Bone and mineral metabolism in older adults with Parkinson’s disease

SUZAN ABOU-RAYA1, MAHDIAH HELMI2, ANNA ABOU-RAYA3

1Geriatric Division, Department of Internal Medicine, Faculty of Medicine, University of Alexandria, Alexandria, Egypt
2Department of Biochemistry, Medical Research Institute, Alexandria, Egypt
3Rheumatology Division, Department of Internal Medicine, Faculty of Medicine, University of Alexandria, Alexandria, Egypt

Address correspondence to: S. Abou-Raya. Tel: (203) 5924601; Fax: (203) 5457611. Email: suzanraya@yahoo.com

Abstract

Objectives: Parkinson’s disease (PD) and osteoporosis are two common chronic disabling conditions in older adults that adversely affect quality of life. The aim of the present work was to study the relationship between bone changes and PD.

Methods: eighty-two patients with established PD aged 65 years or older and 68 age-, sex- and body mass index (BMI)-matched healthy control subjects were recruited. Exclusion criteria included other known causes of osteoporosis. Data including BMI, sunlight exposure, Hoehn and Yahr stage, disease duration and history of previous falls and/or fractures were collected. Bone mineral density was measured using dual energy x-ray absorptiometry. Sera were analysed for ionised calcium, vitamin D, bone alkaline phosphatase (BALP) and urinary N-terminal telopeptide of type I collagen (NTx). Physical and mental performance was also assessed.

Results: the findings show that the bone mineral density (BMD) of all PD patients was significantly lower compared to controls. PD patients had significantly decreased vitamin D levels, significantly increased BALP and NTx levels, reduced physical and mental performance and more falls and/or fractures in comparison to healthy controls.

Conclusion: PD is associated with an increased incidence of osteoporosis, falls and fractures. PD is thus a risk factor for osteoporosis and appropriate therapeutic interventions should be initiated to slow or prevent disability.

Keywords: Parkinson’s disease, osteoporosis, older adults, elderly
Introduction

Parkinson’s disease (PD) and osteoporosis are two common chronic conditions in older adults that are gaining importance for healthcare due to the associated morbidity and mortality. PD and osteoporosis are both chronic disabling conditions in older adults that adversely affect quality of life.

PD is a chronic, common neurological condition, the prevalence of which increases with advancing age [1–2]. The prevalence of PD increases from 0.6% between 65 and 69 years to 3.5% between 85 and 89 years and 70% of patients are older than 55 years when they experience their first symptoms [1, 3–5].

PD is a movement disorder characterised by tremor, rigidity, slowness of movement and postural imbalance leading to immobility and frequent falls [1, 6, 7]. Evidence suggests that PD patients are at increased risk of falls, more related to intrinsic (disease-related) factors than extrinsic (environmental) factors [7–9]. Furthermore, it has been reported that PD patients have a higher incidence of hip fractures than the general population [9–12].

Osteoporosis is a skeletal disorder characterised by compromised bone strength and increased fracture risk [13]. It is one of the most important diseases encountered in geriatric practice. During their lives, women lose about 60% of their trabecular bone and about 35% of their cortical bone. Fractures are thus commoner in older people. The lifetime risk of any fracture of the hip, spine or distal forearm is about 40% in white women and 13% in men [13–15].

Patients with PD have increased rates of osteoporosis which may not be related solely to immobility [16]. In both conditions, there is an increased fracture risk [15, 16].

The examination of the association of these common problems in our increasing ageing population is important if we are to devise interventions to slow or prevent disability. The increasing morbidity, disability and mortality associated with fractures in older adults make finding new determinants of osteoporosis a priority. Accordingly, the aim of the present study was to evaluate the relationship between bone changes and PD.

Methods

Participants

One hundred and twenty-six consecutive patients aged 65 years and above with established PD who presented to our institution for follow-up visits were enrolled in this study. They fulfilled diagnostic criteria for PD, and were evaluated with the Unified PD Rating Scale (UPDRS) [17] and the Hoehn and Yahr (H and Y) staging [18].

Patients were excluded if they had other known causes of osteoporosis, systemic inflammatory or connective tissue disease; renal, hepatic, cardiac or thyroid impairment; a history of therapy with corticosteroids, oestrogen, bisphosphonates, calcitonin, calcium or vitamin D.

Healthy subjects were recruited by advertisements, physician referrals and from senior citizen centres to serve the purpose of controls. Controls were screened for participation eligibility with the same exclusion criteria being applied as in patients. Sixty-eight age-, sex- and body mass index (BMI)-matched healthy control subjects were ultimately recruited.

Data including demography, disease duration, disease severity, medication usage, diet and sunlight exposure, Hoehn and Yahr stage and history of previous falls (a history of falls was obtained from patients and/or close family members, caregivers or friends particularly in people with cognitive impairment) and/or fractures (history of fractures was obtained both by patient recall and by checking medical records) were collected. Diet content for daily intake of vitamin D and calcium was assessed by a food frequency questionnaire. The patients were asked to complete a questionnaire about diet and exposure to sunlight. The mean weekly dietary calcium and vitamin D intake was calculated for each participant. Sunlight exposure was assessed by a questionnaire administered to the participants. Sunlight exposure of <15 min a week was taken to mean that the subject did not go outdoors.

The study was approved by the Ethics Committee and the Institutional Review Board of our institution. Informed consent was obtained from all subjects and the study was conducted in accordance with the ethical standards for research involving human subjects described in the Helsinki Declaration.

Bone density measurement

Bone mineral density (BMD) measurements using dual-energy X-ray absorptiometry (DXA) were performed at the lumbar spine (LS) and proximal femoral neck (FN). The DXA machine (Hologic 4500A, version 9.03; Hologic, Inc., Waltham, MA) was used to measure BMD (g/cm²) using standard protocols. The difference between an individual’s BMD and the mean for a reference population is expressed in standard deviation (SD) units. Z- and T-scores were calculated where the Z-score is the SD of the individual's BMD compared to the mean BMD score of a similar sex-, age-, weight- and height-matched population and the T-score is the SD of the individual’s BMD compared with the mean BMD score in a young healthy population. BMD was categorised as normal, low bone density (osteopaenia) or osteoporosis as defined by the WHO. WHO defines osteopaenia as a bone density between 1 SD and 2.5 SD below the bone density of a normal young adult. Osteoporosis is defined as 2.5 SD or more below that reference point. Our institution follows the National Osteoporosis Foundation screening guidelines recommending bone density testing for all women aged 65 or older and younger postmenopausal women who have had a fracture or who have one or more risk factors for osteoporosis.
Biochemical measurements

Serum samples collected at baseline after an overnight fast were stored at −70° until analysed. Serum calcium (Ca) corrected for albumin level, phosphorus (P), creatinine and blood urea nitrogen (BUN) were measured by standard methods.

Serum 25-hydroxycholecalciferol (25-OHD) was measured using a competitive protein binding assay and 1,25 dihydroxycholecalciferol (1,25(OH)_2D) was measured after extraction by a radioreceptor assay (Nichols Institute Diagnostics, San Juan Capistrano, CA, USA). The results were interpolated from the standard reference curve provided with each kit.

Bone alkaline phosphatase (BALP) was determined using radioimmunoassay (RIA, Hybritech Inc., CA, USA). Serum N-terminal telopeptide of type I collagen (NTx) was measured by ELISA (Osteomark NTX serum; Ostex International).

Radiography

Plain x-ray radiographs of the spine to assess vertebral compression fractures (VCFs) were carried out for all subjects.

Disease severity, physical and mental performance assessment

Disease severity was assessed using the UPDRS. Physical performance assessment included the 6-min walk test, the ‘Get-Up and Go’ test, grip strength and instrumental activities of daily living (IADLs). The 6-min walk test was performed according to the protocol of Guyatt et al. [19]. The ‘Get-Up and Go’ test is a timed functional test in which subjects are asked to stand up from a standard chair and walk a distance of ~3 m, turn around and walk back to the chair and sit down again [20]. The normal time required to finish the test is between 7 and 10 s. Grip strength (kg) was measured using a Jamar dynamometer and scored as the maximum of two attempts for the stronger hand [21]. Grip strength measurement was based on longstanding preference which was often the side least affected by PD.

Participants were asked if they needed assistance in performing IADL tasks (preparing own meals, doing own housework and laundry, using the telephone and taking prescribed drugs) using the Lawton IADL Scale [22]. Mental performance was assessed using the Mini-Mental State Examination (MMSE) test for cognition [23].

Statistical analysis

Statistical analyses were performed using the SPSS for Windows 13.0 software (SPSS, Chicago, IL). Data of continuous variables are presented as means and SD. Group differences were analysed using Student’s t-test and the chi-square test. Spearman’s rank correlation was used for correlations. Statistical significance was based on a 5% level.

Table I. Demographic characteristics of the study population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PD patients (n = 82)</th>
<th>Controls (n = 68)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67.5 (7.5)</td>
<td>67.0 (6.9)</td>
<td>0.832</td>
</tr>
<tr>
<td>Sex (males/females)</td>
<td>43/39</td>
<td>36/32</td>
<td>0.689</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.9 (5.7)</td>
<td>23.5 (3.8)</td>
<td>0.677</td>
</tr>
<tr>
<td>Previous fall(s)</td>
<td>38 (46%)</td>
<td>2 (3%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Previous fracture(s)/VCFs</td>
<td>33 (40%)</td>
<td>1 (1.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Sunlight exposure/week</td>
<td>15 min or more</td>
<td>21 (26%)</td>
<td>55 (81%)</td>
</tr>
<tr>
<td></td>
<td>&lt;15 min</td>
<td>61 (74%)</td>
<td>13 (19%)</td>
</tr>
<tr>
<td></td>
<td>&lt;15 min</td>
<td>48 (59%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td></td>
<td>&lt;15 min</td>
<td>45 (55%)</td>
<td>2 (3%)</td>
</tr>
</tbody>
</table>

Values are given as mean (SD) or numbers (percentage).

Results

Eighty-two patients (43 men, 39 women), mean age 67.5 ± 7.5 years, were found to be eligible and agreed to participate. The demographic characteristics are shown in Table 1. The PD patients were 43 males and 39 females (mean ± SD age 67.5 ± 7.5 years). The mean ± SD duration of PD was 6.5 ± 3.5 years. The mean ± SD Hoehn and Yahr staging was 3.0 ± 0.5. Three patients were untreated; the other 79 were treated with anti-Parkinsonian drugs alone or in combination, including levodopa (19 cases), anticholinergics (28 cases), dopamine agonists (26 cases) and amantadine (6 cases). Forty-six per cent (11 males and 35 females) reported a fall(s) in the previous 12 months and 33 PD (7 males and 26 females) patients had experienced fractures. Twenty-one were found to have VCFs on x-ray. Three of the PD patients had sustained humeral neck fractures, two had sustained radial fractures, one had fracture of the ribs, one had fracture of the pelvis and five sustained FN fractures.

The mean ± SD scores of the UPDRS were total 31.7 ± (PD) and osteoporosis 10.8: activities of daily living (ADL) subscale 9.6 ± 5.1 and motor subscale 24.3 ± 5.9. PD patients had significantly reduced grip strength [29.5(9.5) versus 40.4(9.0), P < 0.01] and the 6-min walk test [1.01 (0.9) versus 1.45 (0.7), P = 0.01] and the timed ‘Get-Up and Go’ test was significantly prolonged [12.5 (1.0) versus 8.0 (0.5), P < 0.01] in PD patients compared to the controls. Impairment in one or more of the IADLs was recorded in 66% of the PD cohort and 26% of the controls. Mental performance as reflected by the MMSE score was significantly reduced in PD patients as compared to healthy controls [24.4(3.3) versus 28.1(1.5), P < 0.005].

Table 2 demonstrates the BMD measurements of the study population. The BMD of all PD was significantly lower compared to the BMD of the male PD patients and to the BMD of the female controls.
Table 2. Bone mineral density (BMD) measurements of the study population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PD patients (n = 82)</th>
<th>Controls (n = 68)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral neck BMD (g/cm²)</td>
<td>0.723 (0.09)</td>
<td>0.957 (0.05)</td>
<td>0.005</td>
</tr>
<tr>
<td>Z-score</td>
<td>−2.037 (0.29)</td>
<td>−1.266 (0.25)</td>
<td>0.001</td>
</tr>
<tr>
<td>Lumbar BMD (g/cm²)</td>
<td>0.889 (0.17)</td>
<td>1.114 (0.06)</td>
<td>0.001</td>
</tr>
<tr>
<td>Z-score</td>
<td>−1.753 (0.16)</td>
<td>−0.778 (0.21)</td>
<td>0.001</td>
</tr>
<tr>
<td>Controls</td>
<td>−0.735 (0.35)</td>
<td>−0.183 (0.28)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Values are given as mean (SD). BMD, bone mineral density.

Table 3. Serum biochemical markers in the study population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PD patients (n = 82)</th>
<th>Controls (n = 68)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BALP (U/l)</td>
<td>32.5 (6.5)</td>
<td>20.5 (5.5)</td>
<td>0.05</td>
</tr>
<tr>
<td>NTx (nmol/mmol Cr)</td>
<td>98.5 (23.6)</td>
<td>21.8 (23.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Serum Calcium (mg/dl)</td>
<td>8.8 (0.9)</td>
<td>19.9 (1.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Serum Phosphorus (mg/dl)</td>
<td>3.8 (0.5)</td>
<td>3.9 (0.2)</td>
<td>0.098</td>
</tr>
<tr>
<td>25-OHD (ng/ml)</td>
<td>12.9 (9.9)</td>
<td>21.6 (4.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>1,25 (OH)₂D (pg/ml)</td>
<td>49.5 (11.4)</td>
<td>49.1 (12.5)</td>
<td>0.05</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.44 (0.5)</td>
<td>1.40 (0.3)</td>
<td>0.355</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>36.8 (5.9)</td>
<td>38.3 (6.5)</td>
<td>0.511</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min)</td>
<td>77.6 (11.4)</td>
<td>78.1 (10.5)</td>
<td>0.477</td>
</tr>
</tbody>
</table>

Values are given as mean (SD). BALP, Bone specific alkaline phosphatase; NTx, N-terminal telopeptide of type 1 collagen; 25-OHD, 25-hydroxycholecalciferol; 1,25 (OH)₂D, 1,25-dihydroxycholecalciferol.

The biochemical measurements are represented in Table 3. Significantly lower levels of serum Ca, 25-OHD and 1,25(OH)₂D were found in PD patients compared to controls. The levels of BALP and NTx were significantly higher in PD patients compared to controls. There was a significant positive correlation between BMD and the following: 25-OHD P < 0.01, r = 0.533, and 1,25(OH)₂D P < 0.001, r = 0.511, and ionised calcium P < 0.01, r = 0.579, respectively. A significant negative correlation was found between the BMD and H and Y stage, P < 0.005, r = −0.577, and the disease duration, P < 0.005, r = −0.498, respectively.

Discussion

In order to minimise patient selection bias and to investigate the true effect of PD on bone, patients were excluded if they had other known causes of osteoporosis, systemic inflammatory or connective tissue disease; renal, hepatic, cardiac or thyroid impairment; a history of therapy with corticosteroids, oestrogen, bisphosphonates, calcitonin, calcium or vitamin D.

The results of the present study demonstrated that patients with PD had lower BMD values than age- and sex-matched subjects without PD. The decrease in BMD in both the FN and LS was greater in female than in male PD patients. These findings of an association between lower BMD and PD are consistent with those of previous studies [10, 16, 24, 25].

In this study, more falls and fractures were recorded in the PD cohort than in the control group. In general, the incidence of falls increases with age [26]. Falls are a common phenomenon among PD patients. In the study by Koller and colleagues, 38% of PD patients reported falls and 13% fell more than once a week [27]. It has also been previously reported that PD patients have a higher risk of fractures (particularly hip fractures) than the general population [14, 16]. The increased fracture incidence may be attributed to the higher risk of falls and to the decreased BMD in PD patients observed in the present and previous studies.

Furthermore, the results of this study demonstrated that PD patients had lower levels of ionised calcium and of vitamin D compared to healthy controls. These findings may be attributed to several factors including reduced sunlight exposure as observed in this study, reduced mobility and less dietary intake of calcium and vitamin D which was also observed in the present study. Sato and colleagues reported amelioration of osteopaenia and hypovitaminosis D in elderly patients with PD by vitamin D supplementation [28]. The same authors also reported reduced fracture incidence after vitamin D supplementation.

The present study showed that bone turnover is increased in PD patients rendering these patients more liable to reduced BMD and increased fracture risk.

In this study the PD cohort demonstrated reduced physical performance (in comparison to controls) as reflected by reduced grip strength, slower gait speed, worse IADL and worse ‘Get-Up and Go’ test scores. It is thought that deterioration in physical performance is related to a decrease in mechanical load on bone which can lead to a reduced bone density [29]. Furthermore, deterioration in physical performance, which results in insufficient sun exposure due to a decrease in outdoor activity, may lead to vitamin D deficiency. Thus, reduced physical performance may lead to both a decrease in vitamin D and a decrease in BMD.

The results of the present study also demonstrated cognitive impairment in PD patients which was significant in comparison to age- and sex-matched controls. Foltynie and coworkers found cognitive impairment in 36% of their PD cohort [30]. It is believed that both fronto-subcortical and temporo-parietal changes contribute to cognitive impairment even in early PD [30]. In addition, the findings of this study suggest that cognitive impairment in PD patients was associated with lower BMD values. A plausible explanation for this is that lower cognition translates into less physical activity and hence a reduction in BMD with a greater risk of osteoporosis and fractures.

The findings of this study showed that BMD in PD patients is associated with disease duration, disease severity, ionised calcium, vitamin D levels, NTx and BALP levels.

Overall, the PD cohort in this study were found to have lower BMD, lower calcium and vitamin D levels, less sunlight exposure, reduced physical and mental performance and a...
higher incidence of falls and fractures than healthy age and sex-matched individuals.

The limitations of the present study include sample size and cross-sectional design of the study. Further large-scale longitudinal studies are required to establish a cause–effect association between PD and osteoporosis, two important health conditions affecting a sizeable proportion of the older community and leading to a reduction in the quality of life of these patients.

Conclusions and implications

Older patients with PD have lower BMD, vitamin D levels and reduced physical and mental performance. The importance of low BMD in these individuals is that it increases fracture risk. In addition, the poor physical performance in PD patients further increases the risk of falls and/or fractures. Thus, appropriate screening and preventive strategies should be instigated to maintain bone health in PD patients. Regular assessment of skeletal integrity and vitamin D levels is essential. PD patients should receive adequate advice and education on diet- and bone health-related habits such as sufficient calcium and vitamin D intake, sunlight exposure and exercise. A physical rehabilitation programme should also be made available to PD patients to improve physical and mental performance and consequently enhance quality of life of these older individuals.

Key points

• Parkinson’s disease (PD) and osteoporosis are two common chronic disabling conditions in older adults that adversely affect quality of life.
• Older patients with PD have lower BMD, vitamin D levels and reduced physical and mental performance.
• PD is thus a risk factor for osteoporosis and increased incidence of falls and fractures.
• Appropriate screening and therapeutic strategies should be instigated to maintain bone health and slow or prevent disability in PD patients.

References

Results of carotid sinus massage in a tertiary referral unit—is carotid sinus syndrome still relevant?

MAW PIN TAN1,2, JULIA L. NEWTON1,2, PAM REEEVE2, ALAN MURRAY3, TOM J. CHADWICK4, STEVE W. PARRY1,2

1 Institute for Ageing and Health, Wolfson Centre, Campus for Ageing and Vitality, Newcastle University, Newcastle upon Tyne NE4 5PL, UK
2 Falls and Syncope Service, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK
3 Regional Medical Physics Department, Freeman Hospital, Newcastle upon Tyne NE7 7DN, UK
4 Institute of Health and Society, 21, Claremont Place, Newcastle University, Newcastle upon Tyne NE2 4AA, UK

Address correspondence to: S. W. Parry. Tel: (+44) 191 2825237; Fax: (+44) 191 2825338. E-mail: swparry@hotmail.com

Abstract

Background: carotid sinus hypersensitivity (CSH) is associated with syncope, drop attacks and unexplained falls in older people. However, a recent study has also reported a prevalence of 35% in asymptomatic community-dwelling older people.

Objective: we conducted a retrospective observational study to investigate the haemodynamic and symptom responses of a large cohort of patients undergoing carotid sinus massage (CSM).

Methods: the electronically stored haemodynamic data of 302 consecutive patients, aged 71 ± 11 years, investigated with CSM for unexplained falls and syncope was analysed. Bilateral sequential CSM was performed in the supine and upright positions with continuous electrocardiogram (ECG) and non-invasive beat-to-beat blood pressure monitoring (Taskforce™, CN Systems, Austria). CSH (CSH) was defined by maximal R–R interval ≥3 s (cardioinhibitory) and/or a systolic blood pressure drop of ≥50 mmHg (vasodepressor).

Results: a total of 74/302 (25%) subjects had CSH, 37 (50%) of which were cardioinhibitory (CI) and 37 (50%) were vasodepressor (VD) subtypes. Subjects with positive CSM were significantly older (75.2 vs 70.2 years, P < 0.001), and more likely to be male (32% vs 19%, P < 0.01). CSH was diagnosed with right-sided CSM alone in 45 (61%) subjects and erect CSM only in 36 (49%) subjects. Symptom reproduction was more likely with the CI than the VD subtypes (82% vs 28%; P < 0.001).

Conclusion: CSH was diagnosed in 25% of patients investigated with CSM at our specialist unit, lower than the prevalence of 39% reported for community-dwelling older individuals. This discrepancy may be explained by selection bias and demographic differences, but raises the possibility of CSH being an age-related epiphenomenon rather than a causal mechanism for syncope, drop attacks and unexplained falls. Our observations have important implications for clinical practice and the development of future research strategies.

Keywords: carotid sinus hypersensitivity, syncope, loss of consciousness, non-accidental falls, elderly