European Geriatric Medicine 7 (2016) 18–22

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Research paper

The relationship of vitamin D with bone mineral density in Parkinson's disease patients

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ARTICLE INFO

Article history:
Received 15 June 2015
Accepted 6 August 2015
Available online 29 August 2015

Keywords:
Parkinson's disease
Vitamin D
Bone mineral density
Osteoporosis

ABSTRACT

Objectives: The purposes of the present study were to evaluate bone mineral density (BMD) and vitamin D status in Parkinson's disease (PD) and to identify the correlation of vitamin D with BMD and disease related parameters.
Methods: Fifty-two patients with PD and 39 controls were recruited in study. Hoehn and Yahr (HY) staging scale, parts II and III of the Unified Parkinson's Disease Rating Scale (UPDRS) were used to assess disease stage, daily living activities, and motor activity, respectively. BMD of lumbar spine and femoral neck were assessed by dual energy X-ray absorptiometry. Serum 25-hydroxyvitamin D (25OHD) levels were measured.
Results: Seventeen patients (32.7%) were osteoporotic and 22 (42.3%) osteopenic. Female and male PD patients had significantly lower T scores and BMD values at femoral neck, whereas only female patients showed significant differences in T scores and BMD values at lumbar spine compared to controls. The mean 25OHD levels were significantly lower in PD patients compared with controls. 25OHD levels showed a positive correlation with T scores and BMD values of lumbar spine and femoral neck and a negative correlation with UPDRS part II, UPDRS part III, and HY stage. In partial correlation analysis performed to adjust disease duration, 25OHD levels were also correlated with lumbar and femoral neck BMD values, femoral neck T scores, but not with other studied parameters.
Conclusions: This study demonstrated that PD patients had lower 25OHD levels and decreased BMD values compared to controls and detected significant association of 25OHD levels with BMD values.

1. Introduction

Parkinson's disease (PD) is a degenerative neurological disease associated with loss of self-sufficiency, an increased risk of falls and a high incidence of fracture [1]. As a chronic and progressive neurodegenerative disease, the symptoms of PD include tremor, rigidity, bradykinesia, postural instability [2]. Osteoporosis (OP) is characterized by low bone mass and micro-architectural deterioration, with a consequent increase in bone fragility and fracture susceptibility [3]. Multiple factors contribute to the development of OP including age, gender, height, weight, family history, smoking status and vitamin D levels [4]. Recently, increasing demonstration suggests that patients with PD are at high risk for OP and fracture and it has also been proposed that PD can promote the development of OP [5–10].

The Global Longitudinal Study of Osteoporosis in Women (GLOW) study found PD to be the strongest single contributor to fracture risk compared with other studied factors [11]. Gait impairment, postural instability and falls, polypharmacy, and reduced bone mineral density (BMD) all contribute to fracture risk in PD. Vitamin D deficiency with secondary hyperparathyroidism may contribute to low BMD but disease duration and severity, age and low body mass index (BMI) are also implicated.

The aim of this study was to evaluate vitamin D status and BMD in Parkinson's disease (PD) and to assess association of vitamin D with BMD and disease related parameters.

2. Materials and methods

2.1. Subjects

This cross-sectional study was conducted between May 2014 and October 2014. The study protocol was approved by the local Ethics Committee of Recep Tayyip Erdoğan University,

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http://dx.doi.org/10.1016/j.eurger.2015.08.002
1878-7649/

Faculty of Medicine, Turkey. The study performed in accordance with the principles stated in Declaration of Helsinki and written informed consent was obtained from all participants prior to the study. Fifty-two consecutive patients with idiopathic PD and 39 healthy controls were enrolled. Patients were excluded if they showed other known causes of OP, such as endocrine and rheumatic diseases, or had history of therapy with corticosteroids or anti-osteoporotic medication. Age- and sex-matched healthy controls were recruited from among hospital staff or their relatives. None of control subjects had metabolic, neurological, and chronic diseases likely to affect bone metabolism or was receiving treatment for OP. Sociodemographic characteristics, smoking habits, sunlight exposure, disease severity were recorded. Sunlight exposure was assessed by the patients in terms of the preceding year, being graded as almost none, less than 15 min per week, or longer. The progression and disease severity of PD were evaluated using Hoehn and Yahr (HY) staging scale [12]. In addition, parts II and III of the Unified Parkinson's Disease Rating Scale (UPDRS) were used to evaluate the activities of daily living and the severity of motor dysfunction of all those in the PD group, respectively [13]. Height and weight were measured and body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared.

Table 1
Demographic and clinical characteristics of Parkinson's disease patients and control subjects.

	Parkinson's disease ($n = 52$)	Healthy control subjects ($n = 39$)
Mean age (years)	64.5 ± 9.7	65.4 ± 5.6
Female/male (n)	27/25	23/16
BMI (kg/m²)	28.8 ± 4.2	31.0 ± 3.8
Disease duration (years) (range)	3.4 ± 3.8 (1-20)	–
HY stage	1.7 ± 0.8	–
Stage I *n* (%)	22 (42.3)	–
Stage II *n* (%)	23 (44.2)	–
Stage III-IV *n* (%)	7(13.4)	–
UPDRS part II	10.6 ± 7	–
UPDRS part III	16.4 ± 8.6	–
Sunlight exposure n (%)		
Never	19 (36.5)	–
15 min/week <	22 (42.3)	–
15 min/week >	11 (21.2)	–
25OHD insufficiency n (%)	25 (48.1)	13 (33.3)
25OHD deficiency n (%)	23 (44.2)	5 (12.8)
Osteoporosis n (%)	17 (32.7)	4 (10.3)
Osteopenia n (%)	22 (42.3)	13 (33.3)

Values are expressed as mean ± standard deviation.
BMI: body mass index; HY: Hoehn and Yahr; UPDRS: Unified Parkinson's Disease Rating Scale; 25OHD: 25-hydroxyvitamin D.

2.2. BMD measurements

Using dual energy X-ray absorptiometry (DXA, Lunar Prodigy; Madison, WI, USA), BMD measurements were taken at both of the lumbar spine (L2-4) and left femoral neck. BMD values were expressed in g/cm^2. BMD values were converted into T scores, expressed in standard deviations, using Turkish reference values [14]. We used World Health Organisation (WHO) classification range to categorize subjects as normal ($T > -1$), osteopenic ($-2.5 < T \leq -1$), or osteoporotic ($T \leq -2.5$) [15].

2.3. Laboratory analysis

Serum samples of all participants were collected to evaluation for biochemical analysis. Serum concentrations of calcium (Ca), phosphorus (P), and alkaline phosphatase (ALP) were measured by standard autoanalyzer technique using Architect C1600® Abbott. Serum 25-hydroxyvitamin D (25OHD) was assessed by chemiluminescent microparticle immunoassay (Architect system, Abbott Diagnostic, Germany). Based on serum 25OHD concentration, vitamin D status was categorized as deficient (less than 30 nmol/L), insufficient (range of 30–50 nmol/L), and sufficient (more than 50 nmol/L) (to convert to nanomoles per liter, multiply by 2.496). Serum osteocalcin was measured using electrochemiluminescence on an immulite 2000 analyser (Diamond Diagnostic, US). Serum bone specific alkaline phosphatase (bALP) was determined by radioimmunoassay (Beckman-Coulter, Brea, CA).

2.4. Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 13.0, for Windows (SPSS, Chicago, IL, USA). Continuous variables are presented as the mean ± standard deviation (SD). The normality of the distribution for all variables was assessed by the Kolmogorov-Smirnov test. Intergroup comparisons were made using the Student's *t*-test for normally distributed variables and the Mann-Whitney *U* test for non-parametric variables. To assess the correlations between variables, Spearman's rank or Pearson's correlation analysis were used according to data distribution. In addition, partial correlation analysis was performed to eliminate confounding factor as disease duration in evaluation of association between BMD values, disease related parameters and vitamin D. A value of $P < 0.05$ was statistically significant.

3. Results

The demographic and clinical characteristics of patients and controls are shown in Table 1. Patients and controls did not significantly differ in age or sex ($P = 0.623$, $P = 0.648$), but BMI was significantly higher in controls than PD patients ($P = 0.011$). The mean disease duration in PD patients was 3.4 ± 3.8 (range 1–20) years. The prevalence of OP and osteopenia was 32.7% and 42.3% in PD group and 10.3% and 33.3% in control groups, respectively. In PD group, the mean 25OHD level was 13.4 ng/mL (range 6.4–34.5) with 23 (44.2%) having D vitamin deficiency and 25 (48.1%) having D vitamin insufficiency.

The comparison of laboratory parameters and BMD values between patients and controls is shown in Table 2. The mean age did not differ between either female PD patients and controls or male PD patients and controls. While the mean BMI was significantly lower in female PD patients compared to controls, there was no significant difference in BMI between male PD patients and controls. Female PD patients had significantly lower 25OHD level and higher PTH concentration than controls. Male PD patients had significantly lower 25OHD level and higher bALP and osteocalcin concentrations compared to controls. The mean T scores, Z scores, and BMD values in the lumbar spine and femoral neck were significantly decreased in female PD patients compared to controls. The mean T scores, Z scores, and BMD values in the femoral neck and Z scores in the lumbar spine were significantly lower in male PD patients compared to controls. Although male PD patients had lower mean T score and BMD values in the lumbar spine compared to controls, the differences were not statistically significant.

The comparison of BMD measurements and disease characteristics between female and male patients with PD is shown in Table 3. Female PD patients demonstrated significantly lower T scores and BMD (g/cm^2) values for lumbar spine compared to male PD patients (−2.2 ± 1.2 vs −1.7 ± 1.2, $P = 0.004$; 0.803 ± 0.161 vs 0.951 ± 0.174 g/cm^2, $P = 0.03$, respectively). Femoral neck T scores and BMD (g/cm^2) values, 25OHD levels, disease duration, UPDRS part