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ANALYSIS OF BONE MINERAL DENSITY AND RELEVANT FACTORS IN PATIENTS WITH TYPE 1 DIABETES

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Abstract – We investigated changes in bone mineral density (BMD) and relevant factors of BMD in patients with type 1 diabetes (T1D). A total of 47 patients with T1D and 40 healthy controls participated in this study. The waist-to-hip ratio (WHR) and body mass index (BMI) were calculated after physical examination. The lumbar spine (L2-L4) BMD and left femoral neck BMD were examined. Blood samples were collected. The BMI, WHR, fasting C peptide (FCP), postprandial C peptide (2hCP), lumbar spine and left femoral neck BMD of the patients with T1D were significantly lower than those of healthy controls, while the fasting plasma glucose (FPG), postprandial plasma glucose (2hPG) and hemoglobin A1c (HbA1c) were higher (P <0.05). Duration of T1D and HbA1c were negatively correlated with lumbar spine and left femoral neck BMD. The FCP and 2hCP were positively correlated with lumbar spine and left femoral neck BMD.

Key words: Bone mineral density; body mass index; type 1 diabetes

INTRODUCTION

The incidences of diabetes and osteoporosis have increased and diabetic patients with a high prevalence of osteoporosis are gradually attracting more attention (Watanabe and Okazaki, 2012). There are complex relationships between diabetes and osteoporosis. Patients with T1D have a greater risk of fracture since they cannot reach their potential peak bone mass (Sealand et al., 2013). The change in the bone mineral density (BMD) of patients with T1D has always been disputed. It has been reported that the patients with type 2 diabetes (T2D) have reduced, increased or unchanged BMD (Brown SA, 2004; Abdulameer et al., 2012; Chen et al., 2013). Several studies have reported that patients with T1D have increased bone fracture risk and decreased BMD (Vestergaard, 2007; Eller-Vainicher et al., 2011).

The increased risk of osteoporotic fracture is related to the history of diabetes, diabetes duration and chronic complications (Rakic et al., 2006; Schneider et al., 2012). Meanwhile the risk of bone fracture is related to glycemic control, and the etiologies remain elusive (Neumann et al., 2011; Simmons et al., 2011). What's more, hyperglycemia, autoimmune inflammation, hyperinsulinemia, hypoamylinemia, deficit of insulin-like growth factors-I (IGF-I) and vitamin D may be the potential pathogenic mechanisms of T1D (Moyer-Mileur et al., 2008; Coe et al., 2011; Takeuchi, 2012). Although osteoporosis is one of the complications of T1D, there are few studies about the BMD of patients with T1D in China.

In recent years, research about the BMD of patients with T2D is gradually increasing in China and abroad, while there is relatively less researche about

T1D. The aim of this study was to investigate BMD changes in patients with T1D and the association between BMD and factors such as the course of the diabetes, hemoglobin A1c, fasting C peptide, fasting plasma glucose, 2 h postprandial plasma glucose and 2 h postprandial C peptide. In our study, we collected forty-seven patients with T1D to investigate the changes in BMD and factors relevant related to BMD, using classical statistical methods.

MATERIALS AND METHODS

Study population

Patients with T1D were recruited from inpatients and outpatients in the incretion department of the Third Hospital of Nanchang from February 2010 to February 2012. All patients enrolled in our study conformed to the 1999 World Health Organization criteria for diagnosis of T1D. Healthy people with normal blood glucose from the physical examination center of the Third Hospital of Nanchang and the investigation of epidemiology in community were taken as controls. The study protocol was explained to both cases and controls before participation, and informed consent was obtained from each participant prior to the start of the study.

Assay methods

General information of the study population, such as gender, age, education level, vocation, marriage status, income, duration of diabetes and complications was collected. The height, weight, waist and hip of all participants were measured by physical examination, and the BMI (kg/m^2) and WHR were calculated. Dual-energy X-ray absorptiometry (MEDILINK, France) was used to measure the lumbar spine (L2-L4) BMD and left femoral neck BMD. All of the measurements were completed with the same instrument and operator.

Fasting blood samples of the patients with T1D were collected to measure the levels of FPG, HbA1c and FCP. The levels of 2hPG and 2hCP were detected 2 h after eating 100 g of steamed bread. The control group underwent the oral glucose tolerance test. The fasting blood and the 2 h post-meal blood were collected to measure the biochemical parameters. The venous blood glucose was determined by the method of glucose oxidase using an automatic biochemical analyzer (ADVIA2400, Siemens). Plasma C peptide was measured using the radiate immune assay kit (Shandong 3V, China). HbA1c was detected by high efficiency liquid chromatography using an automatic glycosylated hemoglobin meter (BIO-RAD, America).

Statistical analysis

Statistical analysis was performed by SPSS ver. 13.0 statistical software (SPSS, Chicago, IL), and data were expressed as means ± SD. One-way ANOVA or two independent T-tests were used to analyze all data of the healthy controls and patients with T1D. Pearson's correlation coefficient was used to indicate the correlation. Multiple-factor analysis was performed using the multiple stepwise regression method. There is significantly statistical difference when P <0.05.

RESULTS

The study population included 47 patients with T1D and 40 healthy controls. The mean duration of diabetes was 7.21±3.97 years, and the average age of participants in the T1D and control groups had no obvious difference (20.19±5.21 vs. 21.41±5.39 years, P >0.05). Differences in demographic, physical and biochemical variables between the T1D and control groups are shown in Table 1. The BMI, WHR, FCP, 2hCP, lumbar spine and left femoral neck BMD of the diabetic patients were significantly lower than those of the control subjects (P <0.05), while the FPG, 2hPG and HbA1c of the diabetic group were increased (P <0.05). Since there was a significant difference in the BMI between the two groups, the data were further analyzed by one-way ANOVA after BMI was adjusted. The results indicated that FCP, 2hCP and BMD of the diabetic group were still lower than those of the control group, while the FPG, 2hPG and HbA1c of the diabetic group were significantly increased (P <0.05).

Table 1. Demographic, physical and biochemical variables of T1D patients and control subjects (Data are shown as means ± SD, * $P < 0.05$ vs. control group)

Variables	Type 1 diabetes	Control
Number	47	40
Age (years)	20.190 ± 5.210	21.410 ± 5.390
BMI (kg/m^2)	21.260 ± 3.140*	24.400 ± 3.500
WHR	0.770 ± 0.150*	0.830 ± 0.220
HbA1c (%)	8.100 ± 1.900*	5.100 ± 0.600
FPG (mmol/L)	8.500 ± 2.100*	5.20 0± 0.800
2hPG (mmol/L)	12.520 ± 3.170*	6.720 ± 1.030
FCP (ng/ml)	0.230 ± 0.100*	1.860 ± 0.630
2hCP (ng/ml)	0.320 ± 0.150*	5.410 ± 1.890
lumbar spine (L2-L4) BMD (mg/cm^3)	0.822 ± 0.083*	0.885 ± 0.086
left femoral neck BMD (mg/cm^3)	0.813 ± 0.090*	0.877 ± 0.098

Table 2. The Pearson analysis of BMD and relevant factors in patients with T1D and relevant factors

		Lumbar spine BMD	Left femoral neck BMD
Age	*r* value	0.028	0.033
	P value	0.326	0.347
Diabetic duration	*r* value	-0.145	-0.161
	P value	0.002	0.000
BMI	*r* value	0.012	0.020
	P value	0.561	0.478
HbA1c	*r* value	-0.141	-0.203
	P value	0.001	0.000
FPG	*r* value	-0.079	0.052
	P value	0.073	0.196
2hPG	*r* value	-0.035	-0.055
	P value	0.166	0.249
FCP	*r* value	0.312	0.340
	P value	0.000	0.000
2hCP	*r* value	0.261	0.272
	P value	0.000	0.000

Table 3. The multiple regression analysis of BMD and relevant factors in patients with T1D

	Age	Diabetic duration	BMI	HbA1c	FPG	2hPG	FCP	2hCP
Regression coefficient	-0.001	-0.072	0.002	-0.085	-0.002	-0.033	0.133	0.116
P value	0.347	0.004	0.222	0.001	0.267	0.217	0.000	0.000

Pearson's analysis for the BMD of T1D patients and relevant factors found that the duration of diabetes (r = -0.145, $P = 0.002$; r = -0.161, $P = 0.000$) and HbA1c (r = -0.141, $P = 0.001$; r = -0.203, $P = 0.000$) were negatively correlated to lumbar spine BMD and left femoral neck BMD, while FCP (r = 0.312, $P = 0.000$; r = 0.340, $P = 0.000$) and 2hCP (r = 0.261; $P = 0.000$; r = 0.272, $P = 0.000$) showed positively cor-

related with the lumbar spine BMD and left femoral neck BMD (Table 2). The other variables, such as age, BMI, FPG and 2hPG had no association with lumbar spine BMD and left femoral neck BMD (P >0.05; Table 2).

Furthermore, multiple regression analysis was performed with lumbar spine and left femoral neck BMD as dependent variables and the other relevant factors as independent variables. The analysis results indicated that the duration of diabetes (r = -0.072, P = 0.004), HbA1c (r = -0.085, P = 0.001), FCP (r = 0.133, P = 0.000) and 2hCP (r = 0.116, P = 0.000) were directly associated with lumbar spine and left femoral neck BMD after adjusting BMI (Table 3). The other factors, such as age, BMI, FPG, and 2hPG were not correlated with lumbar spine and left femoral neck BMD (P >0.05; Table 3).

DISCUSSION

In this study, the lumbar spine and left femoral neck BMD of patients with T1D were lower than those of the control group were. The BMD of lumbar spine and left femoral neck were reduced by 7.1% and 7.3%, respectively. Mastrandrea et al. (2008) found that patients with T1D had reduced BMD and increased risk of postmenopausal osteoporosis fracture by studying 63 cases of female patients with T1D, and Hamilton (2009) came to similar conclusions in Australia. Some researchers have found that the BMD of premenopausal women with T1D was 3-8% lower than that of healthy women and that the risk of osteoporosis fracture increased (Strotmeyer et al., 2006). Therefore, the change in the BMD in patients with T1D was in conformity to the results of the abovementioned studies. However, some researchers have observed that there were minor differences in body composition, and no differences in BMD between healthy controls and patients with long-standing childhood and adolescence onset T1D (Ingberg et al., 2004). These inconsistent conclusions may be related to the small sample size, i.e., only a few tens of cases. Collecting a large amount of studying subjects is actually quite difficult because the number of patients with T1D is small. In addition, genetic factors play very important roles in the BMD, and the results may be changed among different races and different areas (Travison et al., 2011).

This study found that the BMD of lumbar spine and left femoral neck were negatively correlated to the duration of disease and HbA1c, and positively related to the FCP and 2hCP. The complications of diabetes could lead to a decrease in BMD since the incidence rates of complications increase with the duration of diabetes. The level of HbA1c reflects the glycemic control of patients in recent 3 months. Glycemic control will become worse and the BMD will be reduced when the level of HbA1c is increased. Heilman et al. (2009) have found that the BMD of patients with T1D was reduced and the lower BMD was associated with poor glycemic control. Nevertheless, some researchers considered that blood glycemic control and diabetes duration could not influence the BMD of patients with T1D (Hadjidakis et al., 2006). Because the level of C peptide reflects the function of islet β cells and the endogenous insulin secretion which have a relationship with BMD, the level of C peptide of patients in T1D is related to the BMD (Rakel et al., 2008). With regard to the mechanism of the reduced BMD of patients with T1D, studies have found that the levels of IL-6 and IL-8 of patients with T1D rose and the levels of BMD and IGF-1 (insulin-like growth factor-1) fell, and the lower level of BMD in patients with T1D was associated with worse glycemic control and higher levels of inflammatory factors (AboElAsrar et al., 2012; Joshi et al., 2013). Rachon et al. (2003) found that the BMD and IL-6 of postmenopausal patients with T1D were increased and reduced respectively, which also indicated that the BMD of patients with T1D may be related to autoimmunity and the levels of inflammatory factors. In addition, some studies have found that vitamin D receptor-gene polymorphisms are closely related to BMD in patients with T1D (Kocabas et al., 2010; Pesta, 2012). The BMD of patients with T1D also has a close relationship with diabetes complications, antidiabetic drugs, glycemic control and life style. Therefore, other parameters, such as calcium, phosphorus, albumin, creatinine, 25-hydroxy vitamin D3, need to be further analyzed

to observe the factors related to the bone metabolism of patients with T1D.

In a word, the BMD of patients with type 1 diabetes is reduced and BMD is related to the duration of diabetes and the levels of HbA1c and C peptide. The results of our study provide some reference to the treatment of osteoporosis of patients with T1D and may facilitate the taking of effective countermeasures; the specific mechanism still needs to be further studied with larger sample size.

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