Prevalence and Factors Associated With Decreased Bone Mineral Density in Young and Middle-Aged Male Schizophrenic Patients

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Abstract

Objective: The prevalence and factors of decreased bone mineral density (BMD) in young and middle-aged schizophrenic male subjects were examined in this study.

Methods: The sample included male patients, diagnosed with schizophrenia, between 18 and 45 years old. In the large-sample, cross-sectional study, cluster sampling method was adopted. 200 male inpatients in total, between 18 and 45 years old, diagnosed with schizophrenia, were included and interviewed in Beijing. The clinical assessment instruments included the Positive and Negative Syndrome Scale (PANSS) and a questionnaire with disease-related investigations and general information. The laboratory measurements concluded calcium, phosphorus, total cholesterol, prolactin (PRL), thyroid stimulating hormone, fT3, T3, fT4, T4, testosterone and fasting blood-glucose (FBG). Dual-energy X-ray absorptiometry was used to test BMD.

Results: The prevalence of osteopenia or osteoporosis was 33.5% (n=67). The prevalence of fracture in decreased BMD group was 17.9% (12/67), significantly higher than that in the normal BMD group (8.3% (11/133), p<0.05). Decreased BMD was associated with PANSS-negative scores, PANSS-total scores, body mass index (BMI), smoking and weight. Multiple logistic regression analysis revealed that BMI and PANSS-negative scores had statistically significant difference between two groups.

Conclusion: Prevalence of decreased bone mineral density was higher in young and middle-aged male subjects with schizophrenia in China. And the prevalence of fracture was more than twice in the decreased BMD group compared with the normal BMD group. PANSS-negative symptom was a risk factor, while BMI was a protective factor.

Keywords: Schizophrenia; Bone density; Risk factors

Introduction

Schizophrenia is a severe and predominantly chronic-relapsing disorder that is associated with marked functional impairments [1]. Moreover, schizophrenia has a greater health issues compare with the general population [2-4]. Osteoporosis, a serious public health issue [5], with abnormally low bone mineral density (BMD), is an important co-morbidity in schizophrenia. It can affect bone density in many ways, such as medical conditions, unhealthy lifestyle behaviours or, possibly, the prolactin-elevating effects of antipsychotics [6]. Although long-standing hyperprolactinemia can have an impact on the rate of bone metabolism and, when associated with hypogonadism, may lead to decreased bone density in both female and male subjects, the relative contribution of antipsychotic-induced hyperprolactinemia in bone mineral loss in patients with schizophrenia remains unclear [7].

A meta-analysis for comparison of BMD in patients with schizophrenia and healthy controls revealed significantly lower BMD in patients with schizophrenia than in the healthy controls (ES=0.589, 95% CI: 0.811–0.367, P<0.001) [8]. And it emphasized the importance of further screening for the risk of osteoporosis in young-aged schizophrenic patients, especially those taking prolactin-raising antipsychotics, which are in high risk of fracture.

In China, the prevalence of osteoporosis among Chinese subjects remains low compared to that in Caucasian population. Although the prevalence of osteoporosis is approximately 50% lower in men than that in women, a higher mortality rate was observed in men after osteoporotic fracture. However, research in men was less sufficient [9]. Young and middle-aged schizophrenic patients usually do not pay attention to the changes of their bone density and have many potential risk factors of osteoporosis. Our study mainly aimed to explore the related risk factors and prevalence of decreased BMD in young and middle-aged schizophrenic male subjects.

Methods

Settings and subjects

This was a cross-sectional study. Subjects with schizophrenia were included from Changping Traditional Chinese Medicine Hospital in April 2014. Inclusion criteria were: male patients with a diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition diagnostic criteria [10] with ages from 18 to 45 years old. Exclusion criteria were: taking any drugs...
known to be effective for BMD got any diseases known to be effective for BMD. 704 cases of subjects were screened, of which 200 cases were qualified for our study. The mean age of the patients was 36.8 ± 4.4 years old.

**Clinical assessment**

The Positive and Negative Syndrome Scale (PANSS) [11] was used to rate symptom severity. A questionnaire was used to assess the general information and disease-related investigations. Details included gender, date of birth, education level, illness duration, previous disease histories, previous medication history, smoking and drinking history, body mass index, waist, daily exercise, and equivalent chlorpromazine (CPZ) doses of current antipsychotics [12].

**Laboratory assessments**

Blood draws were completed between 7 am and 9 am the next morning by specially trained research nurses at a fasting state for 8-12 h. Blood sample (5 ml) was centrifuged at 3,000 rpm for 5 min after standing at room temperature for 1 h. Then the serum, approximately 1.5 ml, was separated and carefully transferred to a disposable cup, stored in ultra-low (-80) refrigerator until analysis. Before the detection began, the stored serum samples were taken out from -80 refrigerator and placed at 4 refrigerator to thaw, standing at the room temperature for equilibrium and detected within 48 h on the detection day.

Detections of hormones, fasting blood glucose (FBG), total cholesterol, calcium and phosphorus were batched completed by a standardized trained technical staff at Clinical Laboratory of Changping District Hospital of Integrated Chinese and Western Medicine.

**BMD assessment**

A dual-energy X-ray absorptiometry (GE Healthcare Bio-Sciences Corp., Piscataway, NJ, USA) was used to measure bone density. BMD testing was determined in the lumbar spine (L1–L4) and femoral neck. T-score values, which compare the patients results with standardized peak bone mass for ethnic- and gender-specific groups between 20-30 years. Osteoporosis is defined as a BMD that falls at least 2.5 standard deviation (SD) below the standardized values, and osteopenia as a BMD value that falls 1 SD below normative values. A BMD value higher than -1.0 SD means normal.

**Statistical analysis**

Data were analyzed using the SPSS 19.0 statistical package for Windows. Sociodemographic and clinical characteristics was compared between groups. Data of continuous variables was performed by independent samples t-test. And categorical variables were performed by the chi-square test. Multiple logistic regression analysis was carried out to adjust for relevant covariates and to determine the risk factors of decreased BMD. Level of significance was set at 0.05 (two-tailed).

**Ethics**

This study protocol and informed consent was approved by the Ethics Committee of Peking University’s Institute of Mental Health. Informed consents were obtained from the subjects or their legal guardians before recruited into the group.

**Results**

The prevalence was 33.5% (67/200), for osteopenia or osteoporosis among the 200 participants.

Participants with osteoporosis or osteopenia were assigned into the decreased BMD group, while the other participants into the BMD normal group. It was statistically significant in PANSS-negative scores, PANSS-total scores, BMI, daily smoker, and weight between the two groups. Details are shown in Table 1. PANSS-negative scores, BMI were significantly associated with decreased BMD by the multiple logistic regression analysis. Details are shown in Table 2.
And the social burden of fractures is enormous. Therefore, for young and middle-aged male patients, more attention should be paid to the quality of the bone, especially in schizophrenic patients.

The PANSS-negative scores were significant on this study, according to our previous study in postmenopausal women with schizophrenia [18]. We can conclude that PANSS-negative scores are significantly important to schizophrenia patients. In fact, a recent review demonstrated low levels of physical activity in schizophrenia patients and a significant relationship with negative symptoms [19]. Another study found the risk factors of decreased BMD specific to schizophrenia include lower levels of physical activity and sedentary lifestyle, staying indoors and poor diet in schizophrenia [20]. They lack of physical activity, reduced sun exposure, combined tobacco and alcohol abuse, inadequate nutritional intake, and vitamin D deficiency. Therefore, schizophrenia patients should pay more attention to improve negative symptoms for prevent the occurrence of BMD.

Consistent with previous studies [21], we concluded that BMI is a protective factor in bone mineral density. Since modest increase in BMI can enhance BMD [22], weight gain that results from medication effect may possibly act as a protecting role against BMD loss especially for patients receiving antipsychotics [23]. While we found that daily smoking may be a risk factor of decreased BMD in young and middle-aged male schizophrenic patients. There were 37.3% and 24.1% daily smoker in decreased BMD group and BMD normal group. A study had shown that smoking only accelerate the loss of bone mass after 50 years of age [24]. While other studies found that daily smoking was significantly reduced bone mineral density for young men and premenopausal women [25,26]. The effect of smoking on bone mineral density is not consistent. But tobacco smoking remains the leading preventable cause of mortality [27]. Smoking rates remain high in persons with mental illness, in particular schizophrenia. People with severe mental illness are also more likely to be heavy smokers, less likely to quit [28,29]. Therefore, we should focus on smoking in young people with schizophrenia, and we should pay special attention to the problem of bone mineral density decline. Moreover, quitting smoking may be one of the ways to prevent bone density decrease.

We have no significant difference in the results of PRL, which is consistent with the results of some studies [30-32]. However; some of studies had shown the opposite conclusion. The difference in this result is considered as follows: 1) Doctors often try to avoid the use of lead to an elevated PRL drugs in hospitalized patients, so elevated PRL patients can restore to normal levels soon, which cannot cause reduced bone mineral density. 2) The use of second generation antipsychotics having minimal influence on PRL, so as to avoid hyperprolactinemia that could result in bone loss. 3) The path-physiology of the decreased BMD among schizophrenic male patients might be different from that of female patients. Therefore, the research of PRL needs more research and testing.

In the present study, some methodological shortcomings are as follows. As a cross-sectional study, instead of a prospective study, we can only found factors that may be associated with decreased bone mineral density in schizophrenia, but could not determine the causal relationship. Large-sample, prospective studies are needed in the future to further confirm the results of this study.

**Conclusion**

Prevalence of decreased bone mineral density was higher in young and middle-aged male subjects with schizophrenia in China. And the
prevalence of fracture was more than twice in the decreased BMD group compared with the normal BMD group. PANSS-negative symptom was a risk factor, while BMI was a protective factor.

Disclosure

The authors report no conflicts of interest in this work.

References