Parkinson's Disease: Update on Medication Management

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ABSTRACT

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder. Its estimated prevalence is 1 million individuals in the United States, with approximately 60,000 people newly diagnosed in the US every year. The incidence and diagnosis of PD will increase in the next decades as our population ages. Nurse practitioners will need to be familiar with the presentation and progression and pharmacologic treatment of PD. This disease has a broad range of motor and nonmotor manifestations. The present article reviews medication treatment for both motor and nonmotor symptoms of PD.

Keywords: carbidopa, dopamine agonists, dyskinesia, levadopa, Parkinson's disease

INTRODUCTION

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder caused by the death of neurons in the midbrain.[1] There are 2 major neuropathologic findings in PD; the first is the loss of pigmented dopaminergic neurons of the substantia nigra pars compacta (Figure) and the second is the presence of Lewy bodies. Although Lewy bodies can occur in other neurologic disease states, they are a characteristic finding in PD. Between 60% and 80% of dopaminergic neurons can be lost before the cardinal motor symptoms of PD become evident.[2]

The estimated prevalence of PD is 1 million individuals in the United States and 5 million worldwide.[3] Approximately 60,000 people are newly diagnosed in the US each year.[4] Aging is a major risk factor for the development of PD, but disease onset may start earlier—10% of people with PD are < 45 years of age.[5] The incidence and diagnosis of PD will increase in the next decades as the population ages. Primary care providers, including nurse practitioners (NPs), will need to be familiar with PD presentation, its progression, and the pharmacologic treatment of this disease.

Medication management is usually initiated when the motor effects of PD have a detrimental effect on daily functioning, such as when gait disturbances, tremors, or bradykinesia interfere with activities of daily living (ADLs). NPs should complete a comprehensive evaluation of impairments in ADLs for all PD patients, including the ability to continue employment or social activities. NPs are instrumental in picking up early symptoms of PD, can be effective in screening for PD, and can monitor for motor and nonmotor side effects of PD therapy and disease progression, and thus can greatly influence the quality of life of the PD patient and caregivers.[6]

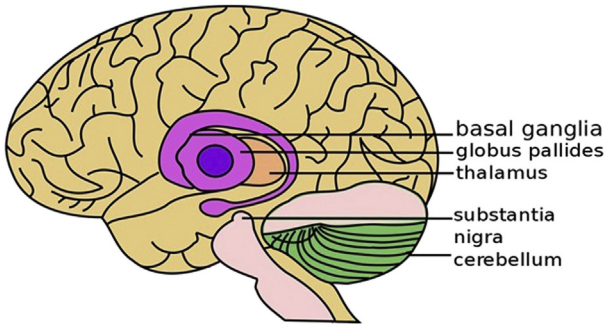
Pharmacologic therapy for PD has advanced in recent decades for symptomatic relief of both motor and nonmotor symptoms, but there is no medication therapy that will stop the progression of the disease. Disease modification trials have focused on slowing the progression of motor features such as bradykinesia, rigidity, and tremor, as assessed by the Unified Parkinson's Disease Rating Scale,[7] and the ongoing need for symptomatic dopaminergic therapy to improve these symptoms and functional quality of life.

Progressive cell destruction in extranigral sites leads to motor symptoms such as postural instability, freezing, and falls, or nonmotor symptoms, which are poorly responsive to levodopa. In addition, drug-induced motor complications contribute to significant disability for PD patients.[8]

DIAGNOSIS

There is currently no test or lab work that can diagnose PD, although research is exploring genetic

Figure. The basal ganglia in the midbrain



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markers. Another test being explored is the dopamine transporter scan, which uses a chemical injected intravenously to label the dopamine transporter in the brain and visualized with a single-photon emission computerized tomography scan. Currently, the test is in the exploratory stages, and has not been able to differentiate between Parkinson's disease and other atypical parkinsonian syndromes, such as progressive supranuclear palsy.[9]

PD is a clinical diagnosis with bradykinesia as one of the hallmark symptoms along with resting tremors (often described as "pill rolling"), gait disturbance, and rigidity. PD is also characterized by rigid and unexpressive facies and slow, low-volume speech. A diagnosis of PD will usually include 2 of the aforementioned major signs to formulate a diagnosis of PD.[5]

The Unified Parkinson Disease Rating Scale is a tool used to follow the longitudinal course of PD[7] and can be used to monitor the effectiveness of medication therapy on reduction of PD symptoms and the patient's quality of life. It is divided into 3 major sections: (1) mentation, behavior, and mood; (2) ADLs; and (3) motor function. These areas are evaluated by the provider by interviewing the patient. A maximum score of 199 indicates worst disability and 0 indicates no disability.[10]

PHARMACOLOGIC THERAPIES FOR PD

Pharmacologic therapies are meant to reduce symptomatology and improve quality of life. Currently, although there are no therapies that slow down or cure PD, pharmacologic therapies do allow for a longer and more productive life in PD patients.

Medication therapy should consist of an individualized plan and must consider symptom presentation, other concurrent health issues (and medications), and the patient's age. Starting doses (as indicated by the package insert) can vary greatly depending on a person's needs, metabolism, and tolerance to the side effects.[11] Every patient with PD needs to be treated individually as no 2 patients will be alike.

The following is a list of classes of medications used to treat PD:

1. Carbidopa/levodopa therapy.
2. Dopamine agonists.
3. Anticholinergics.
4. Monoamine oxidase inhibitor B (MAO-B) agents.
5. Catechol-*O*-methyltransferase (COMPT) inhibitors.
6. Other medications.

Levodopa Therapy

PD is caused by the loss of dopaminergic input to the basal ganglia; levodopa is the most effective drug for treatment of the motor symptoms of PD. It works by being converted to dopamine in the brain.[12] Levodopa taken alone causes nausea and vomiting, and therefore it is given in combination with carbidopa (Sinemet; Merck, Kenilworth, NJ). Carbidopa (a peripheral decarboxylase inhibitor) blocks conversion of levodopa to dopamine in the peripheral circulation and liver and is not effective alone, but, when combined with levodopa, reduces the side effects of nausea and vomiting and increases absorption of levodopa in the brain. Another side effect of levodopa therapy that needs to be monitored is orthostatic hypotension. All levodopa medications should be started at a low dose and increased slowly to reduce side effects, especially in the elderly. Patients generally have a good response to levodopa therapy, but, as PD progresses, response to the drug shortens, and the effectiveness wears off before the next dose. The patient's motor symptoms range between being "on" (a good levodopa response, which includes reduction in stiffness and tremors, and improved balance, muscle control, and walking) and medication "off" times (levodopa effect wears