

Parkinson Disease: Sleep Disorders

Description/Etiology

Parkinson disease (PD) is a progressive neurodegenerative disorder of the central nervous system related to a deficiency of the neurotransmitter dopamine, which causes a chemical imbalance that affects voluntary movement. This chronic, debilitating condition is insidious in onset, usually begins unilaterally with mild symptoms, and eventually manifests bilaterally with increasingly severe symptoms. PD is characterized by a variable combination of rigidity, postural instability, bradykinesia, and tremor. Advancing disease erodes all functional abilities, causing autonomic dysfunction, musculoskeletal deformities, sensory symptoms, sleep disturbances, dermatologic problems, and psychiatric symptoms. Early diagnosis is challenging because clinical symptoms typically do not appear until dopamine levels and pigmented neurons are reduced by 80% and 60%, respectively (for more information on PD, see *Quick Lesson About ... Parkinson Disease*).

Impaired sleep is a common nonmotor complication of PD that has a major impact on patient and caregiver quality of life (QOL). Sleep impairment can manifest at any stage of PD and typically becomes more severe as the disease progresses. Nocturnal sleep disorders include sleep fragmentation, early awakening, difficulty falling asleep (i.e., sleep initiation), altered dreaming (with vocalization, terrors, and nightmares), restless legs syndrome (RLS), nocturia, sleep-disordered breathing (SDB), and rapid eye movement sleep behavior disorder (RBD), which is characterized by symptoms that range from increased muscle tone to physical activity and shouting. RBD might occur in the prodromal stage of PD or in the course of PD. Daytime sleep disorders include excessive daytime sleepiness (EDS) and sudden onset of sleep (i.e., sleep attack). The etiology of PD-related sleep disorders is thought to be multifactorial and include deterioration of the part of the brain that controls the sleep-wake cycle, medication side effects, and drug-induced sleep disturbance. Risk factors for EDS include male sex, poor nighttime sleep quality, and use of antihypertensive medications. Iron-deficiency anemia is associated with RLS. SDB is associated with more rapid progression of neurodegeneration in patients with PD. The presentation of SDB in PD is atypical, as SDB is most often related to obesity, and obesity is not present in most patients with PD.

Treatment of sleep disorders in PD is aimed at targeting the major sleep complaint and its underlying mechanism. Although there is no way to prevent the progression of PD, pharmacotherapy can control symptoms, preserve patient independence, and slow progression. Treating sleep disorders in PD has been shown to improve sleep, depressive symptoms, and motor dysfunction and to lessen fatigue. Treatment strategies involve pharmacologic agents such as dopamine agonists and education about lifestyle modification.

Facts and Figures

An estimated 35–60% of patients with PD have RBD. EDS affects ~ 50% of patients with PD and SDB is present in 20–60% of persons with PD.

Risk Factors

Common dopaminergic medication side effects, such as sleepiness, hallucinations, confusion, and psychosis, can compound existing sleep problems. Risk factors for sleep disorders in patients with PD include constipation, obesity, adenotonsillar hypertrophy, nasal obstruction, severe foot dystonia (i.e., muscle contraction), tremors and rigidity, leg and

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arm contortions, leg cramps, sleep-onset blepharospasm (i.e., eye muscle twitching), pain, sleep-related respiratory dysrhythmias, and comorbid conditions, including Alzheimer's disease.

Signs and Symptoms/Clinical Presentation

Symptoms of sleep disorders in patients with PD are general fatigue, drowsiness, not feeling refreshed after sleep, and falling asleep during periods of inactivity. A sleep attack presents as a spontaneous episode of dozing.

Assessment

› Patient History

- Assess risk factors, including medications taken, and ask about PD onset
- Assess sleep patterns and presence of movements or behaviors at night

› Physical Findings of Particular Interest

- Other conditions that contribute to the development of sleep disorders can be present; these include pain, paroxysmal nocturnal dyspnea, gastroesophageal reflux disease (GERD), constipation, and nocturia secondary to prostatism

› Diagnostic Tests/Studies

- Diagnosis is made by sleep history, which can include a subjective sleep assessment and/or objective assessment using tools such as the Epworth Sleepiness Scale (ESS), the Parkinson's Disease Sleep Scale (PDSS), the Pittsburgh Sleep Quality Index (PSQI), and the Scale for Outcomes in PD Sleep Scale (SCOPA-S). The Multiple Sleep Latency Test and polysomnography can be ordered to diagnose sleep disorders
- The patient's bed partner can be asked to complete a sleep questionnaire to further identify sleep problems

Treatment Goals

› Promote Optimum Sleep, Physiologic Function, and Emotional Well-Being

- Assess vital signs, all physiologic systems (especially neurologic), level of patient disability, and **fall risk**; follow facility protocols for fall prevention and educate the patient and family on PD pathophysiology and treatment option risks and benefits (for details of PD treatment unrelated to sleep disorders, see *Quick Lesson* referenced above)
- Review diagnostic study results on sleep evaluation, and ask patient/caregiver about problems with sleep
- Assess patient/caregiver anxiety level and coping ability; evaluate for knowledge deficits and educate on general sleep hygiene measures that can be tried before or in addition to the use of pharmacologic options
 - Regular daytime activities, exposure to direct sunlight in the morning, and implementation of a schedule for bedtime and awakening can regulate circadian rhythm disruption
 - Hospitalized patients should follow their normal bedtime routine as much as possible and be provided a quiet and restful environment for sleep
 - Bed rails and physical therapy can improve nighttime mobility
- Assess for nocturnal bladder symptoms as a cause of sleep disorders; if appropriate, reduce fluid intake in the evening, place a commode or urinal at the bedside, and/or request referral to a urologist for evaluation and treatment
- Assess safety of the sleep environment
- Discuss optimization of the dopaminergic medication regimen to improve nighttime mobility, decrease RLS, and prevent EDS; changes in the medication regimen can include giving small bedtime doses, using long-acting or timed-release agents, and giving selegiline, a non-drowsy dopaminergic agent that is taken in the morning
 - Clinician can titrate and reduce the dopaminergic regimen to treat sleep disorders involving hallucinations; downward titration can worsen PD symptoms, and patient input is essential to determine if QOL improves
- Administer other prescribed pharmacologic agents prescribed for sleep disorders, including modafinil for EDS, a mild sedative for insomnia, clonazepam for RBD, iron supplements for iron-deficiency anemia associated with RLS, clonazepam or quetiapine for hallucinations, melatonin for improving sleep circadian rhythm and cognitive function, and/or antidepressants for depression
 - There is no completely effective treatment for EDS or sleep attacks

Food for Thought

- › Authors of a recent literature review discovered a high prevalence of restless legs syndrome in patients with PD, which might be related to iron and dopaminergic alterations observed in both disorders. The authors suggested two theories about the relationship between the disorders: in the first restless legs syndrome might be an early manifestation of PD. Alternatively, dopaminergic therapy used to treat PD might be an important factor in the development of restless legs

syndrome. Given that early diagnosis of PD can be difficult because its clinical symptoms do not appear until the later progression of the disease, understanding the relationship between restless legs syndrome and PD might be useful for earlier detection (Ferini-Strambi et al., 2018)

- › Authors of a recent systematic review of eight studies about the efficacy of non-pharmacologic interventions for patients with PD experiencing sleep disturbances found three main types of therapies being used, which included complementary (e.g., Chinese herbal medicine, touch therapy, caffeine), cognitive behavioral, and physical exercise interventions. Only half of the studies reported success with the interventions; researchers concluded that the severity of motor symptoms in patients with PD and their gradual functional decline might impact the efficacy of the available interventions (Lee et al., 2018)
- › Researchers explored the relationship between sleep disturbances and pain in patients with PD and found that in 144 patients, 52.1% reported pain, 65.3% identified pain severity as moderate or higher; musculoskeletal pain was the most common type identified. Most patients who experienced pain had longer disease progression and were older. Researchers identified lower sleep efficiency, depressed mood, increased nonrapid eye movement stage one, and poorer activities of daily life as independent predictors of pain in these patients (Fu et al., 2018)
- › Researchers analyzed the prevalence of PD in patients with rapid eye movement (REM) behavior disorder (pRBD) and compared the clinical characteristics they identified in patients with pRBD, using the first Mayo Sleep Questionnaire (MSQ), with those of patients with PD without RBD. Nearly half (48.5%) of 140 participants had pRBD. Patients with pRBD were found to have a significantly higher daily levodopa equivalent dose and higher prevalence of symptomatic hypotension. Researchers concluded that the MSQ can be a cost-effective tool to screen for RBD (Gomutbutra et al., 2018)
- › Researchers analyzed the efficacy of the prodromal criteria for determining PD in 121 patients with REM behavior disorder and found that 39.7% of the participants with the disorder had progression to dementia with Lewy bodies and PD, which increased to 67.9% after a 4-year follow up. Researchers found that patients who met the criteria had significantly faster neurodegeneration compared to patients who did not, which suggests the prodromal criteria is a promising and effective tool for predicting PD in patients with REM behavior disorder (Fereshtehnejad et al., 2017)

Red Flags

- › Patients with PD taking dopaminergic medications should use caution when driving or operating machinery, especially if they have a history of EDS, sudden onset of sleep, or sleep-related breathing disorders
- › Amphetamines should not be prescribed for EDS because of severe side effects and the potential for abuse
- › Sedatives and evening doses of dopaminergic medications can have unpleasant side effects, including hallucinations, involuntary movements, vivid dreams, confusion, increased risk for falls, sleep apnea, and increased EDS
- › Medications for PD must be continuously monitored for efficacy and have significant risk for toxicity and adverse effects—patient and caregiver knowledge of indications and side effects for each drug, close patient observation, and timely communication with the clinician are essential

What Do I Need to Tell the Patient/Patient's Family?

- › Encourage patients to maintain physical and mental health and to maintain independence with ADLs as much as possible while utilizing a schedule for bedtime and awakening
- › Encourage joining a local support group, which can provide social interaction, family care services, and disease education
- › Educate to never take over-the-counter sleep aids without consulting the treating clinician

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