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A comparison of bone quality and its determinants in young opioid-dependent women with healthy control group

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ABSTRACT

Background: Little is known about bone quality and its determinants in patients with opioid addiction. The goal of this study was to compare bone quality and its determinants in young opioid addicted women with a local group of young healthy women.

Method: Using cross-sectional design, 104 women (mean age 29.9 yrs, range: 20–40 yrs, SD = 7.8) with previous opioid addiction and current methadone substitution (3–30 mg, daily) for 1–16 weeks were compared to 117 healthy women (mean age 31.0 yrs, range: 20–40 yrs, SD = 5.9). Bone quality was examined with quantitative ultrasound. Anthropometric characteristics (body weight, fat free mass (FFM), fat mass) were obtained by bioelectrical impedance analysis. Substance use and other risk factors for low bone quality were assessed by questionnaire-based interviews.

Results: More than one-quarter (34%) of patients had osteopenia (n = 31) or osteoporosis (n = 4), compared to 16% of the healthy control group having osteopenia (n = 18). Bivariate correlation analysis demonstrated that age, body weight, and FFM correlated with bone quality ($p < 0.05$) in healthy women, which were not found in patients. Multivariate analyses showed that in healthy controls, the determinants of bone quality were age, body height, physical activity, and BMI, but in patients, the determinant of bone quality was duration of drug intake.

Conclusions: Long-term opioid dependence in young women may lead to low bone quality. Efforts to increase awareness of low bone quality in young opioid addicted women should be considered so that effective treatment may be employed to lower future fracture risk.

1. Introduction

Osteoporosis is a systemic disease, characterized by a progressive loss of bone quality and micro-architectural deterioration, predisposing people to fractures after minimal trauma or falling (Rachner et al., 2011). Several risk factors, such as advanced age, low body mass index (BMI) and life-style factors as well as decreased mobility, have been reported to be the determinants of bone quality in the general population (Lima et al., 2009; Morin et al., 2009).

Low bone quality has been found among illicit drug users and opioid users on methadone maintenance treatment (MMT) both in men and women. A cross-sectional study in Switzerland reported a high prevalence of low bone mineral density (BMD) in 144 long-term opioid-dependent men (Gotthardt et al., 2016). Kim et al. (2006) reported that more than three quarters of the sample of patients (33 men, 59 women) with opioid dependence had low BMD. However, contrasting studies exist. For example, Grey et al. (2011) found that BMD in 83 opioid dependent patients (48 men, 35 women) was lower than normal throughout the skeleton in men, but not women. In general, studies focusing on young opioid-dependent women are limited, and the effect of opioid dependent on bone quality in young women is unclear and merits thorough investigation (Milos et al., 2011).

Several potential mechanisms have been proposed to analyze the bone quality in the opioid-dependent people. Some reports found that chronic abuse of opioid drugs may be associated with altered bone metabolism and reduced trabecular bone mass (Perez-Castrillon et al., 2000). Other researches established that opioids abuse can suppress hypothalamic secretion of gonadotropin-releasing hormone and consequently decreases the level of gonadal hormones (Katz and Mazer, 2009), and chronic hypogonadism is a prominent cause of osteoporosis in both sexes (Seeman, 2002). Moreover, life-style factors and comorbidities associated with long-term opioid consumption, such as smok-

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ing, alcohol use disorders and lower physical activity level may influence bone quality in young opioid dependent women (Slemenda et al., 1989). To our knowledge, body composition was an important determinant of bone status (Ding et al., 2016). Increased mechanical loads stimulate bone formation and suppress resorption, whereas unloading has the opposite effect (Ehrlich and Lanyon, 2002; Rodan, 1997). Body weight (BW) and fat-free mas (FFM) were found to have positive relationship with bone quality (Morin et al., 2009; Lima et al., 2009). However, it's uncertain that if these relationships also exist in patients with opioid addiction, and what's the difference compared with young healthy women.

Within a large cohort of young opioid dependent women and a healthy control group, the aim of our study was (1.) to evaluate bone quality in patients comparing with the healthy controls, and (2.) to find the determinations (among the risk factors) to bone quality in young opioid dependent women and in the healthy controls, so that the therapeutic interventions may be employed to prevent or treat drug-induced osteoporosis.

2. Material and methods

2.1. Design, participants and recruitment process

This was a cross-sectional study of long-term opioid dependent women living in the middle area of China. 206 Subjects were recruited from the Women's Specific Drug Rehabilitation Center of Anhui Province between November 2015 and March 2016. Inclusion criteria were:1.) newcomers (within 4 months), 2.) age 20–40 years, 3.) previous drug consumption of > 3 years.

After the medical examination and the questionnaire-based interviews, the exclusion criteria reduced the number of potential participants to 135. Exclusion criteria were: 1.) HIV infection; 2.) Individuals with history of fractures in previous 24 months; 3.) type 1 diabetes; 4.) significantly impaired renal or hepatic function, or chronic kidney disease; 5.) pregnancy, because of the altered hormonal household.

Patients not willing to participate or who had withdrawn consent were also excluded. Finally, a total of 104 patients aged 20–40 years were recruited.

Meanwhile, a total of 117 age- and BMI-matched healthy women were used as control group to compare bone quality and anthropometric data. All controls were recruited from Anhui province and assessed in Anhui National Physical Fitness Monitoring Center in Hefei of Anhui province. All subjects answered the questionnaires regarding lifestyle, medical history, and current medication. Individuals with history of fractures in previous 24 months, type 1 diabetes, significantly impaired renal or hepatic function, and chronic kidney disease were excluded. Women not willing to participate or who had withdrawn consent were also excluded.

All participants provided informed consent, and the study was conducted in accordance with the guidelines in Institute and Intelligent of Machines, Chinese Academy of Science. The study was approved by appropriate institutional research ethics committee.

2.2. Questionnaires – background characteristics

The questionnaires-based interviews were taken to obtain more information about patient group and healthy controls. The questionnaires include six parts: medical history, history of drug use, physical activity level, nutritional calcium intake, smoking status, and education level, as shown in Table 1. The history of drug use was taken only in patient group.

In order to ensure accuracy in survey results, we told all the subjects the purpose of this survey. The answers of patients were compared with medical examination and the official data, and any discrepancies would be confirmed by the individuals.

Table 1
Questionnaires to the Patient and Control group.

Questions	Data Type
Medical history:	
1. Individuals with history of fractures in previous 24 months	0 = No 1 = Yes
2. Pregnancy	0 = No 1 = Yes
3. Type 1 diabetes	0 = No 1 = Yes
4. Significantly impaired renal or hepatic function, or chronic kidney disease	0 = No 1 = Yes
History of drug use (Patients only):	
1. Type of drug use: (1) Heroin, opium, morphine, and other opiates (2) Cocaine (3) Marijuana (4) Amphetamines (5) Hallucinogens (6) Other drugs	Multi selection
2. Age at onset of drug intake (year)	Quantitative
3. Duration of drug intake (years)	Quantitative
4. Frequency of drug use: (1) 3–7/week or more; (2) 1–2/week; (3) 1–2/month; (4) seldom	Single selection
5. Way of drug use: (1) injection (2) non injection	Single selection
6. Duration of methadone intake (weeks)	Quantitative
7. Daily methadone dose (mg)	Quantitative
8. Duration of drug intake (years)	Quantitative
Physical activity level:	
1. Average physical activity (20 min brisk walking, fitness training or sport) (hours/week)	Quantitative
Nutritional calcium intake:	
1. Diet habit: (1) well-balanced diet, regular intake of calcium-rich foods (2) Occasionally intake of calcium-rich foods (3) Low nutritional calcium intake, seldom intake of calcium-rich foods	Single selection
Smoking status:	
(1) often (2) occasionally (3) seldom	Single selection
Education level:	
1. Years of education (years)	Quantitative

2.3. Measurements of anthropometric characteristics

Body height (BH) was measured to the nearest 0.1 cm using a stadiometer (GMCS-I, XinDongHuaTeng Corp., China). BW, FFM, and fat mass (FM) were measured by bioelectrical impedance analyzer (BX-BCA-100, Broshare Technology Corp., Hefei, China); the REG. NO. of BX-BCA-100 in the China Food and Drug Administration (CFDA) is 2210038. In addition to abstinence from diuretics, alcohol, intense exercise and fluids as detailed earlier, subjects emptied their bladder 30 min before the bioelectric impedance analyses (BIA) measurement was taken. Subjects stood on bare feet with the heel and toe of each foot in contact with the metal footpads, with arms hanging on each side, lightly holding the analyzer handgrips. Coefficient of variance (CV) of the impedance measure was 0.4%. Values obtained from BIA were supported by skinfold measurements using harpenden calipers.

2.4. Measurements of bone quality

Bone quality was assessed by a quantitative ultrasound (QUS) device (BX-BDI-500A, Broshare Technology Corp., Hefei, China). The REG. NO. of BX-BDI-500A in CFDA is 20152230048. Speed of sound (SOS; m/s) and broadband ultrasound attenuation (BUA; dB/MHz) were measured on the right calcaneus with the subjects in an upright seated position. The stiffness-index (SI), a combination of SOS and BUA, is calculated by the system according to the following formula: $SI = 0.67 \times BUA + 0.28 \times SOS–420$ (Njeh et al., 1997) and has a lower precision error than either SOS or BUA alone. In general, SI value impresses the bone quality as measured by QUS, and higher SI value indicates better bone health. Meanwhile, values were also expressed as T-score, which was generated based on the SI in QUS device (Liu et al., 2012). Bone health of subjects was classified into normal (T-score more than −1.0), osteopenia (T-score between −2.5 and −1.0), and osteoporosis (T-score less than −2.5). The measurement took 5 min