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

Yang Shen, Zhiyong Li, Yichen Huang, Jing Yan and Ying Liang*

National Clinical Research Center for Mental Disorders, Peking University Sixth Hospital, Institute of Mental Health, Key Laboratory of Mental Health, Ministry of Health, Peking University, Beijing, China

***Correspondence:** Ying Liang, National Clinical Research Centre for Mental Disorders, Peking University Sixth Hospital, Institute of Mental Health, Ministry of Health, Peking University, Beijing, Haidian District, China, Tel :8610 82801955; Fax: +8610 82801955; E-mail: liangying1980@bjmu.edu.cn

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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 score 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 condition, 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 (ESs=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.

	Decreased BMD		**Normal BMD**				
	group (n=67)		**group (n=133)**				
	N	**%**	**N**	**%**	**χ2**	**df**	**P**
Age (years)					2.13	2	0.344
<30	8	11.9	8	6			
30-39	40	59.7	84	63.2			
≥ 40	19	28.4	41	30.8			
FBG					2.11	1	0.106
≤ 6.1	66	98.5	124	93.2			
>6.1	1	1.5	9	6.8			
Illness duration					3.248	2	0.197
0-10	38	56.6	58	43.6			
11-20	25	37.3	67	50.4			
21-30	4	6	8	6			
Smoking	25	37.3	32	24.1	3.84	1	0.05
Drinking	13	19.4	18	13.5	1.17	1	0.279
Fracture	12	17.9	11	8.3	4.07	1	0.044
	Mean	**SD**	**Mean**	**SD**	**T**	**df**	**P**
Age of onset	25.4	5.5	25.5	5.6	0.05	198	0.961
Exercises (min/day)	34.1	17.3	36.4	16.3	0.94	198	0.347
CPZ	444.6	122.7	454.8	243.3	0.32	198	0.747
PANSS positive	12.3	5.3	11.1	5.2	-1.47	198	0.144
PANSS negative	14.4	9.1	11.9	4.8	-2.06	198	0.042
PANSS total	50	14.6	45.8	13.2	-0.07	198	0.039
Weight	65.7	12.4	70.9	12.1	2.87	198	0.005
Height	170.3	5.5	170.6	4.9	0.38	198	0.707
BMI	22.6	4	24.4	4	2.94	198	0.004
Systolic pressure	118.1	6.8	119.5	7.2	1.33	198	0.184
Diastolic pressure	76	6.2	75.6	5.6	-0.47	198	0.64

Total cholesterol	3.71	0.7	3.75	0.74	0.37	198	0.714
Calcium	2.3	0.7	2.2	0.1	-1.44	198	0.151
Phosphorus	1	0.4	1	0.2	-0.2	198	0.841
Waistline	84.7	15.1	87.5	12.3	1.39	198	0.167
TSH	2.5	1.9	2.5	2	-0.1	198	0.918
T3	0.9	0.3	1	0.7	1.7	198	0.09
fT3	2.4	0.4	2.6	1.1	1.02	198	0.309
T4	7.3	2	7.4	2.1	0.28	198	0.783
fT4	1.1	1.4	1.2	1.6	0.35	198	0.723
PRL	13.7	12	17	14.5	1.59	198	0.114
Testosterone	4.4	7.4	3.3	1.2	-1.28	198	0.205
LH	8.2	5.2	7.7	5.1	-0.58	198	0.566
FSH	14.6	13.7	13.3	13.6	-0.64	198	0.525

Table 1: Comparison of demographic and clinical characteristics between decreased BMD group and BMD normal group of young and middle-aged male schizophrenic patients.

Factors	B	SE	Wald test	p-Value	Odd ratio	95% cl
PANSS	0.06	0.027	4.24	0.039	1.06	1.00-1.12
negative BMI	-0.12	0.05	6.86	0.01	0.88	0.81-0.97

Table 2: Decreased BMD associated factors (multiple logistic regression analysis).

Discussion

Our study revealed that 33.5% (67/200) of Chinese young and middle-aged male schizophrenic patients exhibited decreased BMD. We did not find previous study about BMD in young and middle-aged Chinese people. Only one study reported that osteoporosis prevalence was 7.7% in males aged 50-59 years in Chinese Han population. BMD is smooth and steady before 40 years old on BMD, and downtrend after 40 years old, drop rapidly between 50 and 60 years old [13]. While our result found that the prevalence of young and middle-aged schizophrenic patients was much higher than the older general population in China. And it suggested that Clinical psychiatrists should pay more attentions to the decreased bone mineral density in young and middle-aged male subjects with schizophrenia.

In our study, the prevalence of fracture in the decreased BMD group (17.9%) is more than twice the BMD normal group (8.3%), and it is statistically significant. It is similar to one study that reported osteoporosis fractures of males on psychotropic in 23% [14]. Some reports proved that decreased BMD is generally recognized as the main risk factor for hip fracture [15,16]. Bone density decreased by 1 standard deviationswill double the risk of fracture, which are consistent with our study [17]. For young and middle-aged male patients, they usually do not pay attention to the changes of their bone density. But they are one of the main undertakers of social labours. 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, accordance with 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 are 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 causing 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.

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