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Pain experience in Parkinson's disease patients: preliminary results of a cohort study

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Abstract

Background: Pain is frequent in Parkinson's disease (PD) and has a great impact on life quality. The aim of the study was to establish the presence of the pain in a cohort of PD patients.
Material and methods: Study sample consisted of 102 consecutive PD patients, (mean age 61.51 ± 8.87 y.o.; disease duration 65.78 ± 41.34 mo.; 55 women and 47 men) evaluated for pain presence and divided into groups with and without pain: "PD pain +" and "PD pain -"
Results: The groups were similar according to ages (61.02 ± 9.61 vs. 62.51 ± 7.69 y.o.) and levodopa dose (729.85 ± 483.29 vs. 708.31 ± 357.50). Pain was present in 64 patients (62.7%) of all study group; more frequent in women (56.3% vs. 43.8%, p> 0.05), with motor fluctuations (72.4% vs. 27.6%, p> 0.05), with dyskinesia (64.0 % vs. 36.0%, p> 0.05) and restless leg syndrome patients (72.7% vs. 27.3%, p> 0.05). Akinetic-Rigid (0.83 ± 0.80 vs. 0.64 ± 0.56, p> 0.05), and quality of life scores (59.70 ± 25.46 vs. 53.84 ±35.76, p> 0.05) were insignificantly higher in "BP pain + "patients. They had longer disease duration (74.19 ± 39.99 y.o. vs 53.29 ± 41.06 y.o. p=0.017), higher depression (16.36 ± 11.97 vs. 8.09 ± 6.42, p=0.000), psychological (10.28 ±6.20 vs. 4.77 ± 2.82, p=0.000) and non-motor symptoms (66.27 ±39.25 vs. 46.68 ± 32.56, p=0.015) scores.
Conclusions: Pain is common in PD, especially in long disease associated with motor complications, depression and other non-motor symptoms.
Key words: Parkinson's disease, pain.

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Introduction

Pain is recognized as a non– motor feature of Parkinson's disease [1] that can appear at any time during the disease course, from the prodromal to late stages [2]. Often the pain appears before the diagnosis of Parkinson's disease, and determines the investigations.

The prevalence of pain in the Parkinson's disease patients is higher than in controls, and could go to 40–75% [1]. PD patients are twice likely to suffer from chronic pain than age-matched non-PD control and also are more likely to receive prescription of analgesics than the general population [3]. Female gender, dyskinesia, postural abnormalities, motor complications and depression are the main predictors for the development of pain in PD [4].

Pain is a significant and troublesome non-motor symptom, experienced by Parkinson's disease patients as a range of different pain syndromes, varying in their cause, origin, location and chronicity [5]. It adversely affects health-related quality of life [6], but remains an under-diagnosed and properly under-treated symptom [5].

Pain is considered one of the most disabling non-motor symptoms in Parkinson's disease, with a strong impact on patients' quality of life, sometimes even greater than that of motor symptoms [7]. In the general population, chronic pain has shown a clear correlation with the severity of depression and reduced quality of life [8].

Although peripheral mechanisms may also contribute, recent studies have indicated that their role is not as important as of central mechanisms to abnormal pain processing [9]. It is presumed that in PD, disease-related states (motor complications, dystonia, rigidity and bradykinesia) as well as medical conditions (osteoporosis, rheumatic disorders) can trigger spontaneous pain which is then abnormally processed and results in painful manifestations in specific body parts [10].

Material and methods

The study was conducted on a cohort of consecutive patients diagnosed with PD at the specialized tertiary clinic with an expert in movement disorders. They were assessed on the basis of a structured questionnaire for general demographic and clinical data. The presence of pain was recorded as a subjective self-reported symptom by the patient. Based on this criterion, the patients were divided into two groups, with and without pain: (1) "BP pain +" and (2) "PD pain -". In all these patients motor

(UPDRS III) and non-motor ((1) Non-Motor-Symptoms (NMS) Scale, (2) Scales for Outcomes in Parkinson's disease – Psychosocial Functioning (SCOPA-PS Scale), (3) Beck Depression Inventory Scale, (4) Montreal Cognitive Assessment (MoCA Scale) symptoms of Parkinson's disease were assessed; as well as (5) quality of life score Parkinson's Disease Questionnaire (PDQ-39). The data analysis was performed via statistical program StatsDirect, using descriptive, variation, and correlational analysis. Student's t tests or Mann-Whitney tests were used as appropriate. P values less than 0.05 were considered statistically significant.

Results

The study group consisted of 102 consecutive PD patients. The mean age in the cohort was 61.51 ± 8.87 y.o. with mean disease duration of 65.78 ± 41.34 mo. By sexes, PD patients, were distributed as follows: 55 were women (53.9%) and 47 were men (46.1%)). Pain, as a self-reported symptom was present in 64 patients (62.7%) of all the study group; and in 90% of cognitively preserved patients, according to MoCA (Montreal Cognitive Assessment test) scores ranging from 30 to 24. In this study pain was encountered more frequently in women (36p (56.3%)) than in men (28p (43.8%), p> 0.05).

No differences were established in the ages of "PD pain +" and "PD pain -" patients (61.02 ± 9.61 vs. 62.51 ± 7.69 y.o.) in the study, as well as in levodopa equivalent daily taken dose (729.85 ± 483.29 vs. 708.31 ± 357.50), in both groups.

Patients with motor complications were more prone to complain pain. So, the majority of the patients with motor fluctuations reported the presence of pain (21p (72.4%) vs. 8p (27.6%), p> 0.05). A similar situation was encountered in the subgroup of dyskinesia patients (16p (64.0%) vs. 9p (36.0%), p> 0.05). An expected result of the study was a significantly more presence of pain in the restless leg syndrome subgroup of patients (8p (72.7%) vs. 3p (27.3%), p> 0.05).

"PD pain +" patients exhibited an akinetic– rigid phenotype of disease, with higher Akinetic-Rigid Scores (0.83 ± 0.80 vs. 0.64 ± 0.56, p> 0.05), revealing more motor impairment. Also, they had a longer disease duration (74.19 ± 39.99 y.o. vs. 53.29 ± 41.06 y.o. p=0.017), compared to pain free patients.

Other non-motor symptoms were more prevalent in "PD pain +", objectified by higher Non-Motor-Symptoms scores (NMS: 66.27 ±39.25 vs. 46.68 ± 32.56, p=0.015), by contrast with "PD pain -" patients. PD patients complaining pain were more depressive, and had a higher psychological involvement, as highlighted by Beck and SCOPA-PS tests (Beck DI: 16.36 ± 11.97 vs. 8.09 ± 6.42, p=0.000), psychological (SCOPA-PS: 10.28 ±6.20 vs. 4.77 ± 2.82, p=0.000)

The quality of life scores (PDQ39: 59.70 ± 25.46 vs. 53.84 ±35.76, p> 0.05) were higher in "PD pain +" patients, but did not reach the statistical significance.

Discussion

The data on prevalence of pain in PD patients (62.7% of all the study group) are in line with the existing data that states a pain prevalence ranging from 40 to 75% in PD patients [1]. A complete consensus on the relationship between pain and gender in the literature does not exist [11]. There are studies reporting that pain is more frequent in females than males and there are also studies reporting that a pain-gender relationship in PD does not exist [12]. However, in some reports, with a large cohort of patients, aiming non-motor symptoms were assessed [13], pain was reported as more prevalent in PD females than in PD males, which is in agreement with the received study results.

There were similar ages (61.02 ± 9.61 vs. 62.51 ± 7.69 y.o.) between groups in the study. Younger age has been reported to be associated with pain in some studies [7], while disease progression has been reported as a risk factor for pain in PD in others [14].

There was not found significant difference in levodopa equivalent daily dose in "BP pain +" and "BP pain –" patients (729.85 ± 483.29 vs. 708.31 ± 357.50). While no correlation has been found between spontaneous pain and daily levodopa dose, some studies have reported that pain of variable quality and localization may fluctuate in intensity during OFF and ON states, particularly in presence of dyskinesia [9]. In this study pain was more prevalent in patients with motor fluctuations (21p (72.4%) vs. 8p (27.6%), p> 0.05), and with dyskinesia (16p (64.0%) vs. 9p (36.0%), p> 0.05). Some uncontrolled observations indicate that spontaneous pain may be minimized by strategies like continuous dopaminergic release and stimulation that usually improve levodopa-related motor complications [4]. Painful symptoms tend to worsen in PD patients who are off medication. For many individuals, however, pain sensations occur in strict relation to the motor fluctuations of the disease, and are ascribed to non-motor fluctuations [11].

Patients with pain in the present study had higher Akinetic-Rigid Score (0.83 ± 0.80 vs. 0.64 ± 0.56, p> 0.05) – indicator of a more severe disease. Another study found also significant correlations between UPDRS part II (p< 0.001), UPDRS part III (p = 0.002), rigidity (p = 0.001), bradykinesia (p = 0.001) and PIGD subscores (p = 0.009), dyskinesia (p = 0.001), wearing off (p = 0.001) with pain [15]. A positive relationship was established between chronic pain occurring in PD patients and the severity of the disease in the literature [12].

PD pain patients also had longer disease duration (74.19 ± 39.99 y.o. vs. 53.29 ± 41.06 y.o. p=0.017). A significant correlation was previously described between chronic pain, Hoehn & Yahr stage of PD and patients age [15]. No relationship between pain and age at diagnosis, disease duration, motor examination or PD stage was observed in several studies [14]. Thus, conflicting results are reported regarding the role of PD progression in the onset of pain, and this could be related to different pain

subtypes occurring at different times in the course of PD. Thus, some studies reported that all types of pain are more prevalent in patients with late-stage PD than in early stages, while only nociceptive arthritic pain was more prevalent in early-stage PD [16].

Concerning other non-motor symptoms, the pain PD patients in this study had higher scores for: depression, psychological and non-motor symptoms. There is a bi-directional relationship among depression, common non-motor symptoms of PD and pain. Chronic pain may be a risk factor for depression, especially in the elderly people. Pain may negatively affect the prognosis of depression, and persistent pain may accelerate depression. From the other perspective, depression may affect the perception of pain, and may contribute to the pain becoming severe and refractory to treatment [17]. Results are inconsistent in the literature regarding pain-depression relationship in PD. In fact, depression is more common in PD patients suffering from pain and furthermore, PD patients with major depression suffer from more severe pain compared to patients without depression [18]. Also, pain is described as closely related to other non-motor symptoms as fatigue, daytime sleepiness, and sleep disorders.

Thus insignificantly, quality of life score PDQ39 was higher in "PD pain +" patients. It is known that, independently from the other motor symptoms of PD, chronic pain, accompanying the disease, adversely affects the daily living activities and quality of life of patients and becomes thus the cause of morbidity and disability. Another study, comprising 265 consecutive PD patients, reported that in patients with less than 6 years disease duration, pain was the fourth most discomforting non-motor symptom related to PD, while in patients with more than 6 years disease duration pain was reported to be the sixth most discomforting non-motor symptom related to PD [19].

Also, in BP, pain has been shown to be a major factor affecting quality of life related to physical and mental health [20] and also leads to reduced autonomy. A significant relationship between pain and depression has been reported in BP, suggesting that pain issues should be considered when treating BP patients with depression and vice versa. However, pain is an independent predictor of poorer quality of life, independent of its close relationship with depression. Pain has an effect on quality of life that is greater than motor impairment and comparable to the effect of motor complications [21]. So, pain is an important factor affecting the health-related quality of life, that's why prevention of chronic pain and / or treatment of the already existing pain may have significant effect in increasing PD patient quality of life.

Conclusions

Pain is common in patients with Parkinson's disease and affects women more than men. It is more prevalent in patients with longer disease duration, in those with more severe motor impairment, also in patients who have developed motor fluctuations. Pain is associated with high depression scores and is more prevalent in patients with other PD specific non-motor symptoms.

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LR conceptualized the idea, wrote the manuscript. LR, OG, SO and IO revised and finalized the text. All authors revised the manuscript critically and approved the final version of the manuscript.

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Ethics approval and consent to participate
The research project was approved by the Research Ethics Committee of *Diomid Gherman* Institute of Neurology and Neurosurgery (protocol No 4, 29.09.2022).

Conflict of Interests
No competing interests were disclosed.