



Measurement and correlation of fatigue and sleep quality in Parkinson's disease: a cross sectional study

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ABSTRACT

Background: Fatigue corresponds to a non-motor symptom of high prevalence in Parkinson's disease (PD) affecting about one third of patients with the disease. This symptom negatively affects daily activities, contributing to the deterioration of the quality of life of these subjects. **Objectives:** To estimate fatigue in PD and to correlate with demographic characteristics, sleep, disease stage, motor function and daily activities. **Methods:** The sample consisted of patients with PD. The following measuring instruments were used for the study: Hoehn and Yahr scale, Fatigue Rating Scale, Unified Parkinson's Disease Rating Scale, Parkinson's Disease Sleep Scale. **Results:** This study highlights the high prevalence of fatigue in subjects with PD, and the screening and treatment of this symptom is extremely relevant in clinical practice. There were no significant correlations between fatigue and other variables analyzed. **Conclusions:** Most participants reported fatigue as a relevant problem, so it is important the use of instruments for fatigue screening in clinical practice and the need to develop therapies related to this symptom in the PD.

Keywords: Parkinson's Disease; Fatigue; Sleep; Sleep Disorders; Daily Activities.

INTRODUCTION

The systematic review with meta-analysis of Franssen et al., shows that fatigue corresponds to a non-motor symptom of high prevalence in Parkinson's disease (PD) affecting about one third of patients with the disease⁽¹⁾. This symptom negatively impacts daily activities, contributing to the deterioration of the quality of life of these subjects⁽²⁾. A universally accepted definition for fatigue in PD has not yet been found in the scientific literature, and this can be attributed to its subjective character and commonly described as mental and physical fatigue⁽³⁾. According to Friedman⁽⁴⁾, the physical form of fatigue corresponds to a sensation of corporal exhaustion and decrease of the energy to perform activities, whereas the mental fatigue is related to the fatigue during or after the accomplishment of activities with cognitive exigencies. Another type of fatigue also reported in PD corresponds to peripheral fatigue described as muscular exhaustion, which may be due to tremors caused by repeated contractions⁽¹⁾. In this sense, even fatigue being a symptom frequently found in patients with PD, its association with other motor and non-motor symptoms has not yet been fully elucidated.

Solla et al.⁽⁵⁾ described that affective and sleep disorders seem to influence the presence and severity of this symptom in PD, and probably more than one mechanism contribute to the onset of fatigue, making the study of this symptom in PD important for therapeutic management. Stocchi et al.⁽⁶⁾ reported that fatigue is associated with depression and sleep disorders and some studies have shown a relationship of fatigue in PD with female, age, depression and daytime sleepiness⁽⁷⁾, while Wen et al. found that there is a relationship between fatigue and the severity of PD, depression and sleep disorders⁽⁸⁾. There are few studies developed in Brazil⁽⁹⁾ that use instruments to assess fatigue in PD and to associate their implications to motor capacity, level of impairment and sleep, as well as the other limitations or disorders produced by the presence of symptoms, restricting the development of studies and the elaboration of effective therapeutic approaches. Therefore, the present study has high scientific relevance, aiming to verify the prevalence of fatigue in PD and correlates it with demographic characteristics, sleep quality, level of impairment in PD, motor function and activities of daily living.

METHODS

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This is a cross-sectional, observational study, performed at the Integrated Clinic of the Faculdade de Ciências da Saúde do Trairi (Facisa/UFRN). The research was approved by the institution's Ethics Committee, with protocol 1.839.643 (CAAE: 58656516.0.0000.5568). The sample was composed by subjects with PD from the Physiotherapy Outpatient Clinic of the Integrated Clinic of the Facisa/UFRN. The patients that were on drug therapy, able to walk with or without auxiliary devices were eligible for the study. The excluded criteria were subjects with cognitive impairment, evaluated by the Mini Mental State Examination - MMSE⁽⁹⁾ or those with other diseases associated with fatigue as heart and lung disease, kidney failure, anemia, liver failure or cancer. Participants signed the Informed Consent Form and began evaluations that were performed individually at the Outpatient Clinic of Physiotherapy by therapists duly trained with the following instruments: Socio-demographic evaluation sheet; Mini Mental State Examination – MMSE; Hoehn and Yahr Scale; Unified Parkinson's Disease Rating Scale – UPDRS; Parkinson Fatigue Scale; Parkinson's Disease Sleep Scale. The pre-structured socio-demographic evaluation sheet contained relevant data for the clinical evaluation of the participant. The Mini Mental State Examination – MMSE allows assessment of cognitive function and dementia, and has a total score of 30 points. Bruck et al.⁽¹⁰⁾ considers a score of 20 as a cutoff point for illiterates and variations from 25 for elderly schooling.

The Hoehn and Yahr Scale – H&Y was used to evaluate the staging of the disease. It has eight stages to classify the severity of PD and allow the subject to be qualified for motor impairment through global measures of signs and symptoms. In this instrument the stages I, II and III correspond to mild to moderate disability, while stages IV and V comprise subjects with more severe disability⁽¹¹⁾. The Unified Parkinson's Disease Assessment Scale - UPDRS evaluates signs, symptoms and certain tasks through clinical observation and self-report, being subdivided into 4 domains. In the present study, domains II and III were used to evaluate aspects of daily life and motor aspects, respectively. The score for each item ranges from 0 to 4, in which the minimum value suggests normality and higher value indicates a more serious commitment⁽¹²⁾. For the evaluation of fatigue was used the Parkinson Fatigue Scale - PFS-16, validated in Brazil by Kummer et al.⁽⁷⁾. This scale was designed to estimate fatigue exclusively associated with PD. PFS-16 is composed of 16 items that encompasses the aspect of physical fatigue and its impact on the daily life of the affected subject through self-report. In this instrument for each question, the response options were: "strongly disagree", "disagree", "do not agree or disagree", "agree" and "strongly agree", being scored from 1 to 5, respectively. The PFS-16 total score was calculated according to the mean response of all items; those with a score of 33 or higher constitute subjects who point fatigue as a problem.

The Parkinson's Disease Sleep Scale (PDSS) was used to evaluate sleep disturbances. It is composed by 15 individual items that are associated to sleep disturbances in the PD, being the maximum total score equal to 150 (i.e., the patient is free of symptoms associated with sleep disorders). PDSS allows the evaluation of nocturnal sleep conditions characteristic of PD. For question 1: bad= 0 and excellent= 10; for question 15: frequent= 0 and never= 10; and the other ones: always= 0 and never= 10⁽¹³⁾.

Data Analysis

A descriptive analysis of the sample data was performed to characterize the sample. The data were stored and analyzed by the BioEstat 5.3. The Shapiro-Wilk test was applied to analyze the normality of the data. Considering that the data presented abnormal characteristics, the Spearman test was used to assess the correlations between demographic characteristics, sleep quality, level of impairment in PD, cognitive function and motor function. The correlation coefficient was interpreted according to Munro⁽¹⁴⁾: 0.00-0.25: low or no correlation; 0.26-0.49: low correlation; 0.50-0.69: Moderate correlation; 0.70-0.89: strong correlation; 0.90-1.00: very strong correlation. The level of significance was $p= 0.05$.

RESULTS AND DISCUSSION

The initial sample consisted of 20 subjects eligible for the study, but 10 were excluded because 3 refused to participate, 2 were not found, 2 were not diagnosed, 1 was restricted to the bed, 1 had amputation in the lower limb and did not attend by personal limitations and 1 presented cognitive deficit. The remaining 10 subjects composed the final sample of the study and were evaluated for sociodemographic aspects (table 1). In our sample, 80% presented scores that point to the presence of fatigue (score equal to or greater than 33 in PFS-16), and more than half point to fatigue as one of the three worst symptoms. In the performed analysis, the demographic factors (age and duration of PD) had no correlation with fatigue. The staging of the disease evaluated by H & Y and motor impairment presented a low correlation with fatigue, whereas aspects of daily life evaluated in the UPDRS II presented a moderate correlation with fatigue (table 2). In sleep assessment (PDSS) four patients had scores that indicated poor sleep quality (PDSS < 82), although two others have reported reliance on medication to maintain sleep quality. There was no correlation between sleep and variables analyzed in this study.

Fabbrini et al.⁽¹⁵⁾, reported high frequency of fatigue, with 58% of subjects with PD. In the study of Kummer et al.⁽⁷⁾ for PFS-16 validation and assessment of fatigue severity in PD developed with 87 subjects, reported fatigue as one of the three worst symptoms. Tanaka et al.⁽¹⁶⁾ evaluated the fatigue in 110 Japanese patients through PFS-16, pointing out that more than half had fatigue. However, the author

**Table 1.** Characterization of the sample.

Variables n=10	Frequency (%)	Median (1°Q 2°Q)
Gender (M/F)	60%/40%	
Education		
Illiterate	30%	
Incomplete Elementary School	40%	
Complete Elementary School	10%	
High School	20%	
Age (years)		65 (62; 67)
Duration of PD (years)		7 (2;7)
MMSE		21 (20;23)
H&Y		3 (1;5)
UPDRS II		15 (9;17)
UPDRS III		15 (11;19)
PDSS		81 (68;76)

Note: 1°Q= First quartile; 2°Q= Second quartile; MMSE= Mini Mental State Examination; H&Y= Hoehn & Yahr; UPDRS= Parkinson's Disease Rating Scale; PDSS= Parkinson's Disease Sleep Scale; M = male; F = female..

Table 2. Correlation between PFS-16 and other continuous variables.

PFS-16 versus	Spearman's q	p-value
Age (years)	-0.1420	0.6956
Duration of PD	0.4708	0.1696
H&Y	0.3606	0.3060
UPDRS II	0.5046	0.1368
UPDRS III	0.3653	0.2992
PDSS	0.1524	0.6742

Note: PFS-16= Parkinson Fatigue Scale; H&Y= Hoehn & Yahr; UPDRS= Parkinson's Disease Rating Scale; PDSS= Parkinson's Disease Sleep Scale; p-value=0.05.

states as a limitation of his study the fact that the scale used (PFS-16) disproportionately emphasizes physical fatigue, not evaluating other types of fatigue reported by subjects with PD. The present study corroborated the findings of the literature demonstrating a high prevalence of fatigue (80%) in patients with PD who were evaluated. We support the claims of Tanaka et al.⁽¹⁶⁾ as the limitations of the PFS-16 instrument, since the mental and peripheral fatigue can affect the patient with PD, however the PFS-16 was chosen because it is the only one developed specifically for PD, allowing to evaluate the impact of the symptom on aspects of daily operation⁽³⁾.

In the present study there was no correlation between fatigue and age, while the diagnosis of the disease showed a low positive correlation with fatigue. The results of the study of Tanaka et al.⁽¹⁶⁾ were similar and concluded that physical fatigue is not related to demographic factors. Shanches and Cardoso⁽¹⁷⁾ reaffirm in their results that no correlation was found between age and time of disease of patients with fatigue. Although it

was not a focus of this study, some authors comment on a possible influence of climatic factors on fatigue, and the routine experiments indicate that they prefer heat to cold, suggesting that warm weather does not increase fatigue⁽¹⁸⁾. Regarding the association between the stage of the disease and its relation to fatigue, there was also no correlation, corroborating with the results of the literature^(9,17). Friedman et al.⁽¹⁸⁾ related fatigue to a common problem that can be reported in the early stages of the disease. The association between fatigue and disease progression is unclear. Motor symptoms such as tremor, bradykinesia, stiffness and postural instability have been the focus of numerous studies⁽³⁾. These symptoms lead to motor impairment and gait disturbance, in addition to gradually impairing mobility and functional activities⁽¹⁹⁾, and consequently has a negative impact on daily activities. In the study of Alves et al.⁽²⁰⁾, bringing updates on the subject in PD, have shown that the fatigue increased during a 8-year period, justified by the increase in motor deficiency. In our study, motor symptoms were evaluated (UPDRS III), and no correlation with fatigue was found. Both fatigue and sleep disorders are considered frequent non-motor symptoms in PD patients, but there are no clear associations between both symptoms^(21,22). Havlikova et al.⁽²³⁾ observed that fatigue is not related to nocturnal dysfunction nor daytime sleepiness, but a strong relationship was found between fatigue and depression, making possible a mental fatigue. In our study, we attempted to correlate fatigue and sleep disturbances, and the sleep assessment instrument (PDSS) emphasized nocturnal sleep disorders such as restlessness legs, disturbing dreams, hallucinations, cramps, tingling, also evaluating the quality of sleep and excessive daytime sleepiness. In our findings, 40% of the patients presented indicative of poor sleep quality (PDSS <82), some participants reported using medications with active principles to stimulate sleep and, consequently, presented better sleep quality; And there was no correlation between fatigue and sleep. The present study conducted a survey of the medications (frequency, time and dosage) of the participants and all of them used medication daily to control Parkinson's symptoms (levodopa and combination drugs). Other studies associate the use of drugs with greater fatigue^(17,24). It is also important to highlight the daily use of medication for the treatment of depression by several participants in our sample, such as: citalopram, amitriptyline hydrochloride, escitalopram; considering a possible association of this symptom with fatigue^(18,22). It was noted the use of medications with varied active principles that caused adverse reactions to drowsiness and that could cause sudden sleep during daily activities, being possible the influence in the scores of the sleep screening instrument used in our research. There is still insufficient data for the use of pharmacological or non-pharmacological therapy for fatigue in patients with PD⁽²⁵⁾. In recent literature rasagiline and modafinil are suggested to improve physical fatigue and no quality articles have been



found reporting effects and efficacy of exercise in reducing fatigue in PD⁽²⁶⁾. Acupuncture is indicated as a non-drug therapeutic alternative with effective effect on fatigue⁽²⁷⁾.

CONCLUSIONS

This research highlights the high prevalence of fatigue in patients with PD, and the screening and treatment of this symptom is extremely relevant in clinical practice. Most of the participants reported fatigue as a relevant problem, so it is important the use of instruments for fatigue screening in clinical practice and the need to develop therapies related to this symptom in PD. There were no significant correlations between fatigue and other variables.

AUTHORS CONTRIBUTION

WLG: critical review; LGCS and NMS: Data collection and treatment, manuscript writing; GKSD and RCSCF: Data collection and treatment; EWAC, ROC and NMFVL: design and development, methodological design, critical review.

CONFLICT OF INTERESTS

The authors declare that there was no conflict of interests.

AUTHORS DETAILS

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