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Excessive daytime sleepiness in Parkinson's disease as assessed by Epworth Sleepiness Scale (ESS)

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Abstract

Objective: To assess daytime sleepiness in patients with Parkinson's disease (PD) using the Epworth Sleepiness Scale (ESS).

Material and methods: One hundred and forty-nine patients with PD (126 men, 23 women) and 115 age matched controls recruited from relatives of medical staff or spouses and other family members accompanying patients to the Movement Disorder Clinic of the All India Institute of Medical Sciences in New Delhi were included in the study. An ESS score of ≥ 8 was considered abnormal. Data obtained were analyzed using Chi square test for categorical variables and Student's *t*-test for continuous variables.

Results: The mean age of patients with PD was 58.37 (S.D. = 10.45) years, and that of controls 56.50 (S.D. = 11.45) years, with a mean duration of disease of 5.68 (S.D. = 3.85) years. The mean ESS score was 4.9 (S.D. = 3.63) and 2.17 (S.D. = 2.54) in PD patients and controls, respectively ($P < 0.05$). Thirty-two patients with PD (21%) had an ESS score of >8 whereas only 3% of controls scored ≥ 8 on the ESS ($P < 0.05$). Higher ESS scores were associated with a higher Hoehn and Yahr (H&Y) stage of disease and higher Unified Parkinson's Disease Rating Scale (UPDRS) (part I, III and total) scores ($P < 0.019$, $P < 0.013$ and $P < 0.011$, respectively).

Conclusion: Excessive daytime sleepiness was more common in PD patients as compared to controls. Higher ESS scores correlated significantly with higher H&Y stage and higher UPDRS (part I, III and total) scores.

Keywords: daytime sleepines; Parkinson's disease; Epworth Sleepiness Scale

1. Introduction

Daytime sleepiness is now increasingly reported in patients with PD, the frequency reported ranging from 26 to 65% [1–3]. Excessive daytime sleepiness (EDS) in PD patients may occur due to drug therapy (Levodopa, Selegiline), primary sleep disorders (insomnia, restless legs syndrome) or disruption of circadian rhythm [4]. Due to its direct impact on road safety and public health, EDS has now become a symptom of concern for the treating physician [5,6]. For this reason it is necessary to screen PD patients for increased propensity to sleep during the day. The methods for evaluating EDS range from overnight polysomnography (PSG) followed by multiple sleep latency test (MSLT), maintenance of wakefulness test (MWT) and Epworth sleepiness score (ESS). We selected the ESS as the best measure to assess EDS on an outpatient basis, as it was inexpensive and relatively easy to administer in 5 min. The ESS has been validated extensively by various studies and found to be reliable [7–9]. In comparison with the MSLT and MWT, the ESS was found to have a sensitivity of 93.5% and a specificity of 100% [10]. Similarly, item and factor analysis has shown that the ESS is a unitary scale with high internal consistency and has a high test–retest reliability over a period of 5 months in normal subjects [7].

We conducted this study to evaluate the frequency of daytime sleepiness in Indian patients with PD using the ESS [7–10].

2. Material and methods

For the study 149 consecutive PD patients from the Movement Disorder Clinic at the All India Institute of Medical Sciences (AIIMS) were recruited from October 1998 to August 2000. Diagnosis was based on the UK PD severity Brain Bank diagnostic criteria [11–13]. PD

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patients in all stages were included. For comparison, we studied a group of 115 age-matched healthy controls comprised of doctors, nurses, relatives and attendees of neurology outpatients from various strata of the society. Patients and control subjects suffering from any chronic debilitating disease that could affect sleep, such as chronic obstructive airway disease, ischemic heart disease, stroke, and painful joint disease, were excluded from the study. Controls with chronic use of sedatives, hypnotics, drugs or alcohol were excluded. Informed consent was obtained from all patients and controls. One interviewer collected the demographic profile, clinical details and information about sleep on a preformed questionnaire during a consultation lasting approximately 30–40 min. PD patients were also evaluated using the UPDRS [14], H&Y PD staging [15] and Schwab and England scale of activities of daily living [16]. The motor evaluation for the UPDRS was done when each patient was most alert.

As depression can lead to impairment of sleep, patients as well as controls were evaluated for depression using the ICD 10 diagnostic criteria [17] and Hamilton depression rating scale [18]. Dementia was excluded in both patients and controls using the DSM IV criteria [19]. All participants completed a sleep questionnaire containing 23 questions—12 from the Case Western Reserve Health Sleep Study Questionnaire [20], eight evaluating PD related sleep problems, two assessing the use of alcohol and nicotine, and one from the Epworth sleepiness scale (ESS)—designed to collect information about the subjective experience of the night's sleep [7–9]. (As most of the Indian population uses the bus as a mode of transport rather than car, in the ESS questions relating to travel, the word 'car' was replaced by the word 'bus'.) Higher scores on the ESS implied a greater average propensity to fall asleep. Normal values range from 2 to 10 [21]. We took the score of ≥ 8 for separating the two groups (with and without EDS), based on the mean +2 standard deviation of the control population (2.11 + 2.54).

Questions pertaining to difficulty with sleep initiation, frequent awakenings, nocturnal pain, insomnia, frightening dreams/nightmares, frequency of urination, stiffness at night, difficulty in shifting position at night, breathing difficulty at night, snoring, choking, pausing for breath at night, feeling tired and sleepy during the day, morning headaches, restless sensation in the legs, sleep walking (questions 5–21) had a five point rating on a 0–4 scale, depending on frequency of occurrence of the particular symptom [0, never; 1, rarely (i.e. less than once a week); 2, sometimes (i.e. 1–2 times/week); 3, frequently (i.e. 3–4 times/week); 4, always or almost always (i.e. 5–7/week)]. Restless legs syndrome was indicated by one question asking the subjects if they experienced restless sensation in the legs, worse in the evenings, and disappearing when walking.

2.1. Statistical analysis

Demographic statistics and mean and standard deviation were performed for all the variables. Chi square test was used to evaluate the categorical variables and Student's *t*-test for continuous variables. Yate's correction factor was used.

3. Results

One hundred and forty-nine PD patients and 115 controls were evaluated. The mean age for the PD patients was 58.37 (S.D. = 10.45) years, and 56.50 (S.D. = 11.45) for controls ($P > 0.05$). The demographic data for patients and controls are shown in Table 1. The mean age of onset of PD was 53.04 (S.D. = 11.16), with mean duration of disease being 5.7 years (3.85). The presenting symptom was tremor in 69%, rigidity in 30% and dystonia in 1%. The total UPDRS score was 40.95 (S.D. = 21.53) with a mean H&Y score of 2.11 (S.D. = 0.78.) The mean levodopa dosage was 445.49 mg/day (275.35 mg). An ESS score of ≥ 8 was observed in 32 patients (21%) as compared to 3% in the control population (Table 1).

Patients with ESS >8 were older in age ($P = 0.006$), with a later age of onset ($P = 0.009$) and had a higher UPDRS score. The bradykinesia score, sleep latency, nighttime awakening, body mass index (BMI), levodopa dose, and RLS were not significant (Table 2).

The only dopamine agonist freely available in India is bromocriptine. EDS, as assessed on a score of 8 or more on the ESS, was observed in only 5/19 patients on bromocriptine, but did not correlate with the dosage. The ANOVA and unpaired *t*-test revealed no statistically significant variation between the various drugs used and the ESS score. This observation is probably due to the small sample in each group studied.

4. Discussion

The present study of subjects from the Indian population revealed an increased ESS score in patients with Parkinson's disease as compared to healthy controls. This

Table 1
Demographic data of PD patients and healthy controls

Variables	Parkinson'disease N = 149 Mean (S.D.)	Controls N = 115 Mean (S.D.)	*P* value
Age (years)	58.37 (10.45)	56.50 (11.45)	NS
Age of onset (years)	53.04 (11.16)	–	
Duration of disease (years)	5.7 (3.85)	–	
ESS score	4.91 (3.63)	2.17 (2.54)	$P < 0.05$
ESS score ≥ 8 *n*(%)	32 (21.47)	4 (3)	

Table 2
Comparison of ESS group 1 and group 2

Variable	Group 1 (≤7)	Group 2 (≥8)	*P* value
Age years	57.15 (10.48)	62.81 (9.18)	0.006
Age at onset years	51.88 (11.30)	57.78 (9.66)	0.009
Mentation	2.08 (1.67)	2.97 (2.51)	0.019
ADL UPDRS	10.78 (7.27)	13.78 (9.02)	0.052
Motor UPDRS	25.75 (13.58)	32.75 (15.22)	0.013
Total UPDRS	38.62 (20.45)	49.50 (23.54)	0.011
Bradikinesia	9.61 (4.87)	11.47 (6.14)	0.073
Levodopa dose (mg)	431.43 (281)	499 (250)	0.267
BMI	22.88 (3.75)	22.84 (3.96)	0.962

has been reported earlier with differences in the percentage of patients with EDS [1–3]. Hobson et al. reported 51% of 638 PD patients to have EDS and found that an ESS score of ≥7 predicted 75% of episodes of sleep while driving, with ESS having a sensitivity of 70% and specificity of 52% [22]. Factor et al. found that more than 65% of 78 PD patients and 26% of 43 controls experienced daytime sleepiness and napping [2]. Hilten et al. did not find any significant difference between PD patients (44%) and controls (31%) [3]. The lower frequency in our study may be partly explained by the fact that we studied an unselected patient population of consecutive patients, encompassing all stages of disease and socioeconomic strata, attending the movement disorder clinic at the AIIMS. Only those patients were excluded who had higher propensity to fall asleep due to chronic debilitating diseases, alcohol, drugs and hypnotic intake, whereas the above-mentioned studies included patients selected after screening or interview who were probably more likely to suffer from sleep problems.

Various mechanisms are reported regarding the occurrence of sleep disturbances in PD, and some authors have postulated a considerable disruption of circadian sleep pattern in those patients [23,24]. Others have postulated that antiparkinsonian drug therapy can lead to alterations in the central neurotransmitter levels, including alteration in serotonergic activity [25,26]. Jellinger and Langston showed in their studies that, besides degeneration of dopaminergic nigrostriatal neurons, there is also variable cell loss in the mesocorticolimbic pathways and parts of the ascending reticular activating system [27,28]. In our study EDS was significantly higher in PD patients and strongly correlated with higher UPDRS part-I, II, H&Y score. Similar observations have been reported by Tandberg et al.'s questionnaire-based study, in which 15% of PD patients had excessive daytime sleepiness associated with higher H&Y stage of disease and higher UPDRS scores (part I, II and total scores), suggesting that disease severity is a major contributing factor [1,29].

A recent report by Frucht et al. of 'sleep attacks' in PD patients receiving the non-ergot dopamine agonists ropinirole and pramiprexole has generated much interest in dopamine agonists and their role in causing excessive daytime sleepiness, especially without warning [30–32]. Although most recently reported in PD patients on non-ergot dopamine agonists, excessive sleepiness has been reported earlier with levodopa, bromocriptine, pergolide and other dopamine agonists [33]. It is suggested that sudden, irresistible attacks of sleep are a class effect of non-ergot dopamine agonists, attributed to higher D3 selective affinity of newer non-ergot dopamine agonists associated with increased sleepiness due to down regulation of dopaminergic inputs to the reticular activating system [34]. Our study did not address this aspect of sleep problems in PD patients.

In summary, the recognition of excessive daytime sleepiness in PD patients is extremely difficult because PD patients and their caregivers infrequently volunteer such complaints, which must be assessed by a questionnaire such as the ESS or subjecting the patient to MSLT/MWT. The advantage of ESS is that it is relatively simple to administer. However, it is purely subjective, and the association between MSLT and ESS is variable [35]. This variation could be due to the fact that they measure different but complementary aspects of sleepiness. The recognition of EDS in PD will help in providing better quality of life and stimulate clinicians to review the therapeutic options.

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