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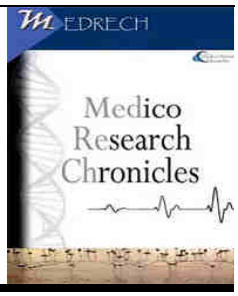

SLEEP DISORDERS IN PEOPLE SUFFERING FROM PARKINSON'S DISEASE

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ABSTRACT

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ORIGINAL RESEARCH ARTICLE

INTRODUCTION:

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disease affecting approximately 1 % of those older than 60 years. (1) In PD degeneration of dopamine neurons, most prominently in the substantial nigra (SN) of the brainstem, is recognized as a characteristic pathologic finding. Deterioration of non-dopaminergic pathways is now recognized as contributing greatly to these disorders, especially the non-motor symptoms such as neuropsychiatric problems, dysautonomia, fatigue, and sleep disorders. (2) Sleep disturbances affect more than two-thirds of patients with Parkinson's disease and include frequent nighttime awakenings with difficulty falling asleep, insomnia, excessive daytime sleepiness (EDS), and REM sleep behavioral disorder (RBD). Sleep disturbances and excessive daytime sleepiness are common in Parkinson's and their frequency relates to the stages of the disease, PD medications, and depression. Almost all PD patients have nighttime symptoms that can interrupt sleep and cause fatigue and daytime sleepiness. Sleep disorders in PD can be caused by a variety of causes, including the disease itself, medication-related factors, and physiological changes of circadian rhythm, sleep architecture changes associated with advancing age, dementia or depression.

Frequent night awakenings can be caused by recurrent tremors at the early stage of sleep, difficulty in turning in bed due to nocturnal akinesia as the effects of daytime administration of dopaminergic drugs wear off at night, and nocturia. In addition, periodic leg movements in sleep (sometimes associated with restless legs), fragmentary nocturnal myoclonus, sleep apnea, REM sleep behavioral disorders (intense dreamlike motor and behavioral problems), and parasomnias (nocturnal hallucinations and nocturnal wandering with disruptive behavior) may all

disrupt sleep in PD. Nocturnal tremor and akinesia due to the PD and nocturia in the elderly can cause arousals. Sleep disorders in PD are related to neurodegeneration of pathways involved in sleep regulation, or treatment side effects. Recent evidence suggests that deterioration of non-dopaminergic pathways may, in fact, occur earlier in the course of PD than deterioration of dopaminergic systems, and that associated sleep disorders may predate the appearance of classic PD motor symptoms. (6, 7) Dopamine is known to have a complex role in sleep and arousal. Dopaminergic neurons in the ventral tegmental area are part of the basal ganglia-thalamo-cortical limbic circuitry, and project to the prefrontal cortex and striatum, thus possibly regulating arousal. (8). More recent evidence points to dopaminergic cells in the ventral periaqueductal gray matter having extensive connections with the sleep-wake regulatory systems. (9) Degeneration of non-dopaminergic pathways in various areas of the brainstem and basal ganglia have been recognized as integral to PD. These areas include the cholinergic nucleus basalis of Meynert and pedunculopontine nucleus (PPN), noradrenergic neurons in the locus ceruleus, serotoninergic neurons in the raphe, and orexinergic neurons in the hypothalamus. (22) Many of these pathways have been closely linked to arousal and sleep functions. Significant overlap and interaction exist between the neuroanatomic substrates of motor and non-motor symptoms. Pathways from key dopaminergic areas of the brain (substantia nigra pars compacta, ventral tegmental area) project extensively and thus contribute to a variety of non-motor functions such as cognition, arousal, and pain. (9, 10).

Motor symptoms at night can manifest as slowed movements, difficulties turning in bed, nocturnal and early morning dystonia, pain, tremors, cramps, all of which lead to frequent night wakes, most commonly in the lighter stages of sleep. The tremor of PD typically disappears with the progression of sleep but may reappear with arousals, movements, and sleep stage changes including the onset/offset of REM and during phasic bursts of REM. When tremor is present, the amplitude is reduced. Tremor is typically absent during delta and tonic REM sleep, but can nonetheless cause considerable sleep disruption. (11) Daytime sleepiness may in part be a specific feature of PD itself rather than simply a function of impaired nocturnal sleep. (13) Nocturia is often cited as the most common non-motor cause of sleep disturbance in PD. (4) Although PD-related dysautonomia is likely a factor, the contribution of the diuretic and arousing effects of sleep-disordered breathing must also be recognized and dealt with accordingly. (14)**.** Parasomnias are undesirable behaviors occurring during sleep, such as vivid dreams, nightmares, hallucinations, and RBD. They are frequently seen in PD patients and may be idiopathic or occur secondary to the disease process itself or its treatment. Most prominent among these in our discussion is RBD. RLS is generally of mild severity in PD patients but can contribute especially to sleep initiation difficulties. (15) **.**PD patients have a higher prevalence of sleep-disordered breathing than age-matched that not suffered from Parkinson's disease. A number of studies have documented respiratory disorders when the patient is completely awake in PD. These problems include respiratory in coordination, pathological upper respiratory tract nose, and abnormal movement of structures over glottis and abnormal respiratory cycle. Studies that have tested patients with Parkinson's during sleep have reported obstructive and central apnea and hypoventilation episodes. Most often these occur in patients at advanced stages of the disease and cause nighttime wakefulness and daytime sleepiness.

AIM:

To assess the frequency and nature of sleep disturbances in persons with Parkinson Disease (PD)

METHODOLOGY:

We evaluated 153 patients suffering from PD, which were hospitalized in the Neurology Department, at UHC 'Mother Teresa' and compared them to a sample of 116 age-matched healthy controls.

We performed a clinical evaluation of PD patients, including the Unified Parkinson Disease Rating Scale- UPDRS score, Hoehn & Yahr score, and Levodopa daily dose. Both groups were evaluated using a questionnaire consisting of 23 questions, identifying patterns of sleep disturbance, the frequency and quality of the disorder. The questionnaire was designed based on the International Classification of Sleep Disorders (ICSD) by consulting with the neurologist and psychiatrist. Both patients and family members were present in the evaluation and we studied sleep disorders like insomnia, nightmares and excessive daytime sleepiness that were present in the last year.

The questionnaire test was created with the purpose of studying the longevity and quality of sleep during the night, nightmares, co-morbidities, polypharmacy, quality of life, daytime sleepiness and functional independence.

The data gathered in the PD patients were studied, correlating the sleep disorder quality and scale with the stage of the disease. (Hoehn & Yahr score, UPDRS score, and Levodopa daily dose). The healthy control group data was studied, considering the patient's co-morbidities and lifestyle.

RESULTS:

153 patients with Parkinson's disease and 153 people at the healthy control group were evaluated. A database was created and we studied the results of both groups with a head to head comparison about sleep disorders.

The average age of PD patients was 58,37 years (SD 10,45) and with average disease duration of 5,7 years since the initial diagnosis (SD 3,85). The mean age of control group was 56,50 years(SD 11,45); (p>0,05).

Sleep problems were detected in 66 (42%) PD patients as compared to 12% of the control group.

According to the data gathered, we have these conclusions:

- Insomnia is present in 32% of PD patients as compared to 5% of the control group.
- Nightmares were detected in 32% of PD patients compared with 5% of the control group.
- Excessive day time sleepiness was seen in 15% of PD patients as compared with 6% of the control group (p<0,025).

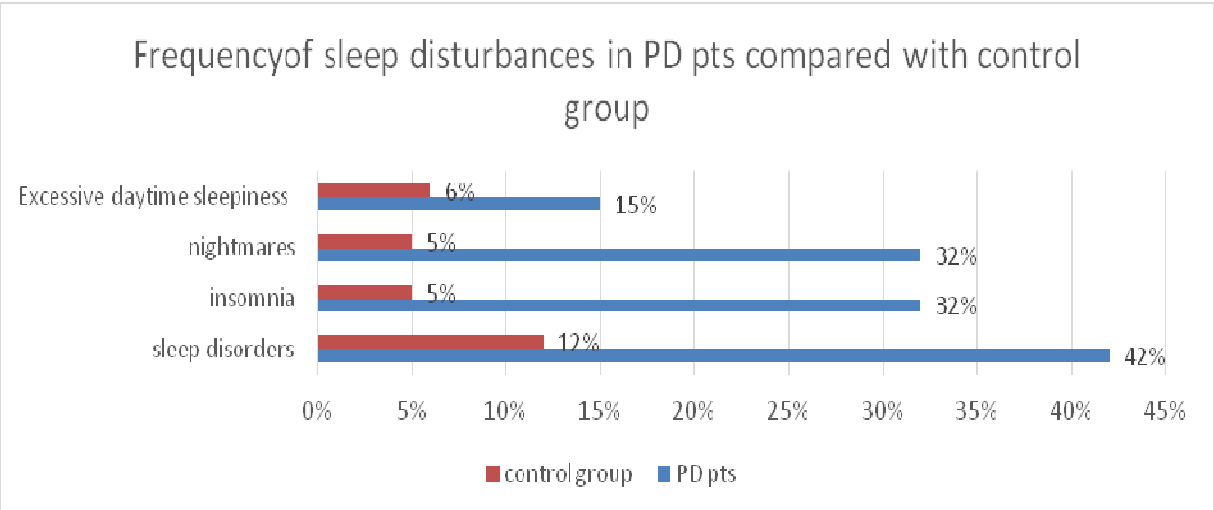

Fig 1: Frequency of sleep disturbance

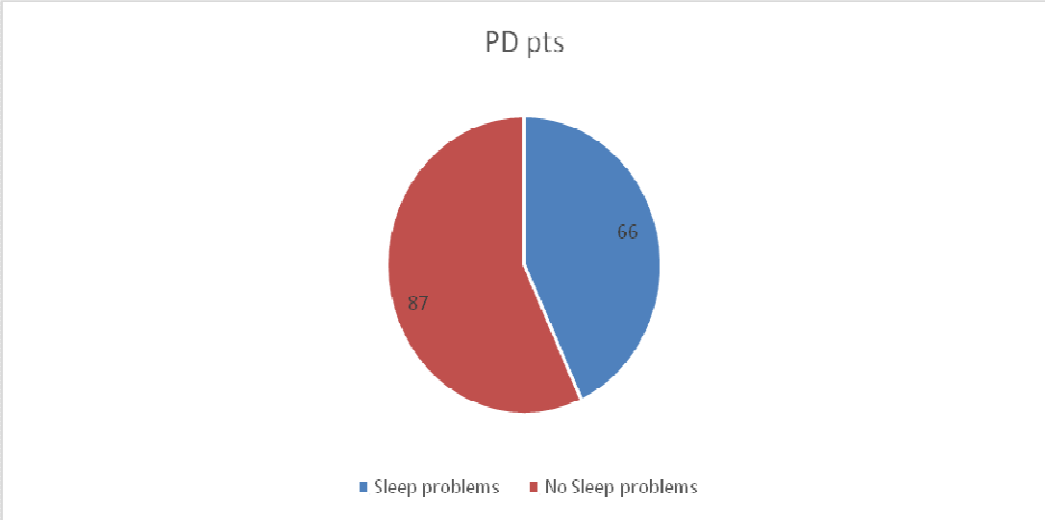

Fig 2: Sleep problems

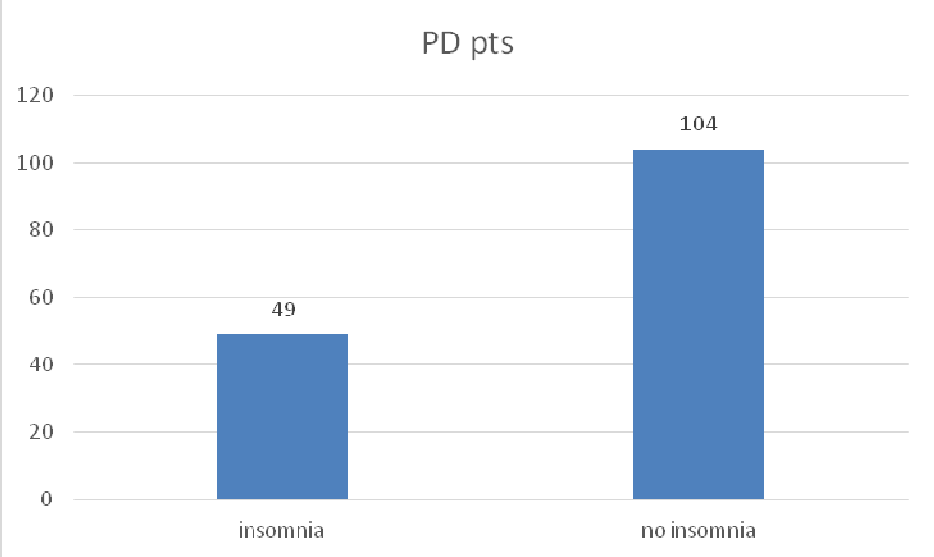

Fig 3: PD Points

Presence of nightmares was significantly associated with:
- Higher Hoehn and Yahr score(p<0,002),
-high UPDRS score(p<0,000) and
-Levodopa dose(p<0,0025).

DISCUSSION

Excessive daytime sleepiness correlated with higher Hoehn and Yahr stage (p<0,004), and Levodopa dose (p<0,04), but was met with a lower frequency than the above-mentioned sleep disorders in PD patients, but not in the control group. The state of excessive sleep during the day was longer in PD patients as compared to the control group (p<0,000).

According to our data, insomnia and nightmares were met with the same frequency in the PD patients, but also in the healthy control group.

CONCLUSION:

Multiple logistic regression analysis showed an association of sleep disturbances with UPDRS Part III, Levodopa dose, Hoehn and Yahr Score.

Sleep problems are much more common in PD patients compared to the control group (P<0,001), and correlate with increased severity of the disease.

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