Journal of Clinical Neuroscience 28 (2016) 43–46

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

# Rapid eye movement sleep behaviour disorder in women with Parkinson's disease is an underdiagnosed entity

Rohan R. Mahale [a,*], Ravi Yadav [b], Pramod Kr. Pal [b]

[a] Department of Neurology, M.S. Ramaiah Medical College and Hospital, MSRIT Post, New BEL Road, Bangalore 560054, Karnataka, India
[b] Department of Neurology, National Institute of Mental Health and Neurosciences, Bangalore, Karnataka, India

ARTICLE INFO

*Article history:*
Received 24 August 2014
Accepted 30 August 2015

*Keywords:*
Parasomnias
Parkinson's disease
RBD
REM behaviour disorder of sleep
Sleep
Women

ABSTRACT

Rapid eye movement sleep behavior disorder (RBD) is common in Parkinson's disease (PD). Little information exists about RBD in women with PD. The aim of this study was to determine the clinical expression of RBD in women with PD and note any differences in women with PD with and without RBD. One hundred fifty-six patients with PD were recruited. There were 37 women with PD and probable RBD was diagnosed using the RBD Screening Questionnaire. Other scales included Pittsburgh Sleep Quality Index, Parkinson's Disease Sleep Scale, Epworth Sleep Scale, Hamilton Anxiety Rating Scale and Hamilton Depression Rating Scale. Probable RBD was diagnosed in 10 women with PD (27%). Most often (70%) RBD occurred after the onset of parkinsonian symptoms. Women with probable RBD were older, had shorter duration of PD symptoms, lower tremor score, and higher axial signs score. They had insomnia (80% *versus* non-probable RBD patients 44%, p = 0.019), and poor sleep quality with excessive daytime sleepiness. Anxiety and depression were common in women with probable RBD. Episodes were brief and confined to vocalization and simple limb movements. No injury to self or bed partners was noted. Women with PD have fewer fights and less aggressive dream enacting behaviour than men, but suffer from significant disturbed sleep, and levels of anxiety and depression.



## 1. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder which has been the focus of much recent research. Patients suffer from both motor and non-motor symptoms. Sleep disturbances occur in up to 96% of patients with PD [1]. Rapid eye movement (REM) sleep behaviour disorder (RBD) is a one of the sleep parasomnias associated with neurodegenerative disorders, in particular the synucleinopathies that include PD [2]. RBD is characterised by violent dreams and the subsequent acting out of dreams during REM sleep [3]. The prevalence of RBD as assessed by questionnaire or interview alone is usually lower (15–47%) than assessed by polysomnography (33–58%) [3,4]. Idiopathic RBD shows a striking sex predominance, with up to 90% of the patients being male [2]. However in PD, recent studies have shown sex differences in terms of clinical expression of RBD while the frequency of RBD remains similar [5]. Women with PD suffering from RBD have not been well studied. The present study aimed to determining the clinical expression of RBD in women with PD and to note any difference in women with PD with and without RBD.

## 2. Methods

### 2.1. Subjects

One hundred fifty-six consecutive patients with PD (mean age, 55.4 ± standard deviation of 11.2 years) who visited the Neurology Out-Patient Services, Movement Disorder Clinic, and those admitted to the Neurology ward of the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India were included in the study. PD was diagnosed according to Queen Square Brain Bank criteria [6]. The study period was from October 2010 to December 2011 and was approved by the Institute Ethics Committee (NIMHANS). All subjects gave written informed consent after full explanation and a detailed description of study method. The study was prospective, cross-sectional and hospital based.

### 2.2. Assessment of RBD

The presence of RBD was determined using the Rapid Eye Movement Sleep Behaviour Disorder Screening Questionnaire (RBDSQ), a

* Corresponding author. Tel.: +91 80 4050 3125; fax: +91 80 2218 3276.
*E-mail address:* rohanmahale83@gmail.com (R.R. Mahale).

http://dx.doi.org/10.1016/j.jocn.2015.08.046
0967-5868/

well validated diagnostic screening tool for RBD both in the general population and in PD patients [7,8]. RBDSQ is a 10 item no/yes questionnaire with maximum score of 13 and cut-off value of 5 points was used to diagnose probable rapid eye movement sleep behavior disorder (pRBD). RBDSQ is based on the minimum criteria (criteria B+C) of International Classification of Sleep Disorders–1 for the diagnosis of RBD [9]. These criteria are limb or body movement associated with dream mentation, and at least one of the following: harmful or potentially harmful sleep behaviors; dreams appear to be "acted out"; and sleep behaviors disrupt sleep continuity.

### 2.3. Clinical assessment

The staging of PD was done using modified Hoehn and Yahr staging (H&Y) [10], the severity of PD motor symptoms was assessed using the Unified Parkinson Disease Rating Scale III (UPDRS III) [11], and cognitive function using the Mini-Mental Status Examination [12]. The total levodopa equivalent dose (TLED) was calculated in each patient [13]. Evaluation of sleep was carried out using the Parkinson's Disease Sleep Scale (PDSS) [14], Pittsburgh Sleep Quality index (PSQI) [15] and the Epworth Sleep Scale (ESS) [16]. To assess anxiety and depression, the Hamilton Anxiety rating scale (HAM-A) [17] and Hamilton Depression rating Scale (HAM-D) [18] were utilized. The following subscores of UPDRS III were calculated for all patients: (i) tremor score (UPDRS item 20–21, maximum score 28), (ii) rigidity score (UPDRS item 22, maximum score 20), (iii) bradykinesia score (UPDRS item 23–26 and 31, maximum score 36), (iv) gait/postural stability score (UPDRS item 27–30, maximum score 16), (v) bulbar abnormalities score (UPDRS item 18–19, maximum score 8), (vi) axial signs score (UPDRS item 18–19, 22 and 27–30, maximum score 42) and (vii) limb signs score (UPDRS item 20–26, maximum score 84). The proportion of the UPDRS III motor score accounted for by each subscore was determined. For the tremor score (% of UPDRS III), the tremor subscore was divided by the total UPDRS III score. Similar derivations were made to assess the proportion of the total motor score accounted for 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 (combined bradykinesia, rigidity and postural instability subscores from the UPDRS motor scale) of 0.5 or more, and the akinetic rigid subtype as patients with a ratio of <0.5 [19].

## 3. Statistical analysis

The data was analyzed using the Statistical Package for the Social Sciences version 16.0 (IBM, Armonk, NY, USA). Comparison of women with PD with and without RBD was done using the following variables: age at onset, age at presentation, disease duration, H&Y stages, UPDRS III total score, UPDRS III subscores, TLED, and scores on the HAM-A, HAM-D, PDSS, PSQI and ESS. The clinical presentation of RBD was assessed using the scores on different items of the RBDSQ. 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 skew of the values. For the analysis of continuous variables, non-parametric tests (Mann–Whitney test and Wilcoxon test) were employed. The qualitative data was analyzed using chi-square/Fischer's exact test. A p value <0.05 was taken as statistically significant.

## 4. Results

Out of 156 patients recruited during the study period, there were 37 women with PD (mean age, 54.0 ± 11.6 years). pRBD was present in 27% (10/37) of the women with PD. In the majority of the patients (70.0%) the symptoms of pRBD appeared after the onset of parkinsonism motor symptoms. In the remaining patients, either it appeared before (20.0%) or along with parkinsonism (10.0%).

### 4.1. Demographic features and clinical characteristics

Women with pRBD were significantly older and had later age at onset of motor symptoms of PD. One patient with pRBD had familial PD whereas five patients without pRBD had familial PD. Women with pRBD had shorter duration of PD symptoms before RBD onset, which was statistically significant. There was no significant difference between the groups with respect to the motor subtypes of PD and TLED (Table 1).

### 4.2. Rating scores and disease complications

The mean UPDRS III motor score was similar in both groups. The mean tremor subscore and tremor score (% of UPDRS III) was significantly lower in women with pRBD. Women with pRBD had higher mean axial:limb sign ratio which was statistically significant. There was no significant difference with respect to the mean rigidity, bradykinesia, gait/postural stability and bulbar abnormalities subscores. The bulbar abnormalities score (% of UPDRS III) was significantly higher (13.4 ± 3.9% *versus* 11.3 ± 3.4%; p = 0.05). The percentage of women with pRBD with advanced stage of PD was high (80%) (H&Y stage ⩾2.5). The percentage of patients with falls and dyskinesia were similar in both groups. The mean HAM-A and HAM-D scores were significantly higher in women with pRBD compared to women without pRBD (Table 2).

### 4.3. Sleep scales

Women with pRBD had significantly higher sleep disturbances. They had significantly fewer mean hours of actual sleep per night. The global PSQI was significantly worse in women with pRBD. Women with pRBD were poorer sleepers (global PSQI score >5) (70.0% *versus* 43.2%; p = 0.03). The total ESS score was significantly higher in women with pRBD, with a higher percentage of patients

**Table 1**
Clinical characteristics of women with PD with and without pRBD

| Characteristic | pRBD (n = 10) | Non pRBD (n = 27) | p value |
|---|---|---|---|
| Age (years) | 62.5 ± 10.3 | 51.2 ± 10.7 | **0.01** |
| Age at onset of symptoms (years) | 58.4 ± 11.9 | 45.8 ± 11.2 | **0.009** |
| Duration of disease (years) | 4.1 ± 2.8 | 5.3 ± 4.9 | **0.04** |
| Duration of treatment (months) | 57.6 ± 55.3 | 37.9 ± 38.0 | 0.105 |
| TLED (mg/day) | 675.0 ± 521.5 | 588.5 ± 313.5 | 0.95 |
| Familial PD | 1 (10%) | 5 (18%) | 0.42 |
| Tremor type PD | 3 (30.0%) | 10 (37.0%) | 0.376 |
| Akinetic rigid type PD | 7 (70.0%) | 17 (62.9%) | - |
| *Site first affected* | | | 0.912 |
| Upper limb | 7 (70.0%) | 22 (81.4%) | |
| Lower limb | 2 (20.0%) | 4 (14.8%) | |
| Both | 1 (10.0%) | 1 (10.0%) | |
| *Side first affected* | | | 0.463 |
| Right | 7 (70.0%) | 21 (77.7%) | |
| Left | 3 (30.0%) | 6 (22.2%) | |
| Both | 0 (0%) | 0 (0%) | |
| Falls | 2 (20.0%) | 6 (22.2%) | 0.643 |
| Dyskinesia | 3 (30.0%) | 7 (25.9%) | 0.463 |

Data are presented as mean ± standard deviation or number (%).
Bold indicates statistical significance.
PD = Parkinson's disease, pRBD = probable rapid eye movement sleep behavior disorder, TLED = total levodopa equivalent dose.