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Clinical commentary

Impact of pain and pain subtypes on the quality of life of patients with Parkinson's disease

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ABSTRACT

Pain is a frequent and troublesome non-motor symptom of Parkinson's disease (PD) and has a negative impact on quality of life (QoL). The aim of this study was to investigate the relative impact of pain or a specific pain subtype on the QoL of patients with PD. We included 161 patients with PD. Pain was assessed using the patients' descriptions, a structured interview, and a detailed neurological examination. QoL was assessed using the 39-item Parkinson's Disease Questionnaire (PDQ-39). One hundred and twenty (74.5%) patients with PD had chronic pain. Musculoskeletal pain was the most prevalent type, followed by radicular/neuropathic, dystonic, and central pain. PD patients with pain, regardless of the pain subtype, had a worse PDQ-39 score than those without pain. Multivariate regression analysis after adjusting for disease-related factors and motor characteristics showed that younger PD onset age and the high scores of part II of Unified Parkinson's Disease Rating Scale, Beck Depression Inventory, and Visual Analogue Scale were significant predictors of the poor PDQ-39 score. Pain along with depression, poor activities of daily living, and younger age of PD symptom onset are associated with poor QoL. All subtypes of pain affect QoL of patients with PD. Pain should be considered during the management of patients with PD.

1. Introduction

Parkinson's disease (PD) is a well-known neurodegenerative disorder and characterized by a combination of motor and non-motor symptoms (NMSs) [1]. NMSs of PD are comprised of a variety of symptoms such as neuropsychiatric, sleep, autonomic, gastrointestinal, and sensory dysfunctions [2]. Pain is a frequent and troublesome NMS in PD, and about 40% of patients with PD experience pain or unpleasant sensations [3]. Pain in PD has been classified into musculoskeletal, radicular/neuropathic, dystonia-related, and central or primary [3].

Measurements of quality of life (QoL) are important tools for quantifying the impact of chronic illness. PD has a negative impact on QoL of patients, similar to many other chronic neurological disorders [4]. Both motor symptoms and NMSs are predictors of QoL in patients with PD [5]. The impact of non-motor symptoms such as depression, cognitive impairment, and sleep disturbance on the QoL of patients with PD has been investigated in several studies [4–6]. Despite an increasing number of studies on QoL, it remains uncertain which demographic and clinical factors are the main predictors of QoL in patients with PD.

The contribution of pain to QoL in PD has also been investigated, and PD patients with pain show worse QoL than PD patients without pain [7,8]. However, the relative contribution of the different subtypes of pain in PD to the patient's QoL has not been studied. Therefore, the aim of this study was to investigate the prevalence and characteristics of pain, its subtypes, and the relative impact of pain or a specific pain subtype on the QoL of patients with PD.

2. Patients and methods

2.1. Subjects

We recruited patients from the Movement Disorders Clinic of Chonnam National University Hospital. Consecutive patients who attended the clinic were examined by a movement disorder specialist (S. M. Choi). A total of 161 patients with PD who fulfilled

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the study criteria were included. The inclusion and exclusion criteria are described in a previous report [9]. Briefly, patients were diagnosed with PD according to the United Kingdom Parkinson's Disease Society Brain Bank clinical diagnostic criteria [10]. All patients with PD who had a positive response to levodopa and did not show clinically significant lesions on the brain magnetic resonance imaging (MRI) were included. Exclusion criteria were an unclear diagnosis, the inability to complete the pain assessment, dementia, peripheral neuropathy, systemic inflammatory or connective tissue diseases, a disease that may be associated with pain (e.g., diabetes mellitus), a severe co-morbidity that interfered with daily functioning, and deep brain surgery.

All the participants provided written informed consent to participate in this study. The study was approved by the Institutional Review Board of the hospital and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki.

2.2. Clinical evaluation

Neurologists (H.J. Jung and G.J. Yoon) pre-trained for the survey, performed a structured interview and a detailed neurological examination. Participants were asked about the age of symptom onset, disease duration, and the past and current medication use. The levodopa equivalent dose (LED) of all the medications taken at the time of the interview was calculated [11]. Weight and height were measured in the standing position, and body mass index (BMI) was calculated as the weight in kilograms divided by the square height in meters. The state of the patients' parkinsonism was assessed using the modified Hoehn-Yahr (H-Y) stage [12] and the motor (part III) and activities of daily living (ADL) (part II) subscores of the Unified Parkinson's Disease Rating Scale (UPDRS) [13]. Patients were examined in the "on" condition. Depression was assessed using Beck's Depression Inventory (BDI) [14], and the general cognition was measured with the Korean version of Mini-Mental State Examination (K-MMSE) [15].

Pain was assessed by the patient's history and a self-reported questionnaire, which included the Korean version of the Brief Pain Inventory (BPI) [16]. Pain was defined as unpleasant sensory and emotional experiences that lasted for >3 months according to the International Association for the Study of Pain (ISAP) definition [17]. Headaches and other facial pain were not analyzed. Pain was categorized as musculoskeletal, radicular/neuropathic, dystonia-related, or central parkinsonian, according to the previous report of clinical classification of painful or unpleasant sensations in PD [3]. Musculoskeletal pain is aching, cramping, arthralgic, myalgic sensations in joints and muscles, and may be associated with muscle tenderness, arthritic changes, skeletal deformity, and immobility. Radicular/neuropathic pain is localized to the territory of a nerve or nerve root, and associated with signs of nerve or root entrapment. Dystonia-related pain is associated with sustained twisting movements and postures, and may fluctuate closely with medication dosing. Central parkinsonian pain is presumed to be a direct consequence of the PD itself, and described as bizarre unexplained sensations of stabbing, burning, scalding, and formication [3,18]. Ancillary investigations such as hematological evaluations, nerve conduction studies, electromyography, and imaging were performed in some patients to determine the pain subtype or in those who had clinical evidence of secondary pain. Pain intensity was evaluated using a 100-mm Visual Analogue Scale (VAS) [19]. The patients were asked to express their level of pain by marking it on a 100-mm horizontal line. A score of zero on the leftmost part of the line indicated "no pain", and a score of 100 on the rightmost part of the line indicated "unbearable pain".

The QoL in patients with PD was evaluated by the Korean version of the 39-item Parkinson's Disease Questionnaire (K-PDQ-39) [20]. The PDQ-39 evaluates mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort [20]. In addition to domain-specific scores, PDQ-39 summary index (PDQ-39 SI) was calculated as the mean score of all domains [21].

2.3. Statistical analysis

SPSS, version 20.0 for Windows (IBM, Armonk, NY, USA), was used to perform the statistical analyses. Independent sample t-tests were used to determine the significance of any difference in the PDQ-39 between PD patients without pain and those with pain or each subtype of pain. Univariate linear regression analysis was used to analyze the potential explanatory factors of PDQ-39. Statistically significant variables in the univariate analysis were included in the multivariate linear regression model with the PDQ-39 as the dependent variables. Values with a p-value <0.05 were considered statistically significant.

3. Results

The demographic and clinical characteristics of the patients with PD are shown in Table 1. One hundred and fifty-two (94.4%) out of 161 patients with were on levodopa treatment, and the others were taking only a dopamine agonist or a monoamine oxidase B inhibitor.

The results of the pain assessment are summarized in Table 2. One hundred and twenty (74.5%) patients with PD had chronic pain, while 41 (25.5%) reported no pain. Musculoskeletal pain was the most prevalent type, followed by radicular/neuropathic, dystonic, and central pain. Twenty-one (17.5%) of the 120 PD patients with pain had two types of pain.

For each PDQ-39 domain and PDQ-39 SI, patients with pain had significantly worse QoL scores than patients with no pain. In addition, there were statistically significant differences in all PDQ-39 domains and PDQ-39 SI between PD patients with each subtype of pain and those without pain, except social support (Table 3).

Univariate linear regression analysis was performed to explore potential factors affecting the PDQ-39 SI. There were statistically significant associations between PDQ-39 SI and age of PD symptom onset, disease duration, LED, H-Y stage, UPDRS III & II scores, BDI score, MMSE score, presence of pain, and VAS score (Table 4). Multivariate linear regression results are presented in Table 5, predicting the scores of PDQ-39 SI. The significant predictors were age of PD symptom onset, UPDRS II score, BDI score, and VAS score (Table 5).

Table 1
Demographics and clinical characteristics of the study population (n = 161).

Age (years)	69.7 ± 7.4
Sex (female:male)	93:68
Age of PD symptom onset (years)	62.6 ± 8.5
Disease duration (years)	6.9 ± 4.1
BMI	23.0 ± 3.1
Levodopa equivalent dose (mg)	521.5 ± 254.7
Modified Hoehn and Yahr stage	2.3 ± 0.8
UPDRS part III score	26.6 ± 12.0
UPDRS part II score	13.4 ± 8.3
BDI score	17.1 ± 12.1
MMSE score	25.3 ± 4.7

PD, Parkinson's disease; BMI, body mass index; UPDRS, Unified Parkinson's Disease Rating Scale; BDI, Beck Depression Inventory; MMSE, Mini-Mental State Examination.
Values are mean ± standard deviation.

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