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Original Article

Rapid eye movement sleep behaviour disorder in young- and older-onset Parkinson disease: a questionnaire-based study

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ABSTRACT

Background: Rapid eye movement sleep behavior disorder (RBD) is common in Parkinson disease (PD).
Objectives: To determine the frequency of clinically probable RBD (cpRBD) in young-onset (21 to ⩽40 years; YOPD) and older-onset PD (>40 years; OOPD) and characterize its pattern.
Methods: A total of 156 patients with PD (YOPD-51, OOPD-105) were clinically examined and the presence of RBD was diagnosed using the minimal criteria for diagnosis of RBD (International Classification of Sleep Disorders, ICSD-1). RBD screening questionnaire based on the minimal criteria was used. The bed-partners were also interviewed with Mayo sleep questionnaire. Other scales included Unified Parkinson Disease Rating Scale part III (UPDRS III), Hoehn & Yahr stage, Mini Mental Status Examination, Pittsburgh Sleep Quality Index, Parkinson Disease Sleep Scale, Epworth Sleep Scale, Hamilton Anxiety Rating Scale and Hamilton Depression Rating Scale.
Results: cpRBD was diagnosed in 30 (19.2%) patients, majority being OOPD rather than YOPD (86.7% vs 13.3%; $P = 0.01$). The frequency of RBD was significantly higher ($P = 0.016$) in OOPD (24.8%) compared to those with YOPD (7.8%). Most often (72.4%) RBD occurred after the onset of parkinsonian symptoms. RBD was independently associated with higher global PSQI scores, total ESS scores and total PDSS scores after adjusting for the effects of age, gender, Hoehn & Yahr stage and duration of illness.
Conclusions: Patients with RBD were older with later-onset motor symptoms, a more advanced stage, poorer sleep quality, and more frequent daytime sleepiness. Older-onset PD had a higher frequency of RBD than young-onset PD.

1. Introduction

Parkinson disease (PD) is one of the most widespread neurodegenerative disorders. Apart from the disabling motor symptoms which are amenable to treatment, patients also suffer from several non-motor symptoms such as depression, anxiety, psychosis, and dementia [1]. Sleep disturbances occur in up to 98% of patients with PD, ranging from insomnia to parasomnias [2].

Rapid eye movement (REM) sleep behavior disorder (RBD) is one of the sleep parasomnias characterized by violent dreams and the subsequent acting out of dreams during REM sleep [3]. RBD is often associated with α-synucleinopathies, particularly PD. The prevalence of RBD in the general population is 0.5% [4] and in PD is variable from 15% to 72% [5–8].

Several studies are available from western countries on the prevalence of RBD, its clinical characteristics, and its association with other non-motor symptoms of PD such as psychosis (hallucinations and delusions) and dementia. However, the literature on the frequency of RBD in PD in the Indian subcontinent is scant [9]. It is possible that there may be a difference in the cultural perception of dreams and genetic factors that can influence sleep architecture. Studies on the frequency of RBD in young-onset PD are limited [10,11]. Hence the present study was undertaken primarily to determine the frequency of clinically probable RBD (cpRBD) in PD, and to compare the frequency of cpRBD between two groups of PD patients: young-onset PD (age at onset of motor symptoms 21–40 years; YOPD) and older-onset PD (age at onset of motor symptoms >40 years; OOPD) [12]. The secondary objective was to compare the clinical characteristics of patients with cpRBD between the two groups of PD patients, albeit that this study was questionnaire-based with lack of polysomnographic confirmation of RBD.

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2. Methods

2.1. Patients and setting

The study included 156 consecutive patients with PD (mean age, 55.4 ± 11.2 years) who visited the neurology outpatient services, and movement disorder clinic as well as those admitted in the neurology ward of the National Institute of Mental Health and Neurosciences (NIMHANS) in Bangalore, India. PD was diagnosed according to the UK Parkinson Disease Society Brain Bank criteria (Queen Square Brain Bank criteria) [13,14]. The patients admitted in the ward were for adjustment of medications and no one had delirium. The study period was from October 2010 to December 2011 and was approved by the Institute Ethics Committee. All subjects gave written informed consent after full explanation and detailed description of study method. The patients presenting with features of parkinsonism were clinically examined to rule out Parkinson-plus syndromes and only those patients (n = 156) fulfilling the inclusion criteria for PD and consenting to participate in the study were recruited. Based on the age of onset of motor symptoms of PD, they were grouped into young- and older-onset PD. All 156 patients were interviewed by one of the authors (R.M.). No incentives were offered for participation. The study was prospective, cross-sectional, and hospital-based.

2.2. Investigations

All patients were interviewed and examined with documentation of demographic variables, disease profile including age at onset of motor and non-motor symptoms, and treatment profile. The staging of PD was done using modified Hoehn & Yahr Stage (H&Y) [15], the severity of motor symptoms of PD was assessed using Unified Parkinson Disease Rating Scale part III (UPDRS-III) [16], and cognitive function was assessed using the Mini Mental Status Examination (MMSE) scale [17]. The total levodopa equivalent dose (TLED) was calculated for each patient [18].

Evaluation of sleep was carried out using the Parkinson Disease Sleep Scale (PDSS) [19], Pittsburgh Sleep Quality Index (PSQI) [20] and Epworth Sleepiness Scale (ESS) [21]. In addition, all patients were interviewed with RBD screening questionnaire (RBDSQ) [22] – a well-validated diagnostic screening tool for RBD. The RBDSQ is a 10-item questionnaire, and cut-off value of five points was used to diagnose clinically probable RBD (cpRBD). The bed partner or spouse of all the patients was interviewed with Mayo Sleep Questionnaire (MSQ) question 1, which pertains to RBD. This was used to confirm cpRBD in patients who were unable to recall the sleep-related events. RBDSQ is based on the minimal criteria (criteria B + C) of International Classification of Sleep Disorders (ICSD-1) [23] for the diagnosis of RBD [(B) Limb or body movement is associated with dream mentation. (C) At least one of the following occurs: (criterion C1) harmful or potentially harmful sleep behaviors; (criterion C2) dreams appear to be 'acted out'; (criterion C3) sleep behaviors disrupt sleep continuity]. The details about timing of dream enactment and clinical events were obtained based on structured clinical interview.

Hamilton Anxiety Rating Scale (HAM-A) [24] and Hamilton Depression Rating Scale (HAM-D) [25] were used to assess anxiety and depression respectively.

The following subscores of UPDRS III were calculated for all patients: (i) tremor score (UPDRS 20, 21, maximum score 28); (ii) rigidity score (UPDRS 22, maximum score 20); (iii) bradykinesia score (UPDRS 23–26, 31 maximum score 36); (iv) gait/postural stability score (UPDRS 27–30, maximum score 16); (v) bulbar abnormalities score (UPDRS 18, 19, maximum score 8); (vi) axial signs score (UPDRS 18–19, 22, 27–30, maximum score 42); and (vii) limb signs score (UPDRS 20–26, maximum score 84). The proportion of UPDRS III motor scores accounted for by each subscore was determined. For tremor score (% of UPDRS III), the tremor score was divided by the total UPDRS III score. Similar derivations were made to assess the proportion accounted by rigidity, bradykinesia, gait/postural stability, and bulbar abnormalities [3]. The tremor-dominant subtype of PD was defined as patients with a ratio of tremor to bradykinesia score (bradykinesia, rigidity and postural instability subscore from the UPDRS motor scale) of $\geqslant$0.5, and the akinetic rigid subtype as patients with a ratio of <0.5 [26].

2.3. Statistical analysis

The data were analyzed using SPSS version 16.0. The qualitative data were analyzed using χ^2-test or Fisher's exact test. The continuous variables were expressed as mean ± standard deviation and categorical variables as frequency and percentage. The normality of the distribution was assessed by the skewness of the values. For the analysis of continuous variables, non-parametric testing (Mann–Whitney test and Wilcoxon's test) was employed. $P < 0.05$ was taken as statistically significant. Correlation among various clinical parameters and scales employed in the study to determine the significance was done using Spearman's correlation coefficient.

3. Results

In all, 156 PD patients (51 YOPD and 105 OOPD) were recruited during the study period. There were 30 patients with cpRBD (19.2%). The frequency of cpRBD was significantly higher (P = 0.016) in OOPD (24.8%) compared to those with YOPD (7.8%). In majority of the patients (72.4%) the symptoms of RBD appeared after the onset of motor symptoms of parkinsonism. In the remainder, it appeared either before (20.7%) or along with parkinsonism (6.9%). Due to low frequency of cpRBD in YOPD patients, a comparison with cpRBD in OOPD was not carried out.

3.1. Demographic features and clinical characteristics

Patients with cpRBD were significantly older and had later age at onset of motor symptoms of PD (Table 1). There was no difference between the two groups (cpRBD and non-cpRBD) with respect to gender distribution (70.0% vs 77.8% men). Two patients with cpRBD had familial PD whereas 18 patients without cpRBD had familial PD. The duration of symptoms, duration of treatment, and TLED (mg/day) were higher in the cpRBD group compared to those without cpRBD, but these differences were not statistically significant. There was no significant difference between the groups with respect to the motor subtypes of PD.

3.2. Rating scores and disease complications

The mean UPDRS III motor score was similar in both groups (Supplementary Table 1). The mean tremor score was lower in the cpRBD group but was not statistically significant. The gait/postural stability score (% of UPDRS III) was significantly higher (15.4 ± 6.2% vs 13.3 ± 6.5%; P = 0.04). Patients with cpRBD had higher mean axial:limb sign ratio, which was statistically significant. There was no significant difference with respect to the mean rigidity or mean bradykinesia score. The median H&Y stage in the cpRBD group was 2.5, which was higher than in the non-cpRBD group (P = 0.02). The percentage of patients with cpRBD with advanced stage of PD was high (H&Y stage $\geqslant$2.5). The percentage of patients with falls and dyskinesia were similar in both groups. The mean HAM-A and HAM-D scores were similar in both groups.