

Pain characteristics in Parkinson's disease: An Indian experience

¹Birinder Singh Paul MD(Medicine)DM(Neurology), ²Gunchan Paul MD(Anaesthesia)IDCCM, ¹Gagandeep Singh MD (Medicine) DM (Neurology), ³Sandeep Kaushal MD (Pharmacology), ¹Amarinder Dhaliwal MBBS, ¹Inder Dev Bahia MBBS

¹Department of Neurology, ²Critical Care, ³Pharmacology, Dayanand Medical College & Hospital, Ludhiana, India

Abstract

Background & Objective: Parkinson's disease (PD) is a chronic neurological disease, many a times presenting with non-motor symptoms. Pain is one of the most important non-motor symptom and there is no consensus regarding its exact mechanism and characterisation. This study was planned to evaluate the characteristics of pain and possible factors influencing it, in a cohort of patients with established Parkinson's disease. **Methods:** 104 patients consenting to participate were included in the study. Data regarding age of onset, duration of disease, treatment, Hoehn-Yahr scale, phenotype of PD, UPDRS scores, pain type and distribution of pain were noted. Single and multiple logistical regression models with pain (1/0) as the outcome variable were used to check the association of pain with the above mentioned variables. **Results:** 54.8% of patients with PD experience pain. Presence of sensory symptoms was significantly associated with the pain group (42.1%) than the no pain group (21%). Pain was more pronounced on the side with predominant motor symptoms (72%) and in 68.4 % patients pain responded to dopaminergic treatment. Musculoskeletal pain (82.5%) was the commonest type and lower limbs were the commonest site of pain (43.2%).

Conclusion: Pain in Parkinson's disease has multiple dimensions and characteristics. Pain itself may be the reason for early diagnosis. Proper classification of pain will help in improved management of these patients.

INTRODUCTION

Parkinson's disease (PD) a chronic, progressive, neurodegenerative disease characterised by the loss of dopaminergic pathways, many a times presenting with non-motor symptoms.¹ The most important concern is the motor stiffness, slowness of movement and postural instability. Pain is an underestimated non-motor symptom in PD patients which has a negative effect on the quality of life.² Epidemiological studies estimate the prevalence of pain to be 30-83% and there is a divided consensus regarding the exact mechanism and characterisation of pain.^{3,4} As PD is a multifocal progressive disease hence, pain processing may be affected at multiple levels beginning at the level of peripheral transmission to its interpretation by the higher centres.⁵⁻⁷ Dopamine is involved in pain modulation at different levels including the spinal cord, thalamus, periaqueductal gray matter, basal ganglia and cingulate gyrus.⁸ Pain can present as a symptom at any time during the course of disease

and may be the presenting symptom before the diagnosis.⁹ Pain has a heterogeneous presentation and different types of pain have been described with variable frequency.⁵ Hence, this study was planned to assess the frequency and type of pain in a cohort of PD patients in an Indian setting, and to characterise the possible factors influencing the presence of pain.

METHODS

The patients who fulfilled the clinical criteria for the diagnosis of PD (United Kingdom Parkinson's Disease Society brain bank criteria) visiting the outpatient department of Neurology at Dayanand Medical College & Hospital from January 2012 to December 2012 were included in the study.¹⁰ Informed consent of the patient and approval by the local ethical committee were taken. Demographic and clinical parameters including age, gender, age of onset, duration of disease, modified Hoehn-Yahr (H&Y) staging, Unified

Parkinson's Disease Rating Scale (UPDRS) scores and treatment history were recorded on a predesigned Performa. The PD population was divided into two phenotypes, PDAR (akinetic rigid) or PDT (tremor predominant) type using the modified ratio developed by Schiess *et al.* based on the UPDRS-III.¹¹ A 12 item akinetic rigid scale and nine item tremor scale was used to assess the phenotype. Each item was rated at five point scale ranging 0-4 (with 0 representing absence of the symptom or normal activity and 4 significant presence of the symptom or impairment). The mean of each scale was calculated and then the ratio (tremor/akinetic score) determined. Patients with a ratio <0.8 were classified as PDAR subjects whereas those with ratio >1.0 were classified as PDT subjects. The presence of sensory symptoms was based on UPDRS –Question 17. A score of > 1 was classified as presence of sensory involvement. UDDRS Section III was used to determine the predominant side affected by PD. The side with a higher total score was taken as the predominant side.

History of any type of pain which the patient complained of were inquired using a questionnaire and was then categorized according to Ford Classification.¹² Pain that was present for at least 3 months with a Visual Analogue Scale (VAS)

score ≥ 3 was included in the study.

Based on this, the PD population was divided into two groups, Group I as PD without pain and Group II as PD with pain. Pain localisation and distribution were also noted. Factors potentially affecting pain were analysed by comparing the two groups.

Patients with history of age-dependent joint, bone or disc diseases were excluded.

All values were expressed as mean (\pm SD) and percentages using SPSS 16.0. Paired t-test was used for categorical variables and chi square was used for continuous variables. The p-value < 0.05 was considered to be significant.

RESULTS

Out of the patients seen in neurology outdoor patient department over one year, 104 patients with diagnosis of PD were seen and included in the study. Forty seven patients were assigned to Group I and 57 patients in Group II. Demographic and clinical characteristics of both the groups are summarized in Table 1. Up to 54.8% of patients with PD reported different types of pain during their course of illness. There was no statistically significant difference between the two groups with respect to age, age of onset, phenotype of

Table1: Demographic and clinical characteristics of a cohort of patients with established Parkinson's disease. Group I are the patients with no pain and Group II with pain associated with parkinsonism

Characteristics	Group I (47)	Group II (57)	p-value
Mean Age	59.91 \pm 10.09	58.04 \pm 8.79	0.36
Age of onset	56.12 \pm 11.76	54.94 \pm 8.97	0.57
Gender (female %)	9 (19.14)	39 (68.4)	0.0006
Phenotypes			
PDT (%)	28 (59.97)	29 (50.8)	0.37
PDAR (%)	19 (40.42)	28 (49.12)	
H&Y stage	2.53 \pm 0.92	2.39 \pm 0.83	0.43
Duration of disease (yrs)	3.69 \pm 2.53	3.04 \pm 2.67	0.20
Duration b/w disease onset & start of treatment (yrs)	3.07 \pm 2.26	2.50 \pm 2.50	0.22
Sensory symptoms UPDRS II (%)	10 (21)	24 (42.1)	0.017
UPDRS IV motor fluctuation	4 (8.5)	7(12.5)	0.58
UPDRS IV mean score	1.33 \pm 0.48	1.44 \pm 0.50	0.39

PDT, Parkinson's disease tremor predominant type; PDAR Parkinson's disease akinetic rigid type; H&Y stage, Hoehn & Yahr stage; UPDRS, Unified Parkinson's Disease Rating Scale

PD (rigid or tremor predominant) and disease severity as assessed by H&Y scale. There was a significant ($p < 0.001$) association of pain with female (68.4%) cohort of PD patients as compared to males. Patients in Group II had a shorter duration (2.5 years) between the onset of disease and start of treatment as compared to Group I (3.07 years). Our study showed a significant ($p = 0.017$) association of sensory symptoms (UPDRS II) with pain. Sensory symptoms were commonly more associated with the PD pain population (42.1%) than the no pain group (21%).

Factors potentially affecting the occurrence of pain was also analyzed (Table 2). In 4 patients (7%) pain was the presenting non-motor symptom overshadowing the motor problems caused by the disease (as they were referred from Orthopedics Outpatient Department). Pain was more pronounced on the side with predominant motor symptoms (72%). Among these patients 68.4 % responded to dopaminergic treatment suggesting a positive effect of PD medication. This effect can be attributed to dopaminergic treatment as this was the only factor modified since diagnosis. Additionally, these patients did not further require NSAIDs for pain relief (after the pain reduction with dopaminergic treatment).

Among the different types of pain, the musculoskeletal pain (82.5%) was the commonest type of pain noted in the PD pain group. The

frequency of various types of pain is shown in Table 2. As shown, 15.2 % patients experience more than one type of pain (akathisia and musculoskeletal). Though pain was heterogeneous in distribution, lower limbs were the commonest site of pain (43.2%) as depicted in Figure 1.

DISCUSSION

Pain is a non-motor symptom that markedly affects the quality of life in patients with Parkinson's disease. It is quite an underestimated and inadequately treated symptom. This is the first

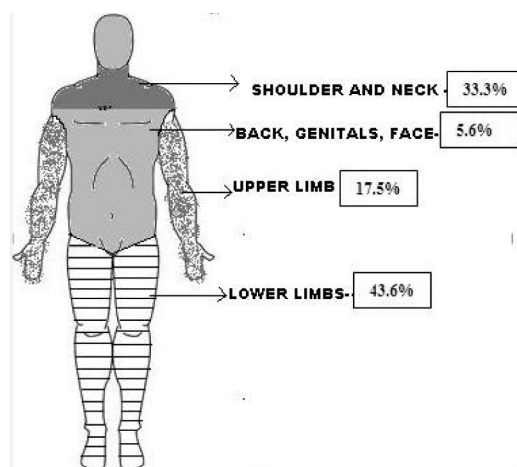


Figure 1. Illustration of the body distribution of pain in patients with Parkinson's disease, lower limb being the most common site of pain

Table 2: Characteristics of pain, type, distribution and the factors affecting pain in patients of Group II (pain associated with Parkinson's disease)

Characteristics of Pain	n =57	%
Presenting symptom	4	7
Pain on the side of disease	41	72
Response to dopaminergic drugs	39	68.4
Musculoskeletal	47	82.5
Radicular-neuropathic	5	8.7
Central	3	5.2
Dystonia related pain	3	5.2
Akathisia/RLS	8	14.1
Two types of pain (musculoskeletal & akathisia)	9	15.8
Sensory symptoms	24	42.1

study that evaluates the characteristics of pain in the Indian population of PD and explores the possible factors influencing the presence of pain in this group of patients. In our study pain as a non-motor symptom was noted in 55% cases while the previous epidemiological studies conducted in the western population report the prevalence of pain ranging from 46% to 83 % in patients with Parkinson's disease.⁵ Beiske *et al.* in a study of 176 PD patients reported that 83% of patients experience pain.³ All the patients in their study were suffering from motor fluctuations which may be reason for higher incidence of pain as compared to our cohort where only 10% patients had motor fluctuations (Table 1). However, there may also be regional differences in the character and frequency of pain. Another study by Tinazzi *et al.* of 117 patients found the incidence of pain to be 40%.¹³ This highlights the differences in the inclusion criteria and definition of pain. As many patients of PD experience painful symptoms and various forms of physical discomfort during the course of illness, we included only those patients who complained of pain for more than three months with a VAS ≥ 3 .

The mean age of onset in our study was 59 years (35-72 years) and there was no correlation of pain with mean age and age of onset of disease. The study by Beiske *et al.* reported the mean age of patients as 69 years but had enrolled patients with motor fluctuations suggesting that the duration of disease was longer in those patients.³ Goetz *et al.* reported that 45% patients had pain and patients with pain were younger than with no pain.¹⁴

Our study suggests a significant association of pain and female gender as reported by other studies as well. Beiske *et al.* reported that female gender was a significant predictor of pain.³ Although the exact reason is not known; it may be related to low threshold of pain perception in females as compared to male. Zambito *et al.* in their study of 106 patients of PD found that patients had decreased threshold to pain and heat as well as lower tolerance to electric and thermal stimuli as compared to healthy controls.¹⁵ Similarly, Mylius *et al.* found similar results in a study of 15 PD patients.¹⁶ However, both did not report any sex based differences in pain perception. On the contrary, laboratory based studies have reported that women are more sensitive than men to experimentally induced pain, as measured by subjective pain threshold, tolerance, or ratings of pain intensity in response to standardized noxious stimuli, as well as by less subjective indices, such as electromyographically measured threshold for

muscle reflexes or pupil dilation in response to noxious stimulation.¹⁷⁻¹⁹ This suggests that sex differences in reports of pain are unlikely to simply be a function of reporting bias but a result of a complex spectrum of factors contributing to sex differences in pain responses. Hormone levels in cycling women also have a substantial impact on pain perception and analgesic response.²⁰

The effect of severity and duration of Parkinson's disease on pain is variably reported by different studies. Although few studies in literature have shown that patients with longer duration of disease with higher incidence of motor complications may be more commonly associated with pain although we could not associate such a relationship. In the study by Tinazzi *et al.*, the mean duration of disease before the onset of pain was 8.2 years compared to 3.04 years in our study.¹³ This suggests that the incidence of pain increases as the duration and complication of Parkinson's disease increase.

In our study, PD population with pain had a short duration between the onset of disease and start of treatment as pain and discomfort might have been severe enough that they overshadowed the motor problems and could be the reason for early referral to a physician. It could be attributed to work culture in our country hence pain symptoms was noted earlier than hypokinesia.

Musculoskeletal type of pain (82.5%) was the commonest type of pain noted our PD patients. Lee *et al.* reported musculoskeletal pain in 40% of their patients while Ford *et al.* reported it to be the most common form accounting up to 90%.^{12,21} In a PD patient there are multiple reasons that can be accounted for the higher incidence of musculoskeletal pain like rigidity, stiffness, lack of spontaneous movements and abnormality of posture. Musculoskeletal pain seems to be related to rigidity or akinesia but in our study there was no difference in occurrence of pain in different phenotypes of PD. This could be attributed to the additional role of basal ganglia in processing of nociceptive and non-nociceptive inputs rather than the contribution of motor abnormalities only.

In our study, 72% of patients complained of pain that was more pronounced on the side where motor symptoms were prominent and in 7% (4 patients) of them pain preceded the first motor sign. Three of our patients presented first to the orthopaedic outdoor for pain. The pain in these patients was also found to be associated with other symptoms as bradykinesia or rigidity hence were referred to the neurology outdoor for further evaluation. They were then diagnosed

as PD hence it was clear that motor symptoms followed the occurrence of pain. However, in one another case the leading question revealed the occurrence of pain few months before the motor symptoms were noted. Further, 68.4% responded to dopaminergic treatment highlighting the concept of dopaminergic mediated pain. Similar finding was reported in a prospective study by Trenkwalder *et al.* who showed that intradermal patches of dopamine agonist markedly improved pain.²² This highlights the fact that proper and early treatment of Parkinson's disease may also improve rigidity and increase the range of movements which could probably decrease the incidence of pain. This would improve quality of life and outcome in these patients.

Another observation noted in our study was the significant association of sensory symptoms with the presence of pain. Gunnar and Gunther in their review described two types of pain in PD, nociceptive and neuropathic.⁶ Neuropathic pain is caused by lesion in the peripheral somatosensory nervous system which suggests a correlation between the presence of sensory symptoms and pain. Hence, pain may also be one of the expanded spectrums of sensory symptoms. From our study we conclude that the female gender and presence of sensory symptoms were possible factors influencing pain in PD patients in Indian population.

Limitation of our study is that it was not blinded. Also we enrolled PD population in the early onset of disease than those with advanced stage and motor complications, hence the pain pattern may be different.

In conclusion, pain in PD is a frequent and important non- motor symptom. It is often an overlooked symptom because PD is primarily a motor disease. The most important diagnostic tool is the clinical history which is necessary to identify the type of pain related to PD. Physicians should be made aware of it so that an effective strategy can be established for proper management of pain including physical therapy and exercise programs apart from dopaminergic treatment.

DISCLOSURE

Financial support: Nil

Conflict of interest: None

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