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ORIGINAL ARTICLE

Non-motor symptoms and quality of life in patients with Parkinson's disease in Northeastern Mexico

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Abstract Parkinson's disease (PD) is a multisystem disorder, and besides the classical motor symptoms it is now known that patients also suffer from a variety of non-motor symptoms that adversely affect quality of life (QOL). Since data on Hispanic populations on this issue are scarce, our aim was to study the association of non-motor symptoms and QOL in patients with PD. This study is a cross-sectional observational study involving patients with PD using the following instruments: Quality of Life Questionnaire (PDQ-8), Unified Parkinson's Disease Rating Scale part III (UPDRS part III), and Non-Motor Symptom Scale (NMSS). We included 52 patients, with a median age of 64 years. Sleep/fatigue and mood/cognitive domains were the most common non-motor symptoms. Only sleep/fatigue, mood/cognition and gastrointestinal domains were associated with worse PDQ-8 scores. After adjusting for confounding variables, NMSS scores were significantly associated with a high PDQ-8 score. Higher NMSS scores were associated with and predicted higher PDQ-8 scores. The focus of management in PD should shift to a comprehensive strategy that incorporates care of non-motor symptoms and improves QOL.

Keywords Parkinson's disease · Non-motor symptoms · Quality of life · Cognition · Sleep

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Introduction

Parkinson's disease (PD) is a multisystem disorder, and besides the classical motor symptoms it is now known that patients also suffer from a variety of non-motor symptoms, such as depression, sleep disturbances, urinary and gastrointestinal (GI) symptoms, among many others [1]. The emphasis of treatment has also shifted from ameliorating motor symptoms to a more comprehensive approach that includes these factors [2, 3]. In recent studies, non-motor symptoms have been shown to be most strongly associated with the patient's quality of life (QOL) [4, 5].

Improving our knowledge of the association between non-motor symptoms and patient QOL could lead to more accurate diagnoses as well as to better therapeutic strategies. Instruments designed specifically to evaluate non-motor symptoms and QOL are increasingly used as outcome indicators in both research and clinical practice for patients with PD and have been used to this effect. In this study we used some of these tools to get an overall picture of the prevalence and impact of non-motor symptoms over QOL in a population of PD patients in Northeastern Mexico.

Patients and methods

We carried out a cross-sectional observational study on 52 consecutive patients with PD from our outpatient clinic at the Department of Neurology of the University Hospital, Monterrey, Mexico, recruited from 2013 to 2014. Diagnosis of idiopathic PD was made by a neurologist with competence in movement disorders according to the UK PD Brain Bank Criteria. All patients

had a brain MRI and drug-induced Parkinsonism was ruled out. This study was approved by the ethics committee of our institution and all patients signed informed consent for inclusion in this study, all in compliance of the Declaration of Helsinki. Besides standard assessment, a semi-structured interview was used to obtain information on disease history and other socio-demographic data and all patients completed the non-motor assessment scale for PD (NMSS), the Parkinson's disease questionnaire-8 (PDQ-8) scale for QOL and the UPDRS part III scale for motor symptoms. All surveys were completed on an "on" period.

NMSS

The NMSS is a 30-item scale for the assessment of non-motor symptoms in PD, containing nine dimensions [6, 7]. Each dimension is scored based on composite severity (from 0 to 3) and frequency (from 1 to 4) of a symptom. Total scores range from 0 to 243 points, with higher scores indicating more symptomatology. The possible scores for each dimension are as follows: cardiovascular (from 0 to 21), sleep/fatigue (from 0 to 48), mood/cognition (from 0 to 72), perceptual problems (from 0 to 36), attention/memory (from 0 to 36), GI (from 0 to 26), urinary (from 0 to 36), sexual function (from 0 to 24), and miscellany (from 0 to 36). When presenting the prevalence of non-motor symptoms, we considered a symptom from any domain to be present when the NMSS score for that domain was >0. An individual symptom was considered to be present when the score of any item was >0.

PDQ-8

A short and self-reported scale to rate QOL, the PDQ-8 evaluates 8 items (mobility, activities of daily livings, emotional well-being, stigma, social support, cognitions, communication, and bodily discomfort) in a 0–4 Likert-type scale [8]. Total scores (0–32) are obtained using a simple calculation where a higher score indicates a worse QOL.

UPDRS part III

One of the most commonly used evaluation tools for PD symptomatology, the UPDRS is a scale for the assessment of function in Parkinson's Disease. UPDRS Part III measures Motor Function. It consists of 14 items with 27 questions, each ranging from 0 to 4. The sum score for the UPDRS Part III ranges from 0 to 108, with higher scores indicating more motor symptoms/impairment [9]. It was assessed by the treating neurologist.

Statistics

Descriptive statistics were used to analyze non-motor symptom prevalence. Asymptotic 95 % confidence intervals around symptom prevalence were calculated. To compare effects of NMSS over QOL, we divided total PDQ-8 scores into quartiles to contrast those with best (quartile <25 %) and worst PDQ-8 scores (quartile >25 %). Categorical variables were assessed using Chi square test and continuous variables were assessed using Student t test or Mann–Whitney U test, where appropriate. Simple correlation analysis using Spearman test was used to evaluate correlations between NMSS, UPDRS part III, Hoehn and Yahr and PDQ-8 scores. Variability in PDQ-8 scores was examined in a multiple regression including NMSS total score, UPDRS part III score, Hoehn and Yahr, and age as covariates. All statistical analyses were assessed using the SPSS computer program (SPSS version 20.0; SPSS Inc., Chicago, IL, USA).

Results

Population

We included 52 patients, with a mean age of 63.4 ± 10.8 years (range 40–87), where 29 (56 %) patients were male. The mean time since diagnosis was 4.5 ± 1.2 years (range 0.3–7 years). Mean total UPDRS score was 58.3 ± 10.8 and mean UPDRS part III scores were 17.5 ± 3.2. Mean NMSS score was 51.8 ± 45.3 and mean PDQ-8 score was 7.3 ± 5.3. Mean Hoehn and Yahr (HY) stage was 2.4 ± 0.9. All patients were receiving levodopa/carbidopa, 6 (11 %) patients were on a dopamine agonist (Pramipexole), 3 (6 %) on a monoamine-oxidase inhibitor (Rasagiline), and 20 (38 %) on an anticholinergic (Amantadine).

Prevalence of non-motor symptoms

Based on NMSS results, sleep/fatigue and mood/cognitive domains were the most common non-motor symptoms in our population. The frequency of any non-motor symptom by domain can be found in Table 1. Total NMSS scores did not differ between males and females (59 ± 54.7 vs. 42.7 ± 29.7, $p = 0.2$). There were no significant differences between males and females in any specific non-motor symptom domain (data not shown).

Common individual symptoms

In the sleep disturbance/fatigue domain, fatigue was the most common symptom. Fatigue was present in 28 (53 %)

Table 1 Frequency of any non-motor symptom by NMSS domain ($n = 52$)

Symptom	n (%)	95 % confidence interval[a] (%)
Sleep and fatigue	40 (76 %)	65–88
Miscellaneous including pain	39 (75 %)	63–86
Mood and cognition	37 (71 %)	58–83
Urinary	33 (66 %)	50–73
GI tract	32 (61 %)	48–74
Sexual	23 (44 %)	30–57
Attention	22 (42 %)	28–55
Cardiovascular and falls	19 (26 %)	23–49
Perceptual problems, hallucinations	14 (26 %)	14–39

[a] Confidence interval for percentages

Table 2 Spearman correlation coefficients

	UPDRS part III (r)	NMSS (r)	PDQ-8 (r)
UPDRS part III		0.489*	0.345**
NMSS			0.577*
Hoehn and Yahr	0.714*	0.476#	0.404#

Significance levels: * $p < 0.001$; ** $p < 0.05$; # $p < 0.01$

patients, with a mean score in question 4 ["Does fatigue (tiredness) or lack of energy (not slowness) limit the patient's daytime activities?"] of 2.7 ± 3.4 (range 0–16). In the mood/cognitive domain, anxiety was the most common symptom, with 30 (58 %) patients answering question 9 ("Does the patient feel nervous, worried or frightened for no apparent reason?"), with a mean score of 2.9 ± 4 (range 0–16). The most common urinary symptom was nocturia in 27 (52 %) patients. In question 24 ("Does the patient have to get up regularly at night to pass urine?") mean score was 3 ± 3.9 (range 0–12). Constipation was the most common GI symptom in 25 (48 %) patients.

PDQ-8

Spearman correlations for PDQ-8, NMSS, UPDRS part III and Hoehn and Yahr scores can be found in Table 2. PDQ-8 scores were more strongly correlated with NMSS scores than with UPDRS part III scores and Hoehn and Yahr stage. Total NMSS scores were significantly higher in patients in quartile >75 % of the PDQ-8 when compared to quartile <25 %. However, individually, only items 2 (sleep/fatigue), 3 (mood/cognition) and 6 (GI tract) in the NMSS scale were significantly different between groups (Table 3). These variables were the only ones significantly correlated with PDQ-8 scores as well ($R = 0.46$, $p = 0.001$ for item 2, $R = 0.52$, $p = 0.001$ for item 3 and $R = 0.34$, $p = 0.01$ for item 6). UPDRS part III scores were higher in the quartile >75 % of the PDQ-8 ($p = 0.007$). Hoehn and Yahr stage was also higher in quartile >75 % of the PDQ-8. Age and gender were similar between groups.

Table 3 Differences between patients by PDQ-8 quartile

	PDQ-8 quartile <25 ($n = 13$)	PDQ-8 quartile >75 ($n = 13$)	p
Age (median)	66	65	0.783*
Sex (male)	6 (46 %)	8 (61 %)	0.431**
Total NMSS	22.1 ± 15.1	90.8 ± 65.7	**0.001***
Sleep/fatigue score	3.8 ± 5.1	12.4 ± 10.5	**0.015***
Mood/cognition score	1.8 ± 4.1	25.9 ± 23.9	**0.002***
GI tract score	1.7 ± 3.5	9.5 ± 9.4	**0.01***
UPDRS part III	10.8 ± 6.9	21.4 ± 11.1	**0.007***
Hoehn and Yahr	1.9 ± 0.9	3 ± 0.8	**0.01**#

Figures are mean ± SD unless stated otherwise

* Student t test; ** Chi square test; # Mann–Whitney U test

p values < 0.05 appear in bold

Table 4 Multivariate linear regression for predictors of PDQ-8 scores

	Regression coefficient	95 % confidence interval	p
NMSS[a]	0.069	0.033 to 0.105	**0.001**
UPDRS part III[a]	0.248	0.094 to 0.405	**0.049**
Hoehn and Yahr[a]	2.71	0.743 to 4.681	0.08
Age[a]	0.017	−0.122 to 0.156	0.075

[a] Per unit increase

p values < 0.05 appear in bold

Regression results for PDQ-8 scores

After adjusting for age, NMSS and UPDRS part III scores could significantly predict PDQ-8 scores (Table 4), but the strongest predictor was NMSS score ($p = 0.001$). Each one unit increase in NMSS score was associated with a nearly 0.07 increase in PDQ-8 score.

Discussion

In this study we found that there is a high prevalence of non-motor symptoms in our PD population, and that they are closely associated with an altered QOL. This association was stronger than an effect explainable by severity of motor symptoms alone, as measured using the UPDRS. This is in accordance with early studies that validated the

NMSS scale, where a higher correlation was found between NMSS and PDQ-8 than with indicators of motor symptom severity [6]. Large population-wide studies have confirmed that there is an inverse correlation between QOL scores and severity of non-motor symptoms [10].

The prevalence of non-motor symptoms in PD varies depending on the population studied and disease stage. In a large multicenter Italian study of over 1000 patients with PD, the most common non-motor symptoms were fatigue (58 %), anxiety (56 %), leg pain (38 %), insomnia (37 %), urgency/nocturia (35 %) and difficulties in maintaining concentration (31 %) [11]. Another study of 159 patients with PD in the United Kingdom found that the most common symptoms were drooling, forgetfulness, urinary urgency and constipation [12]. This study was carried out in ambulatory patients treated in primary care facilities, in an early disease stage. In populations of late-stage PD patients living in nursing care facilities, 77 % of patients were found to meet criteria for PD-related dementia, and besides cognitive complaints, depression and poor nighttime sleep were also found frequently [13]. Gender differences have also been described. In a Chinese study of 428 early stage untreated PD patients found that depression and cognitive alterations were more common in females, whereas no differences were found in motor symptoms [14]. Female propensity for affective disorders could partially explain these results. In our study the most common non-motor manifestations were fatigue, anxiety, cognitive complaints and urinary symptoms. In agreement with our results, an earlier study on 100 Mexican PD patients found that urinary symptoms were most often reported (60 %), followed by depression/anxiety (55 %), sleep disorders (40 %) and cognitive alterations (39 %) [15].

We found that the non-motor symptoms most strongly associated with PDQ-8 scores were in the domains of sleep/fatigue, mood/cognition and GI symptoms, which is in accordance with many published studies. Depression and cognitive complaints are usually among the most troubling non-motor symptoms contributing to an altered QOL [16]. In a study of 158 patients with newly diagnosed PD, using the NMSS, depression, GI symptoms, insomnia and cognitive complaints were found to have the greatest negative impact upon PDQ-39 scores [17]. In other studies, fatigue, cognitive complaints, GI symptoms and depression have been found to be more strongly associated with alterations in QOL [11, 18]. Depression and cognitive complaints have also been shown to be independent predictors of overall disability in PD [19]. These symptoms should be addressed early and aggressively in PD.

The tool used to evaluate QOL in PD patients could explain some of the differences observed between studies. For example, in a recent study, PD-related motor symptoms more strongly affected QOL than non-motor symptoms when using PDQ-39, whereas non-motor symptoms had a greater impact over perceived QOL, as evaluated by the PQ-10 [20]. In our study, using the PDQ-8, NMSS scores were more strongly associated with a worse QOL than UPDRS part III scores. This finding is consistent with studies in patients with both PD and Atypical Parkinsonism who had their QOL affected by NMSS scores more strongly than by the UPDRS part III scores [4, 5]. Even considering these differences it is clear non-motor symptoms are capable of greatly affecting QOL.

Conclusions

In conclusion, depression, cognitive complaints, fatigue and GI symptoms are commonly found in patients with PD and they negatively impact QOL. Mental health services and gastroenterologists should be engaged as early as possible in the ongoing comprehensive care of patients with PD, especially considering the vast array of therapeutic interventions that could significantly improve their QOL [21, 22]. The focus of management in PD should shift to a comprehensive strategy that incorporates care of non-motor symptoms and improves QOL.

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Compliance with ethical standards

Conflict of interest None.

Ethical approval This work was approved by the Ethics Committee of our Institution and adhered to international ethical standards.

Informed consent All participants signed informed consent for inclusion into this study.

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