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Contribution of Musculoskeletal Disorders to Chronic Lumbago in Parkinson's Disease

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Abstract

Purpose: To clarify the impact of bone metabolism disorder on lumbago in Parkinson's Disease (PD). Methods: Data was retrospectively analyzed from 52 patients with PD in our outpatient clinic for more than 1 year (mean age, 63 ± 4 years old; mean duration from onset, 6.3 ± 0.8 years). Patients' characteristics, comorbid musculoskeletal disorders, serum bone metabolism biomarkers, and bone mineral density were examined. Results: Twenty-one PD patients (40.2%) had chronic lumbago. Severe comptocormia and scoliosis were the most common musculosketal disorders in this group (47.6%) affected by lumbago, followed by osteoporosis (14.3%), compression fracture (4.8%). There was no significant difference in the duration of PD, body mass index, frequency of falls, bone mineral density, tartrate-resistant acid phosphatase-5b, osteocalcin, and N-terminal telopeptide between PD patients with or without chronic lumbago. Multivaritae logistic regression analysis identified the independent predictors of chroni lumbago in PD patients as Hoen-Yahr stage (odds ration [OR] = 2.794, 95%CI 1.103 - 7.076), and elevated serum 1,25-OH_2 vitamin D level ([OR] = 0.92, 95%CI 0.86 - 98). Conclusion: Bone metabolism disorders are found to be associated with chronic lumbago in PD patients.

Keywords

Chronic Lumbago, Parkinson's Disease, Bone Mineral Metabolism, 1,25-$(OH)_2$-Vitamin D

1. Introduction

Sensory impairments are one of the non-motor symptoms of Parkinson's Disease (PD), classified as pain, paresthesia, and olfactory dysfunction [1]. The frequency of pain differs greatly depending on the report, from 12% to 74% [2] [3]. This is thought to be due to the fact that not only is pain difficult to assess objectively, it is also

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difficult to differentiate between pain caused by PD and that due to comorbidities. Surveys on pain in PD patients have been reported by two groups [4] [5] since 2008; the most common sites of pain in PD patients were shown to be the legs and back, followed by the shoulders [4]. It was also shown that lumbar vertebra disease was common in elderly PD patients. Elderly people have a high risk of fracture from osteoporosis [6], and lumbar compression fractures are a major factor in the deterioration of the Quality of Life (QOL) of elderly PD patients. Hence, in PD patients with late-life onset who present with low back pain, it is necessary to determine the presence of not only bone disease, but also that of bone metabolism disorders. In this study, we investigated complicating bone metabolism disorders in PD patients who complained of chronic low back pain.

2. Materials and Methods

The subjects were 52 PD patients (mean age, 63 ± 4 years; mean duration of disease, 6.3 ± 0.8 years). All subjects met the diagnostic criteria for sporadic PD of the UK Parkinson's Disease Society Brain Bank, and it was confirmed that dopamine replacement therapy was effective against the parkinsonian symptoms in these patients. All patients underwent brain magnetic resonance imaging (MRI), and those with intracranial organic disease other than PD were excluded. Data on disease duration and severity (Hoehn-Yahr stage), the Unified Parkinson's Disease Rating Scale (UPDRS) score, medication history, falls, and history of lumbar compression fractures were collected from patient interviews and medical records.

Chronic low back pain was assessed and determined from physician interviews. Chronic low back pain was defined as low back pain at the time of the survey that had continued for at least 3 months, and obtained visual analog scale score greater than 5 cm on a 10-cm. Vertebral compression fractures and osteoporosis were examined as osseous diseases that present with chronic low back pain. Vertebral fracture assessment by visual inspection using plain radiographs [7], and the bone mineral density (BMD) of the lumbar vertebrae was measured using dual energy X-ray absorptiometry (DXA). Serum 1,25-OH_2 vitamin D was measured using a radioimmunoassay (RIA), serum osteocalcin was measured using an enzyme immunoassay, and tartrate-resistant acid phosphatase (TRACP)-5b and serum N-terminal telopeptide (NTX) were measured using an enzyme-linked immunosorbent assay (ELISA). Patients determined to have the following in interviews or upon careful examination were excluded: 1) systemic inflammation, connective tissue disease, or secondary osteoporosis or lumbar compression fracture from renal, hepatic, cardiac, or thyroid causes; 2) history of treatment with steroids, estrogen, bisphosphonates, calcium, vitamin D; or 3) intervertebral disc lesions or spinal/cauda equine compression on lumbar MRI or associated nerve symptoms; 4) history of mild depression for more than 12 months, or severe coexisting diseases (such as severe heart failure, severe hypertension, glaucoma, convulsion, and kidney dysfunction).

The results are shown as the mean ± standard error, and the IBM SPSS Statistics version 17.0 (Chicago, IL) software package was used for the statistical analyses. The Mann-Whitney test and chi-square test were used for analyzing the characteristics of patients with and without chronic low back pain. Logistic regression analysis was used to identify factors related to chronic low back pain. A P value of <0.05 was considered to be statistically significant.

3. Results

The patient characteristics are shown in **Table 1**. Chronic low back pain was seen in 40.3% of the subjects. In these patients, the levodopa dosage was significantly higher ($P = 0.003$), the Hoehn-Yahr stage was significantly higher ($P = 0.003$), and the number of those taking anticholinergic agents was significantly greater ($P = 0.023$) than in the group without chronic low back pain. The rates of concurrent musculoskeletal disease with and without chronic low back pain are shown in **Figure 1**. Musculoskeletal deformities in the group of PD patients with chronic low back pain included, in order of descending frequency, severe postural abnormalities (47.6%), osteoporosis (14.3%), and compression fracture (4.8%). In a comparison of background factors in patients with and without chronic low back pain (**Table 2**), the group with low back pain had significantly higher rates of dysuria ($P = 0.018$), chronic pain in locations other than the lower back ($P = 0.030$), and severe lateral flexion posture ($P = 0.030$). In a comparison of bone metabolism markers and BMD in patients with and without chronic low back pain (**Table 3**), serum 1,25-OH_2 vitamin D levels were significantly lower in the group with chronic low back pain than in the group without it ($P = 0.004$). No significant differences were seen between the groups in any of the other bone metabolism markers or BMD.

Table 1. Baseline characteristics.

	Patients with chronic lumbago	Patients without chronic lumbago	P value
N	21	31	
Age, years	73.1 ± 5.0	70.1 ± 8.3	0.21
Male, %	32	57	0.06
Duration from onset	6.7 ± 4.8	5.7 ± 4.1	0.36
BMI, kg/mm^2	21.3 ± 3.5	21.1 ± 3.0	0.83
Waist hip ratio	0.85 ± 0.11	0.85 ± 0.08	0.70
College graduate (%)	66.7	74.2	0.39
High economic status (%)	19.0	29.0	0.57
Hoehn-Yhar stage	3.5 ± 0.8	2.7 ± 0.9	0.00
Medications			
Levodopa (mg)	513 ± 175	364 ± 199	0.00
Pramipexoe (mg)	1.8 ± 1.2 (n = 6)	1.9 ± 0.9 (n = 17)	1.00
Ropinirole (mg)	10.4 ± 4.3 (n = 5)	10.0 ± 3.1 (n = 6)	0.46
Selegiline (%)	28.6	32.3	0.78
Entacapone (%)	19.0	6.5	0.28
Amantagine (%)	47.6	35.5	0.35
Zonisamide (%)	14.3	6.5	0.25
Trihexyphenidile (%)	27.8	4.8	0.02
Donepezil (%)	19.0	6.5	0.16

BMI: body mass index

Table 2. Clinical characteristics with/without chronic lumabago.

	Patients with chronic lumbago	Patients without chronic lumbago	P value
More than moderate postural instability (%)	33.3	19.4	0.14
Scoliosis (%)	52.3	16.1	0.03
Falls (%)	38.1	16.1	0.07
Edema (%)	23.8	9.7	0.17
Urinary incontinence (%)	33.3	3.2	0.02
Wearing off (%)	28.6	22.6	0.62
Poor response to antiparkinson drug (%)	47.6	25.8	0.11
Pain other than lumbus (%)	33.3	3.2	0.03
Psychosis (%)	33.3	25.8	0.56
Sensory abnormalities (%)	38.1	16.1	0.07

Table 3. Serum biochemical samples and bone mineral density with or without chronic lumbago in patients with PD.

	Patients with chronic lumbago	Patients without chronic lumbago	P value
1,25-OH$_2$-vitamin D (pg/ml)	44.8 ± 15.6	60.1 ± 18.4	0.00
NTX (nmol BCE/l)	17.1 ± 5.1	17.7 ± 5.2	0.70
Osteocalcin (ng/ml)	6.2 ± 2.2	5.8 ± 1.7	0.31
TRACP-5b (mU/dl)	451 ± 312	404 ± 212	0.98
BMD (g/cm^2)	0.94 ± 0.21	0.98 ± 0.23	0.97

PD: Parkinson's disease, BMD: bone mineral density, NTX: N-terminal telopeptide, TRACP-5b: tartrate-resistant acid phosphatase-5b.

In the logistic regression analysis, the Hoehn-Yahr stage (odds ratio [OR]: 2.794; 95% confidence interval [CI]: 1.103 - 7.076; P = 0.030) and serum 1,25-OH_2 vitamin D level (OR: 0.950; 95% CI: 0.908 - 0.994; P = 0.027) were shown to be significantly related to chronic low back pain.

4. Discussion

This study demonstrated that: 1) many PD patients with chronic low back pain show advanced postural abnormalities; and 2) a low serum 1,25-OH_2 vitamin D level is an independent factor in PD patients with chronic low back pain.

Advanced postural abnormalities were seen at a higher rate in the group with chronic low back pain than in the group without chronic low back pain (**Table 2**). PD is a disease that occurs mainly in older people, and it is known to worsen over time after onset [8] and to be associated with an elevated incidence of pain [9]. Descending neural transmission of dopamine in the spine plays a major role in the transmission of pain, suggesting the impairment of this pathway as a mechanism of the pain in PD [10] [11]. The nociceptive reflex threshold has also been shown to be lower in PD patients than in healthy people, and there is a high likelihood that the pain in PD differs from a simple comorbidity. Motor fluctuations are a risk factor for the appearance of pain in PD [5], suggesting dopamine system involvement in one mechanism of the sensory impairment in PD [12]. Decreases in BMD with age in this state may result in bone degeneration, contributing to decreases in QOL.

As shown above, the possibility that secondary thoracic vertebra deformation from poor postural control is involved in the development of chronic low back pain is thought to be high. At the same time, many patients in the chronic low back pain group also complained of pain in areas other than the lower back (**Table 2**). With respect to the presence of multiple sites of pain in PD, one may conjecture that pain occurs from respective mechanisms thought to cause pain at local levels and from a central impairment. Thus, it is possible that in the subjects of this study, there was both systemic pain with a central origin and pain from secondary musculoskeletal deformation at local levels. Because a history of lumbar compression fracture or osteoporosis was seen in many patients with chronic low back pain (**Figure 1**), the results of this study indicate the need for both paying attention for the presence of osseous disease and identifying risk factors related to concurrent osseous pain in PD patients with chronic low back pain based on the timing of the development of osseous disease and PD and the trends in both diseases. In this study, low serum levels of 1,25-OH_2 vitamin D were thought to be an independent factor related to chronic low back pain. Sato et al. reported that a lack of physical activity and insufficient sunlight are factors for the low 1,25-OH_2 vitamin D levels in PD, and that the replenishment of 1,25-OH_2 vitamin D as supplements is effective [13]. The 1,25-OH_2 vitamin D level is also a risk factor for decreased trabecular bone and fractures [14], and regular checks of the serum 1,25-OH_2 vitamin D level may enable the prevention of fractures, which are associated with worsened QOL, even in PD patients. In this study, the PD group

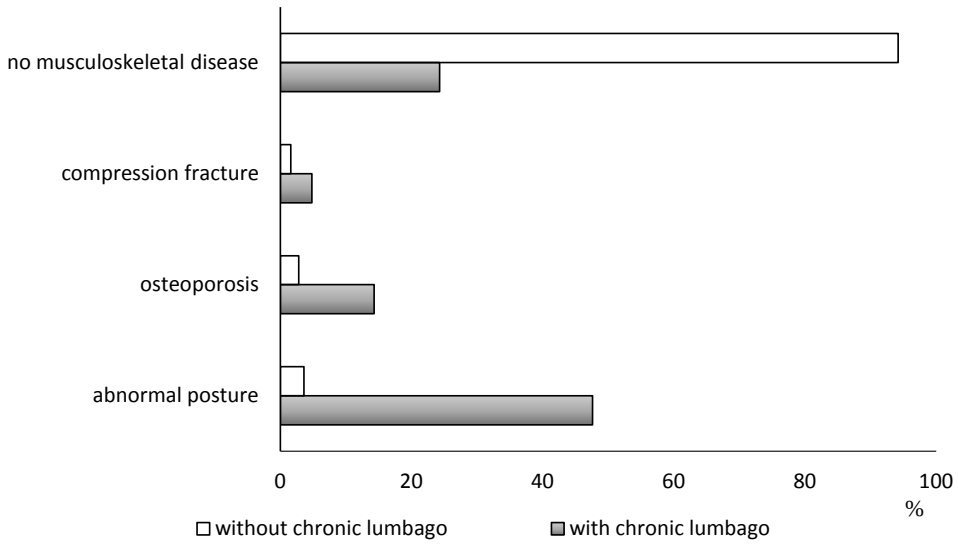

Figure 1. Musculoskeletal disease with/without chronic lumbago in PD.

showing chronic low back pain had a high rate of dysuria (P = 0.018; **Table 2**), but the Hoehn-Yahr stage was also higher in the PD group with chronic low back pain than in those without it. As such, it appears that the presence of bone metabolism disorders due to a decreased absorption of vitamin D in patients with marked dysuria, an autonomic neuropathy, and chronic low back pain is worth investigating. From the evidence for a low serum 1,25-OH_2 vitamin D level in PD, it is possible that the serum 1,25-OH_2 vitamin D level may be an indicator not only for the evaluation of fracture risk, but also for a state of poor bone formation and progression of musculoskeletal degeneration in PD.

In this study, no difference was seen in BMD with and without chronic low back pain, and no association was found between the existence of chronic low back pain and serum bone metabolism markers related to bone resorption or bone formation. Past investigations on BMD in PD patients have reported inconsistent findings, with some reporting no decrease in BMD [15] [16] and others reporting that there was a decrease [17]-[20]. In relation to bone metabolism markers, it was reported that urine deoxypyridine excretion increases in PD patients [21], and that this excretion is reduced when the patients get more exposure to sunlight [13]. The mean BMD of all of the PD patients in this study was maintained at an age-appropriate level, but the bone metabolism function in PD patients is thought to differ greatly depending on environmental factors, the characteristics of the subject group, and the control settings. In the future, it may be necessary to compare PD patients who rarely go outdoors because of a decreased QOL and PD patients who have a daily living level similar to that of healthy people.

5. Conclusion

The present findings suggest that in PD patients with chronic low back pain, in addition to deteriorated motor function, there may also be a vitamin D metabolism disorder due to the PD. Further study is warranted.

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Conflict of Interest

The authors have no conflict of interest to report.

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