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Original Article

Internal Medicine Section

Sleep Dysfunction in Parkinson's Disease

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ABSTRACT

Introduction: Sleep disorders are common in Parkinson's Disease (PD). It can antedate the motor manifestations of PD. It is related primarily to the involvement of sleep regulating structures, secondary involvement through motor, depressive and dysautonomic symptoms and the tertiary involvement through anti-parkinsonian medications.

Aim: The aim of our study is to evaluate the frequency and nature of the sleep abnormalities in Idiopathic Parkinson's Disease, analysing the sleep architecture using polysomnography and to correlate the results with the disease parameters.

Materials and Methods: A cross-sectional study was done in 50 patients who fulfill the "UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria". They were assessed using detailed history and clinical neurological examination. The severity of the disease was assessed based on Unified Parkinson's Disease Rating Scale (UPDRS part III) and the sleep is assessed using Parkinson's Disease Sleepiness Scale (PDSS) and Epworth Sleepiness Scale (ESS). Objective sleep study was done using polysomnography.

Results: Disturbed sleep was reported by 70% of patients. Sixty percent of them had difficulty in falling asleep and 48% had difficulty in maintaining the sleep due to frequent awakenings. Day time somnolence was reported by 30% of patients. Polysomnographic analysis showed reduced total sleep time in 40 patients (80%). Correlation analysis of the total sleep time, sleep efficiency, deep sleep time, REM sleep time with the disease duration, staging, severity, PDSS Score, showed significant positive correlation ($p<0.05$). Sleep related movement disorders like Periodic Limb Movements (PLMS), Restless Leg Syndrome (RLS) also showed inverse correlation with disease duration and severity ($p<0.05$).

Conclusion: Sleep architecture is markedly disturbed in patients with Idiopathic Parkinson's disease. There is a reduction in the total sleep time, deep sleep time and REM Sleep duration. Periodic limb movements in sleep, restless leg syndrome, and obstructive sleep apnea contributes to the sleep fragmentation resulting in defective day time functioning.

Keywords: Day time functioning, Sleep efficiency, Snoring, Polysomnography

INTRODUCTION

Sleep is defined as a periodic reversible physiological state of loss of consciousness from which a person can be aroused by adequate sensory stimuli and it is necessary for the recoupment and well being of the individual. We spend around 8 hours per day for sleep which means 56 hours per week, 224 hours per month and 2688 hours per year, almost nearly 1/3rd of our life we spend for sleep [1].

Sleep helps in energy conservation, physical restoration, memory reinforcement and consolidation, thermoregulation, preserving synaptic efficiency, brain growth and development [2]. Sleep disorders are very common in Parkinson's Disease (PD). Sleep disorders comes under the "non-motor components" of PD [3].

Patients may complain of difficulty in initiating sleep, fragmented sleep due to frequent awakenings in the night, early morning awakenings, inadequate night sleep followed by Excessive Daytime Sleepiness (EDS), snoring, nightmares, hallucinations, vivid dreams, panic attacks, Periodic Limb Movements (PLMS), Restless Leg Syndrome (RLS), REM sleep behavioural disorder, etc. [4]. The factors being anatomical involvement of the sleep regulating structures (degeneration of hypothamic neurons, pendunculo pontine nucleus, locus ceruleus, midbrain raphe nucleus etc.), motor rigidity, depression, dysautonomic symptoms and by anti-parkinsonian medications used in treating PD [5]. Various studies indicate sleep disturbance ranges from 60-98% in PD [6,7]. There is positive correlation with the disease severity, Unified Parkinson's Disease Rating Scale (UPDRS) part III score, L-dopa score, rigidity and bradykinesia [8]. Respiratory dysfunction during sleep occurs in PD which can include apnea and hypopnea. Excessive daytime sleepiness is seen in 15-51% of PD patients [8,9].

Approach to a patient with a sleep complaint includes, a detailed history of sleep, psychiatric, neurologic, medical, drug, family history and a standard sleep questionnaire along with objective documentation of the sleep and its related events using polysomnography (PSG). The Epworth sleepiness scale is used to measure daytime sleepiness.

AIM

The aim of our study is to evaluate the frequency and the nature of the sleep abnormalities in Idiopathic Parkinson's Disease, to analyse the sleep architecture in Parkinson's disease using polysomnography and to correlate the results with the disease parameters.

MATERIALS AND METHODS

A cross-sectional study was done in 50 patients who fulfill the "UK Parkinson's Disease Society- Brain Bank Clinical Diagnostic Criteria" admitted in neurology ward/consulting in Neurology outpatient clinic. Patients who are bed ridden and associated with co-morbidities which affects the sleep like uncontrolled diabetes, LV dysfunction, Bronchial Asthma, Chronic obstructive Pulmonary disease, vascular Parkinsonism, head injury, dementia, Parkinson plus syndrome were excluded. They were assessed using detailed history and clinical neurological examination. The severity is assessed based on Unified Parkinson's Disease Rating Scale

(UPDRS) and the sleep is assessed using Parkinson's disease sleepiness scale (PDSS) and Epworth Sleepiness Scale (ESS). Objective sleep evaluation was done using polysomnography.

RESULTS

Disturbed sleep was reported by 35 patients [Table/Fig-1]. Of them 30 have difficulty in falling asleep and 24 have difficulty in maintaining the sleep due to frequent awakenings. Most of the patients revealed that they woke up in the night mainly to pass urine. Day time somnolence was reported by 15 patients. The study participants were 35 (70%) males and 15 (30%) females with the age group range from 46 to 70 years (mean age is 57.16 years). Females belong to the age group between 48 to 70 years (mean 59.73years) and age range in the males lie between 46 to 70 years (mean 56.05 years). The duration of the disease ranges from one year up to 12 years

	DESCRIPTIVE STATISTICS			
	min	max	mean	S.D
Age(yr)	46	70	57	6.6
Duration(yr)	1	12	5.3	2.29
Staging	1	5	2.9	0.81
UPDRS motor severity	10	40	25.3	7.24
PDSS	80	150	115.9	22.02
ESS	0	16	5.86	5.42
POLYSOMNOGRAPHY				
TS Time (hour)	210	445	310.3	45.82
Latency (minutes)	2	50	22.3	11.45
Efficiency%	55	94	72.9	9.55
Maintanence%	52	99	73.82	11.26
REM episodes	1	3	2.12	0.479
PLMS	0	10	2.7	3.96
AHI	0	20	3.66	5.38

[Table/Fig-1]: Subjective and Objective (Polysomnography) Results
UPDRS - Unified Parkinson's disease rating scale; PDSS - Parkinson disease sleepiness scale; ESS - Epworth sleepiness scale; TS - Total sleep; PLMS - Periodic limb movement syndrome; AHI - Apnoea hypopnoea index

	PEARSON CORRELATION ANALYSIS (n=50)					
	DURATION		STAGING		SEVERITY	
	r	p-value	r	p-value	r	p-value
PDSS	-0.831	<0.05	-0.826	<0.05	-0.955	<0.05
ESS	-0.845	<0.05	-0.836	<0.05	-0.828	<0.05
TST	-0.762	<0.05	-0.745	<0.05	-0.748	<0.05
SL.MAINTANENCE	-0.846	<0.05	-0.845	<0.05	-0.98	<0.05
SL.EFFICIENCY	-0.784	<0.05	-0.842	<0.05	-0.751	<0.05
SL.LATENCY	-0.835	<0.05	-0.854	<0.05	-0.91	<0.05
PLMS	-0.557	<0.05	-0.647	<0.05	-0.506	<0.05
AHI	0.043	>0.05	0.167	>0.05	0.221	>0.05

[Table/Fig-2]: Correlation analysis
UPDRS - Unified parkinson's disease rating scale; PDSS - Parkinson disease sleepiness scale;
ESS - Epworth sleepiness scale; TS - Total sleep
PLMS - Periodic limb movement syndrome; AHI - Apnoea hypopnoea index

with the mean duration of 5.3 years. In more than 50% (n=26) of patients the duration of the disease was between five to ten years. Around 40 patients have Hoehn and Yahr staging of 3 or less. Eight patients came under stage 4 and two patients came under stage 5. The severity of the disease (UPDRS motor score) ranges between minimum score of 10 and a maximum score of 40 with the mean value of 25.3 [Table/Fig-1].

The severity when correlated with the disease duration and Hoehn and Yahr staging showed a significant positive correlation (p<0.05). In our study the PDSS score ranges from 80 to 150 with the mean value of 115.90. The subjective sleep assessment using PDSS score correlates positively with the duration of the disease, staging and the severity of the disease (i.e.) with progression of the disease there is a significant drop in the PDSS score. Day time somnolence (Epworth Sleepiness Score) was reported by 15 patients and it was predominantly seen in whom, the duration of the disease is more and the staging and the severity of the disease were in higher range. A score of > 10 is considered abnormal. In our study the ESS score ranges from zero to sixteen with a mean value of 5.86.

Polysomnography Analysis

The total sleep time ranges from 210 (3h 30min) minutes to 445 (7h 25min) minutes with the mean value of 310 (5h10 min). Total sleep time is reduced in 40 patients (80%). There is a strong positive correlation (p<0.05) of the total sleep time with the duration, staging, severity, PDSS Score. Latency of sleep is the time taken to fall asleep after going to the bed. The normal latency of sleep is 15 to 20 min. The range of this parameter in our study is between 2 minutes to 50 minutes with the mean value of 22.3 minutes. Prolongation of latency of sleep indicates defect in the initiation of sleep. Latency is prolonged in 26 patients (>50%). Sleep efficiency is ratio of number of hours slept divided by number of hours spent in the bed. The normal sleep efficiency is > 85% which is seen only in 12 patients. The sleep efficiency ranges between 55% to 94% in our study with a mean value of 72.9%. There is a significant increase in the N1N2 stages of NREM sleep associated with a decrease in the slow wave sleep(N3) in 80% of our study group (p-value <0.05). Ten patients in our study group had 3 Rapid Eye Movement sleep episodes, 37 patients had 2 REM sleep episodes and 3 patients had only 1 REM sleep stage. The overall duration of REM sleep in the total sleep time is reduced and REM sleep onset latency is also prolonged (>2 hours) in 80% (n=40) of our patients. REM sleep behavioural disorder (RBD) was seen in 10 of our patients (20%) and it showed no correlation with duration, staging, severity of the disease and the sleep scores. Periodic Limb Movements in sleep (PLMS) are repetitive stereotyped movements present in NREM sleep was seen in 15 patients. It is scored as PLMS index. It is expressed as number of PLMS per hour of sleep. The upper limit of the normal PLMS index is five. Pearson correlation analysis showed significant positive correlation (p-value <0.005) of PLMS with disease parameters like duration, staging, severity of the disease and sleep scores like PDSS and Epworth sleepiness score. A maximum number of 8 patients in stage 4 had PLMS, 2 patients in stage 5 and 3 patients in stage 3 had PLMS. RLS was seen in 10 patients (20%), 4 of them were female. All the patients in our study were having RLS had PLMS (100%). Sleep latency is prolonged in nine of the ten patients having RLS. Presence of RLS correlates significantly with the duration of the disease and the disease severity and staging. Documented Apnoeic and hypopneic spells were noted in 21 patients in our study. Classification of severity of Sleep Disordered Breathing (SDB) is based on AHI scoring. AHI score<5 is normal; 5- 15 is mild SDB; 15 – 30 is moderate SDB, >30 is severe SDB. The distribution of AHI index ranges between 0 to 20 with the mean value of 3.66. AHI index didn't show a significant correlation with the disease parameters in correlation analysis (p-value >0.05). Snoring is expressed as snore index, which is the number of snore events per hour [Table/Fig-2]. Snoring was seen in 14 patients and it showed significant correlation with the Epwoth sleepiness score and PDSS Score (p-value <0.05).

DISCUSSION

Sleep disorders are common in Parkinson's disease (PD). Nocturnal sleep disturbance and excessive day time somnolence are more frequent in patients with PD than the healthy control [10,11]. The prevalence and the pattern of sleep disturbance are evaluated through this study. The study group consists of 50 patients with age group ranging between 46 to 70 years with varying duration, staging

(based on hoehn & yahr staging) and severity (based on UPDRS Part III motor score). Their sleep related issues were assessed with standard sleep questionnaire and objective assessment was done using polysomnography recording.

Evaluation with sleep questionnaire: Patients with PD were evaluated with Parkinson's disease sleepiness scale and Epworth sleepiness scale. An ESS score of more than 10 is considered significant. Their subjective sleep quality scores and daytime somnolence scores were noted. Reduced sleep quality were noted in 70% of our patients and excessive day time somnolence was reported in 30% of our patients indicating more of nocturnal sleep disturbance which is in contradiction to the study done by Verban et al., stating that excessive day time somnolence (43% Vs 10% controls) was more common than nocturnal sleep disturbance in PD [12].

We correlated the PDSS Score and ESS score with the disease parameters and it correlated positively with the disease duration, higher staging and severity of the disease ($p< 0.05$). Our observation is similar to the results of the study done by Kumar et al., showing excessive day time somnolence in PD patients when compared to the age matched controls and showed a positive correlation with the higher H &Y staging and higher UPDRS score [13]. A similar study done by Cano-de-la-Cuerda et al., showing that PD severity and depression scores correlate significantly with the diminished nocturnal sleep and excessive daytime sleepiness [14]. This implies that neuronal degeneration in the motor areas and sleep centres progress simultaneously, as the sleep disorders parallels with the disease progression [15].

Total sleep time is reduced in 40 patients (80%) in our study. The total sleep time ranges from 210 (3h 30min) minutes to 445 minutes (7h 25 min). The reduction in the total sleep time strongly correlates positively with the disease duration, severity and staging of the disease. The observation is similar to the study done by Diederich NJ et al., in which he concluded that the total sleep time, deep sleep time, REM sleep time and sleep efficiency (SE) were inversely correlated with disease duration and severity [16]. A similar observation of reduction in the total sleep time in Parkinson's Disease was seen in the study done by Dhawan et al., [17]. The latency of sleep is prolonged in 26 patients (52%) with a maximum latency upto 50 minutes and with mean latency duration of 22.36 minutes. The other investigators also observed prolongation of sleep latency in PD patients upto 30.7 minutes (Kaynak et al.,) [18] and 32.6 min (Wetter et al.,) [19]. The latency of sleep in PD is prolonged than the normal healthy elderly individuals who tends to fall asleep within the normal 20 minutes. The normal sleep efficiency is > 85% which is seen only in 12 of our patients. Sleep efficiency is reduced in 38 patients (76%) which is higher than the previous studies which showed reduced sleep efficiency between 69.2+17.0 (Wetter et al.,) [19]. This sleep efficiency in PD patients was much less than the normal healthy individuals [20]. Sleep in polysomnography is divided into 4 stages {stage 1 (N1)/ stage 2 (N2)/ stage 3 &4 (N3) / REM sleep}. The time spent in N1 N2 stages of sleep increased in 40 (80%) of our patients and deep sleep and REM sleep were decreased in 40 (80%) of our patients. These results showed significant impact of the disease process with the sleep stages. Our findings correlate with the study done by Avidan et al., showing that lighter stages of sleep increase and slow wave sleep and REM sleep decreases in PD [21]. RBD which is the loss of tone in REM sleep associated with acting out of dreams is seen in ten patients (20%) and it showed no correlation with the disease parameters whereas Gagnon et al., reported that 33 patients of PD with the mean age group of 68.7 +7.7 years with the mean disease duration of 7.7+5 had RBD 33 % with REM muscle atonia in 58% of the patients [22]. PLMS is a significant non-motor disorder of Parkinson's Disease causing sleep disturbance. It is expressed as PLMS index. It is the number of events in one hour. PLMS score of >5 are considered abnormal. Our study showed PLMS in 18 patients (36%). Other studies showed PLMS of 22.02+3.6 (Covassin, Naima, et al.,) [23] and 55.4 + 3.47 (Wetter et al.,) [19]. PLMS is associated with arousal and contribute to significant nocturnal sleep disturbance. It is significantly higher than normal healthy age matched controls [19]. PLMS significantly correlates with the staging, severity, duration of disease and sleep scores [24]. Ten of our patients had RLS. All the patients in our study having RLS had PLMS (100%). Around 9 patients having RLS were found to have prolonged sleep latency. RLS also correlates significantly with the duration of the disease and the disease severity and staging, and the sleep scores. Ondo and his colleagues in their study showed that 20.8% of the PD patients have RLS which is twice that of the normal control population. Thus the prevalence of RLS in our study is similar to the study reported by Ondo [25].

Sleep Disordered Breathing (SDB) are apnoea/hypopnea and the aetiology may be obstructive, central or mixed. Classification of severity of SDB is based on AHI scoring. AHI>5 is taken into consideration. The most common type of SDB is the obstructive sleep apnoea [26]. In our study, obstructive sleep apnoea was seen in 21 out of 50 (42%) patients with AHI >5. The AHI score didn't correlate with the disease duration, severity, staging and the sleep scores, Whereas a study done by Arnulf et al., showed a positive correlation of AHI score with the advancement of PD [26]. Snoring is expressed as snore index, which is the number of snore events per hour. In the present study, the snoring was observed in 14 patients (28%) who showed a significant correlation with the ESS score and PDSS score. Snoring is mainly due to impaired upper airway dynamics in PD [27,28].

Based on the results of our study it is very clear that as the disease progresses in severity and as the disability due to the disease increases there is a proportionate decrease in the normal sleep pattern in the patients. Sleep is thus directly and strongly correlated with the disease process. Some of the previous studies proposed that sleep and the motor centres are differently affected in PD and the rate of degeneration of one is different from the other and hence they concluded that, sleep parameters doesn't correlate with the motor severity [29,30]. But our study clearly showed that except certain parameters, most of the variables correlate significantly with the disease severity and the disability scores. Hence, both the sleep and motor centres are involved in PD and degeneration of both the centres occur parallel to each other at a varying pace.

LIMITATION

Limitations of the study are there were no control population, day time dysfunction was not analysed objectively and it was only questionnaire based.

CONCLUSION

Sleep disturbance is very common in patients with Idiopathic Parkinson's disease. The total sleep time is significantly decreased in patients with increased severity, staging and duration of the disease. Patients spent less time in slow wave sleep (N3) and there is significant prolongation of N1/N2 stages of sleep. The mean REM sleep duration is also reduced. REM sleep behaviour disorder is seen in 20% of the patients which did not correlate with the disease parameters. The latency of sleep is prolonged causing difficulty in falling asleep. The sleep efficiency is grossly diminished as there is defect in the maintenance of sleep due to frequent awakenings. Periodic limb movements in sleep, restless leg syndrome, and obstructive sleep apnoea also contribute to the sleep fragmentation resulting in defective day time functioning. Thus the Sleep architecture is markedly affected in patients with Parkinson's disease. It is essential that all the patients with Parkinson's disease should be evaluated for sleep disorders so that appropriate intervention can be taken to improve their quality of sleep.

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