slightly affected prolactin levels were used in terms of BMD in L1, L2, L3, L4, L1-L4 total, femoral neck, femoral trochanter, intertrochanteric area, femur ward's area, and total hip areas.

When the two groups were evaluated in terms of bone loss (osteoporosis or osteopenia) by T scores, no statistically significant difference was found in terms of L1, L2, L3, L4, total lumbar (any body loss between L1 and L4), femoral neck, femoral trochanter, femoral intertrochanteric area, Ward's area, total femoral (any bone loss in the femoral areas measured), and total bone loss (bone loss in any area measured).

A statistically significant positive correlation was found between the BMI of all patients with T scores and Z scores measured in total lumbar, femoral neck, femoral intertrochanteric area, total femoral, and femoral ward's area ($p < .05$).

In the patients who used prolactin-raising antipsychotics, a statistically significant negative correlation was found between the treatment period and L1 vertebra T score at a moderate level ($r = -.317$, $p < .05$); L3 vertebra BMD and T score at a moderate level ($r = -.337$, $p < .05$ and $r = -.345$, $p < .05$); L4 vertebra BMD and T score at a moderate level ($r = -.316$, $p < .05$ and $r = -.336$, $p < .05$); L1-L4 total BMD and Z and T scores at a moderate level ($r = -.434$, $p < .05$; $r = -.343$, $p < .05$; and $r = -.400$, $p < .05$); femoral neck BMD ($r = -.452$,

Table 1. Prolactin levels of the groups in which prolactin-raising antipsychotics and antipsychotics that slightly affect prolactin levels were used

Hormone levels	Group 1 (n=40)	Group 2 (n=40)	p
Increased prolactin level (number, %)	30 (75%)	7 (17.5%)	$<.001^*$
Prolactin level (ng/mL, mean $\pm$ SD)	54.26 $\pm$ 48.45	15.95 $\pm$ 12.03	$<.001^{**}$
*Chi-square test, ** Student's t-test			

Table 2. Clinical variables in the groups in which prolactin-raising antipsychotics and antipsychotics that slightly affect prolactin levels were used

Clinical variables	Group 1 (n=40)	Group 2 (n=40)	p
Disease time (Year $\pm$ SD)	9.65 $\pm$ 9.11	7.15 $\pm$ 6.02	>.05**
Time of antipsychotic usage (Months, mean $\pm$ SD)	81.15 $\pm$ 102.29	27.00 $\pm$ 15.45	<.001*
Body mass index (kg/m ² , mean $\pm$ SD)	28.34 $\pm$ 5.50	26.58 $\pm$ 4.51	>.05**
Chlorpromazine equivalent dose (mg/day, mean $\pm$ SD)	431.25 $\pm$ 240.91	571.67 $\pm$ 397.47	>.05**
SAPS score (mean $\pm$ SD)	18.78 $\pm$ 12.39	18.73 $\pm$ 15.45	>.05**
SANS score (mean $\pm$ SD)	33.65 $\pm$ 18.13	33.65 $\pm$ 22.01	>.05**
Smoking (cigarettes/day, mean $\pm$ SD)	20.25 $\pm$ 19.01	11.08 $\pm$ 14.58	>.05*

* Mann-Whitney U test, ** Student's t test

$p < .05$); femoral trochanteric area BMD and Z score at a moderate level ($r = -.386$, $p < .05$ and $r = -.366$, $p < .05$); femoral intertrochanteric area BMD and Z and T scores at a moderate level ($r = -.422$, $p = .004$; $r = -.368$, $p < .05$; and $r = -.353$, $p < .05$); total femoral BMD and Z and T scores at a moderate level ($r = -.453$, $p < .05$; $r = -.468$, $p < .05$; and $r = -.496$, $p < .05$); and femoral ward's area BMD and T score at a moderate level ($r = -.356$, $p < .05$ and $r = -.314$, $p < .05$) (Table 3).

In patients who used prolactin-raising antipsychotics, a statistically significant negative correlation was found between chlorpromazine equivalent doses and L4 vertebra Z score at a moderate level ($r = -.337$, $p < .05$), L1–L4 total BMD, Z and T scores at a moderate level ($r = -.349$, $p < .05$; $r = -.384$, $p < .05$; and $r = -.343$, $p < .05$), total femoral Z score at a moderate level ($r = -.334$, $p < .05$) (Table 3).

When all patients were examined, no correlation was found between the disease time and BMD in the examined bone area, Z scores, and T scores ($p > .05$).

In the logistic regression analysis that was performed to determine the factors predicting total bone loss, total bone loss was considered as a dependent variable, and age, gender, disease time, time of antipsychotic drug usage, chlorpromazine equivalent doses, prolactin level, exercise, smoking, and body mass index were considered as independent variables. Only body mass index entered into the model which emerged ($p = .004$, $r^2 = .154$). Accordingly, the increase in BMI decreased the possibility of bone loss.

Discussion

In our study, the first 80 patients who were diagnosed with schizophrenia, who had been using medication for at least 12 months, and who met the study inclusion criteria were included in the study. The patients were examined in terms of prolactin levels and BMI. The patients who were in partial or full remission were included in the study controlling the sociodemographic properties as much as possible (patients below 18 years and above 55 years, patients with alcohol/substance abuse or addiction, patients with malnutrition, etc. were excluded). All patients were using a single type of antipsychotic. Although the antipsychotic drugs were within the therapeutic dose range, no dose limitation was made. Our study is a naturalistic follow-up study in this aspect.

The mean age of patients included in our study was 36.59 ± 10.00 years (females, 35.13 ± 9.42 years; males, 37.90 ± 10.38 years). Menopause is defined as the absence of menstrual periods for at least one year (12). In the classification of osteoporosis by etiology, senile osteoporosis is reported to develop above the age of 75 years, and postmenopausal osteoporosis is reported to develop below the age of 65 years (12). In our study, there was no female patient who was compatible with the definition of menopause. The fact that the mean age of patients included was low is important in terms of excluding the confounding effect of postmenopausal or senile osteoporosis on decrease in BMD.

In our study, hyperprolactinemia was found in two (10%) patients who used quetiapine, five (25%) who used olanzapine, 12 (60%) who used haloperidol, and 18 (90%) who used risperidone. These results that were related with the effects of antipsychotic drugs on prolactin levels were found to be compatible with the literature (14,15,16,17).

When the treatment groups were compared in terms of mean prolactin levels, it was observed that the prolactin level in the group in which prolactin-raising drugs were used was higher than that in the group in which antipsychotics that slightly affected prolactin levels were used (Table 1). When the two groups were compared in terms of the number of patients with hyperprolactinemia, the number of patients with a high prolactin level in the group in which prolactin-raising drugs were used was higher than that in the other group (Table 1). The statistically significant difference between the two groups with respect to mean prolactin levels and the number of patients with hyperprolactinemia supports the accuracy of such a classification.

Although a significant difference was found between the group in which prolactin-raising antipsychotics were used and the group in which antipsychotics that slightly affected prolactin levels were used in terms of prolactin levels, no statistically significant difference was found between the groups in terms of BMD in the areas where measurement was made.

When the patients were grouped as patients with bone loss and without bone loss according to the T scores, no significant-

Table 3. Correlation of the disease time and chlorpromazine equivalent doses with BMD, T scores, and Z scores in the group in which prolactin-raising antipsychotics were used

Areas in which equivalent measurements were done in the group in which prolactin-raising antipsychotics were used	Treatment time	Chlorpromazine dose
L1	BMD	
	T	-.317
	Z	
L2	BMD	
	T	
	Z	
L3	BMD	
	T	-.337
	Z	-.345
L4	BMD	
	T	-.316
	Z	-.336
L1-L4 total	BMD	-.434
	T	-.4
	Z	-.343
Femoral neck	BMD	-.452
	T	
	Z	
Femoral trochanteric area	BMD	-.386
	T	
	Z	-.366
Femoral intertrochanteric area	BMD	-.442
	T	-.353
	Z	-.368
Total femur	BMD	-.453
	T	-.496
	Z	-.468
Femoral ward's area	BMD	-.334
	T	-.356
	Z	-.314

ly difference was found between the prolactin-raising group and the prolactin-sparing group.

No consensus has been reached in the studies examining the effects of hyperprolactinemia on BMD in the literature. Some studies have reported that hyperprolactinemia because of the use of antipsychotics or other causes leads to a decrease

in BMD (8,10,18,19,20), whereas some other studies have concluded that it has no effect on BMD (11,21,22,23,24). The results obtained in our study in terms of BMD are compatible with the studies reporting that prolactin levels do not affect BMD values (11,21,22,23,24). Different results obtained in the studies examining the effects of antipsychotic usage and prolactin levels on BMD may be related with many causes. The primary point to be considered is the differences in the methods used between studies. The BMD values measured were compared with healthy control groups in some studies, with reference data in some other studies, and with groups who were receiving different antipsychotic agents without the presence of a control group in some others. Another point is the difference in the number of patients included in studies. Another factor that is difficult to control is the fact that BMD is also affected by factors, including nutrition, physical activity, smoking, and alcohol consumption, other than hormone levels. Besides these possible causes, probably most importantly, patients included in all these studies were not first-attack schizophrenia patients, and the history of treatment was not known.

In studies in which the effect of antipsychotic treatment on BMD was examined and no relationship was found between prolactin levels and BMD, the possibility that shortness of the treatment time may be responsible for this was noted (22,25). In our study, the presence of a relationship between the treatment time and BMD in the group in which prolactin-raising antipsychotic were used was found to be important in terms of indicating that decrease in BMD can be expected with long-term treatment even if no correlation was found between prolactin levels and BMD. In the literature, there is no definite data related with the question of how long it takes an antipsychotic treatment to decrease BMD. However, it may be considered that studies should be extended to a longer time period in the light of our study and previous studies. Further studies are required in this area.

As with antipsychotic treatment time, there are no sufficient data regarding the effects of disease time on BMD. It is not known if a change occurs in BMD in patients with schizophrenia who have not received any treatment. In our study, no correlation was found between the disease time and BMD in the bone areas examined, Z scores, and T scores. However, it may be thought that the presence of negative and positive symptoms may lead to limitation in life and nutrition of patients as the disease time gets extended, an increase in smoking and consumption of alcohol may increase in addition and tendency for osteoporosis may be increased.

Meaney et al. examined the effect of chlorpromazine equivalent doses of prolactin-raising antipsychotics of different groups on BMD and prolactin in 2004 for the first time. In the study, it was revealed that prolactin levels increased as the drug dose increased and BMD in the lumbar vertebrae decreased, and it was reported that this may be related with the degree of occupancy of D2 receptors (7).

In our study, no correlation was found between chlorpromazine equivalent doses and prolactin levels in the patients who used prolactin raising antipsychotics; however, a statistically significant negative correlation was found between chlorpromazine equivalent doses

es and L4 vertebra Z score, LL4 total BMD, Z and T scores, and total femoral Z score. Although no correlation was found between drug doses and prolactin levels, the fact that BMD decreased as the drug dose increased, particularly in the group in which prolactin-raising antipsychotic were used indicated that care should be taken in dose adjustment in antipsychotic treatment.

It is known that osteoporosis develops with a lower rate in obese individuals. In our study, the mean BMI values were found to be above 25 kg/m² in both groups, and the positive correlation between BMI and BMD is compatible with the other studies in the literature (7,21,26). The fact that no correlation was found between prolactin levels and BMD in the treatment groups in our study may be related with the protective effect of overweight from osteoporosis.

The limitations of our study included absence of a control group, lack of knowledge of previous antipsychotic drugs used and pre-treatment BMD values, and the difference in drug usage times between the groups.

BMD may decrease because of many life styles. This study was designed without investigating nutrition, physical activity level, familial history of bone loss, calcium and vitamin D deficiency, and other hormonal parameters. Therefore, it is difficult to test the importance of single variables, including increase in prolactin levels. Ideally, long-term, prospective, randomized studies investigating these factors should be conducted with first-attack schizophrenia patients who have not received treatment before.

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