chapter

15

Drugs Used for Parkinson's Disease

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Objectives

1. Identify the signs and symptoms of Parkinson's disease.
2. Define the vocabulary used for the pharmacologic agents that are prescribed to treat Parkinson's disease.
3. Identify the neurotransmitter that is found in excess and the neurotransmitter that is deficient in people with parkinsonism.
4. Describe the reasonable expectations of the medications that are prescribed for the treatment of Parkinson's disease.
5. Identify the period that is necessary for a therapeutic response to be observable when drugs that are used to treat parkinsonism are initiated.
6. Cite the action of carbidopa, levodopa, and apomorphine on the neurotransmitters involved in Parkinson's disease.
7. Explain the action of entacapone and of the monoamine oxidase inhibitors (selegiline and rasagiline) as it relates to the treatment of Parkinson's disease.
8. Describe the symptoms that can be attributed to the cholinergic activity of pharmacologic agents.
9. Cite the specific symptoms that should show improvement when anticholinergic agents are administered to the patient with Parkinson's disease.

Key Terms

Parkinson's disease (PĂR-kĭn-sĕnz dĭ-ZĒZ) (p. 224)
dopamine (DŌ-pă-mēn) (p. 224)
neurotransmitter (nyū-rō-TRĂNZ-mĭ-tĕr) (p. 224)
acetylcholine (ăs-ē-tĭl-KŌ-lēn) (p. 224)
anticholinergic agents (ĂN-tē-kō-lĭn-ŬR-jĭk) (p. 226)
tremors (TRĒ-mŭrz) (p. 227)
dyskinesia (dĭs-kĭ-NĒ-zhă) (p. 227)
propulsive, uncontrolled movement (prō-PŬL-sĭv ŭn-kŏn-TRŌLD MŬV-mĕnt) (p. 228)
akinesia (ă-kĭ-NĒ-zhă) (p. 228)

PARKINSON'S DISEASE

Parkinson's disease is a chronic progressive disorder of the central nervous system. It is the second most common neurodegenerative disease after Alzheimer's disease. An estimated 1% of the U.S. population that is more than 50 years old, 2% of the population that is more than 60 years old, and 4% to 5% of the population 85 years old or older have this disorder. Thirty percent of patients report an onset of symptoms before the age of 50 years; 40% report that the onset occurred between the ages of 50 and 60 years; and the remainder reports that their symptoms began after the age of 60 years. The incidence is slightly higher in men than women, and all races and ethnic groups are affected. Characteristic motor symptoms include muscle tremors, slowness of movement when performing daily activities (i.e., bradykinesia), muscle weakness with rigidity, and alterations in posture and equilibrium. The symptoms associated with parkinsonism are caused by a deterioration of the dopaminergic neurons in the substantia nigra pars compacta, which results in a depletion of dopamine along the nigrostriatal pathway that extends into neurons in the autonomic ganglia, the basal ganglia, and the spinal cord and causes progressive neurologic deficits. These areas of the brain are responsible for maintaining posture and muscle tone, as well as for regulating voluntary smooth muscle activity and other nonmotor activities. Normally, a balance exists between *dopamine,* which is an inhibitory *neurotransmitter,* and *acetylcholine,* which is an excitatory neurotransmitter. With a deficiency of dopamine, a relative increase in acetylcholine activity occurs and causes the symptoms of parkinsonism. About 80% of the dopamine in the neurons of the substantia nigra pars compacta of the brain must be depleted for symptoms to develop. Orthostatic hypotension, nocturnal sleep disturbances with daytime somnolence, depression, and progressing dementia are often nonmotor symptoms that are associated with Parkinson's disease.

There are two types of parkinsonism. Primary or idiopathic parkinsonism is caused by a reduction in dopamine-producing cells in the substantia nigra pars compacta. The causes are not yet known, but there appear to be both genetic and environmental factors associated with its development. Approximately 10% to 15% of cases appear to be inherited. Secondary parkinsonism is caused by head trauma, intracranial infections, tumors, and drug exposure. Medicines that deplete dopamine and thus cause secondary parkinsonism include dopamine antagonists such as haloperidol, phenothiazines, reserpine, methyldopa, and metoclopramide. In most cases of drug-induced parkinsonism, recovery is complete if the drug is discontinued.

Get Ready for the NCLEX® Examination!

Key Points

- There are many types of sleep disorders, but the most common is insomnia.
- Most cases of insomnia are short-lived and can be effectively treated by nonpharmacologic methods, such as a back rub, eating a lighter meal in the evening, eliminating naps, and reducing the use of alcohol and stimulants such as caffeine and nicotine.
- People who have insomnia that lasts for more than 1 month and who also suffer from daytime impairment of their social and employment responsibilities should be referred to a physician for a complete history and physical assessment. There may be other underlying conditions that must be treated before the patient resorts to the use of sedative-hypnotic agents.
- A variety of sedative-hypnotic drugs are available for pharmacologic treatment; however, the drugs of choice are the newer nonbenzodiazepines (e.g., zaleplon, zolpidem, eszopiclone) because of their wide margin of safety.

Additional Learning Resources

SG Go to your Study Guide for additional Review Questions for the NCLEX® Examination, Critical Thinking Clinical Situations, and other learning activities to help you master this chapter's content.

Evolve Go to your Evolve Web site (http://evolve.elsevier.com/Clayton) for the following FREE learning resources:

- Animations
- Appendices
- Drug dosage calculators
- Drugs@FDA (a catalog of FDA-approved drug products)
- Gold Standard Patient Teaching Handouts in English and Spanish
- Interactive Drug Flashcards
- Interactive Review Questions for the NCLEX® Examination and more!

Review Questions for the NCLEX® Examination

1. The nurse is making rounds on the unit during the night shift and notes that one of the older patients is awake. The nurse reviews the patient's bedtime medication and sees that 5 mg of zolpidem was administered at 2100. For what condition does the nurse evaluate the patient? *(Select all that apply.)*
   1. Impaired coordination
   2. Pain
   3. Hangover
   4. Confusion
   5. Excessive use
2. What does the nurse expect that a patient who is receiving a benzodiazepine who also ingests alcohol may experience?
   1. Erratic sleep and a need for less of the prescribed medication
   2. Additive effects of the alcohol and the sedative-hypnotic agent
   3. Antagonist effects of the alcohol and the sedative-hypnotic agent
   4. Need for a higher dose of the benzodiazepine and frequent assessments
3. A patient has been receiving benzodiazepines for several years. What condition may this cause?
   1. Nephrotoxicity
   2. Withdrawal symptoms if the drug is discontinued rapidly
   3. A rush of morning energy with repeated usage
   4. Seizures during the time that the drug is being administered
4. What is a benefit of using zaleplon and zolpidem?
   1. There is no rebound in insomnia.
   2. They have long half-lives.
   3. They do not diminish stage 3 or 4 or REM sleep as much as benzodiazepines do.
   4. They can be used for only 2 weeks.
5. The term *rebound sleep* refers to:
   1. the disturbance of REM sleep that causes restlessness and nightmares.
   2. difficulty staying asleep after initially falling asleep.
   3. the inability to sleep after discontinuing a sedative medication.
   4. transient restlessness and anxiety.

Life Span Considerations

Parkinson's Disease

Parkinson's disease, which is most often seen in geriatric patients, causes a relative excess of acetylcholine as a result of a deficiency of dopamine. Drug therapy with dopaminergic agents increases dopamine availability, whereas anticholinergic medicines may be taken to counterbalance the availability of acetylcholine. Approximately 40% of patients with parkinsonism have some degree of clinical depression as a result of the reduced availability of the active metabolites of dopamine in the brain.

All drugs that are prescribed for the treatment of Parkinson's disease produce a pharmacologic effect on the central nervous system. An assessment of the patient's mental status and physical functioning before the initiation of therapy is essential to serve as a baseline so that comparisons can be made with subsequent evaluations.

Parkinson's disease is, at present, both progressive and incurable. The goals of treatment are to moderate the symptoms and to slow the progression of the disease. It is important to encourage the patient to take the medications as scheduled and to stay as active and involved in daily activities as possible.

Orthostatic hypotension is common with most of the medicines that are used to treat Parkinson's disease. To provide for patient safety, teach the patient to rise slowly from a supine or sitting position, and encourage the patient to sit or lie down if he or she is feeling faint.

Constipation is a frequent problem among patients with Parkinson's disease. Instruct the patient to drink six to eight 8-ounce glasses of liquid daily and to increase bulk in the diet to prevent constipation. Bulk-forming laxatives may also need to be added to the daily regimen.

The motor symptoms of parkinsonism start insidiously and are almost imperceptible at first, with weakness and tremors gradually progressing to involve movement disorders throughout the body (Figure 15-1). The symptoms usually begin on one side of the body (i.e., asymmetrical onset and progression) as a tremor of a finger or hand, and they then progress to become bilateral. The upper part of the body is usually affected first. Eventually, the individual has postural and gait alterations that result in the need for assistance with total care needs. Varying degrees of depression are the most common (i.e., 40% to 50%) nonmotor symptom associated with Parkinson's disease. Most patients with depression also develop feelings of anxiety, and this sometimes includes panic attacks. Those who develop anxiety before depression are very susceptible to depressive episodes after the anxiety. Apathy or depressed emotions with a lack of willpower or the inability to make decisions often accompany depression. Chronic fatigue, which is another common symptom, may also contribute to depression. Dementia, which resembles Alzheimer's disease, occurs in a significant number of patients, but there is continuing debate as to whether it is part of the Parkinson's disease process or if it is caused by concurrent drug therapy, Alzheimer's disease, or other factors. Dementia is characterized by the slowing of the thought processes, lapses in memory, and a loss of impulse control. The diagnosis of Parkinson's disease is based on a careful history taking, a physical examination, and a positive response to dopaminergic treatment. There are no laboratory tests or imaging studies that can confirm the diagnosis.

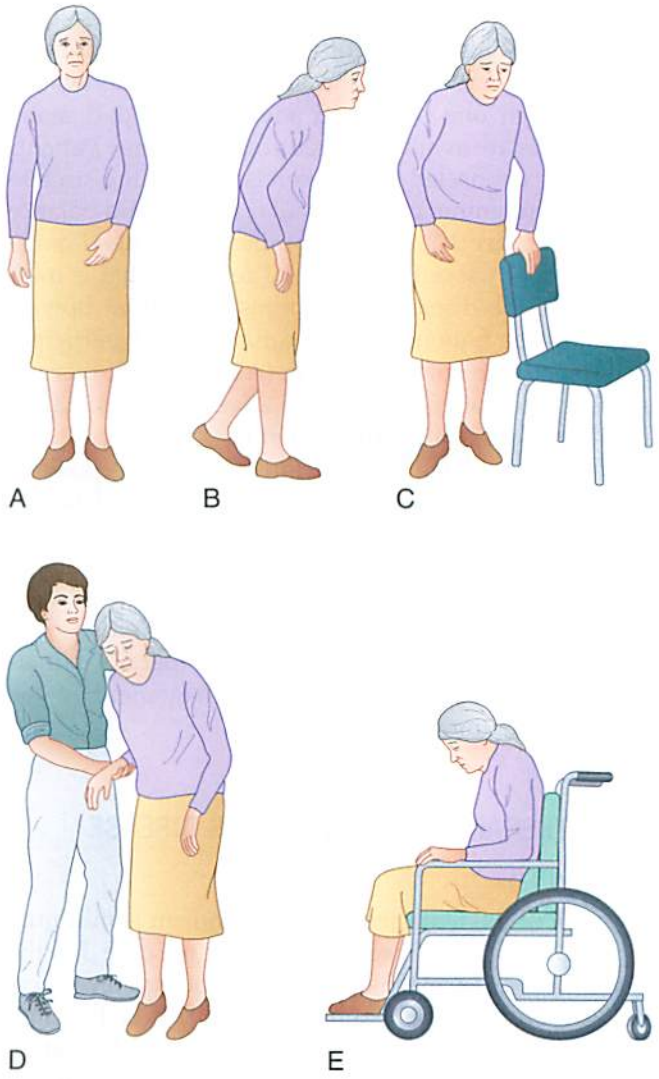

FIGURE 15-1 Stages of parkinsonism. **A,** Flexion of the affected arm. The patient leans toward the unaffected side. **B,** Slow, shuffling gait. **C,** The patient has increased difficulty walking and looks for sources of support to prevent falls. **D,** Further progression of weakness. The patient requires assistance from another person for ambulation. **E,** Profound disability. The patient may be confined to a wheelchair as a result of increasing weakness.

The patient and the family should understand that Parkinson's disease often has a course that takes place over decades; that the rate of progression varies greatly from one person to another; and that many approaches are available to reduce symptoms. Patients should be counseled about exercise, including stretching, strengthening, cardiovascular fitness, and balance training. Patients and their families often need assistance to learn about the medical regimen that is used to control the disease's symptoms and about how to maintain the patient at an optimal level of participation in activities of daily living (ADLs). Drug therapy presents the potential for many adverse effects that all involved parties must understand.

Nurses can have a major influence in the positive use of coping mechanisms as the patient and family express varying degrees of anxiety, frustration, hostility, conflict, and fear. The primary goal of nursing intervention should be to keep the patient socially interactive and participating in daily activities. This can be accomplished through physical therapy, adherence to the drug regimen, and management of the course of treatment.

DRUG THERAPY FOR PARKINSON'S DISEASE

ACTIONS

The goal of the treatment of parkinsonism is minimizing the symptoms, because there is no cure for the disease. Nonpharmacologic therapy focuses on education, support services, exercise, and nutrition. Pharmacologic goals are to relieve symptoms and to restore dopaminergic activity and neurotransmitter function to as close to normal as possible. Treatment is usually started when symptoms progress to interfere with the patient's ability to perform at work or to function in social situations. Drug therapy includes the use of the following: rasagiline or selegiline, possibly to slow the deterioration of dopaminergic nerve cells; carbidopa-levodopa, ropinirole, pramipexole, amantadine, or entacapone in various combinations to enhance dopaminergic activity; and anticholinergic agents to inhibit the relative excess of cholinergic activity (e.g., tremor). Therapy must be individualized, and realistic goals must be set for each patient. It is not possible to eliminate all symptoms of the disease, because the medications' adverse effects would not be tolerated. The trend is to use the lowest possible dose of medication so that, as the disease progresses, dosages can be increased and other medicines added to obtain a combined effect. Unfortunately, as the disease progresses, drug therapy becomes more complex in terms of the number of medicines, dosage adjustments, the frequency of dosage administration, and the frequency of adverse effects. Therapies often have to be discontinued because of the impact of adverse effects on the quality of life. Other drug therapy may also be necessary for the treatment of the nonmotor symptoms of Parkinson's disease.

USES

Rasagiline or selegiline may be used to slow the course of Parkinson's disease by possibly slowing the progression of the deterioration of dopaminergic nerve cells. A dopamine receptor agonist—often carbidopa-levodopa—is initiated when the patient develops functional impairment. Carbidopa-levodopa continues to be the most effective drug for the relief of symptoms; however, after 3 to 5 years, the drug's effect gradually wears off, and the patient suffers from "on–off" fluctuations in levodopa activity. A catechol-*O*-methyltransferase (COMT) inhibitor (entacapone) may be added to carbidopa-levodopa therapy to prolong the activity of the dopamine by slowing its rate of metabolism. Apomorphine may also be administered to treat off periods. *Anticholinergic agents* provide symptomatic relief from excessive acetylcholine. These agents are often used in combination to promote optimal levels of motor function (e.g., to improve gait, posture, or speech) and to decrease disease symptoms (e.g., tremors, rigidity, drooling). See Figure 15-2 for an algorithm for the treatment for Parkinson's disease.

❖ Nursing Implications for Parkinson's Disease Therapy

■ Assessment

Unified Parkinson's Disease Rating Scale. The Unified Parkinson's Disease Rating Scale (UPDRS) is often used to identify the baseline of Parkinson's disease symptoms at the time of diagnosis and to monitor changes in symptoms that may require medicine dosage adjustment. The UPDRS evaluates the following: (1) mentation, behavior, and mood; (2) ADLs; (3) motor examination; (4) complications of therapy; (5) modified Hoehn and Yahr staging; and (6) the Schwab and England ADL scale.

History of Parkinsonism. Obtain a history of the patient's exposure to known conditions associated with the development of parkinsonian symptoms, such as head trauma, encephalitis, tumors, and drug exposure (e.g., phenothiazines, reserpine, methyldopa, metoclopramide). In addition, ask if the person has a history of being exposed to toxic levels of metals or carbon monoxide.

Obtain data to classify the extent of parkinsonism that the patient is exhibiting. A rating scale such as the UPDRS may be used to assess the severity of Parkinson's disease on the basis of the degree of disability exhibited by the patient:

- Stage 1: Involvement of one limb; slight tremor or minor change in speech, facial expression, posture, or movement; mild disease

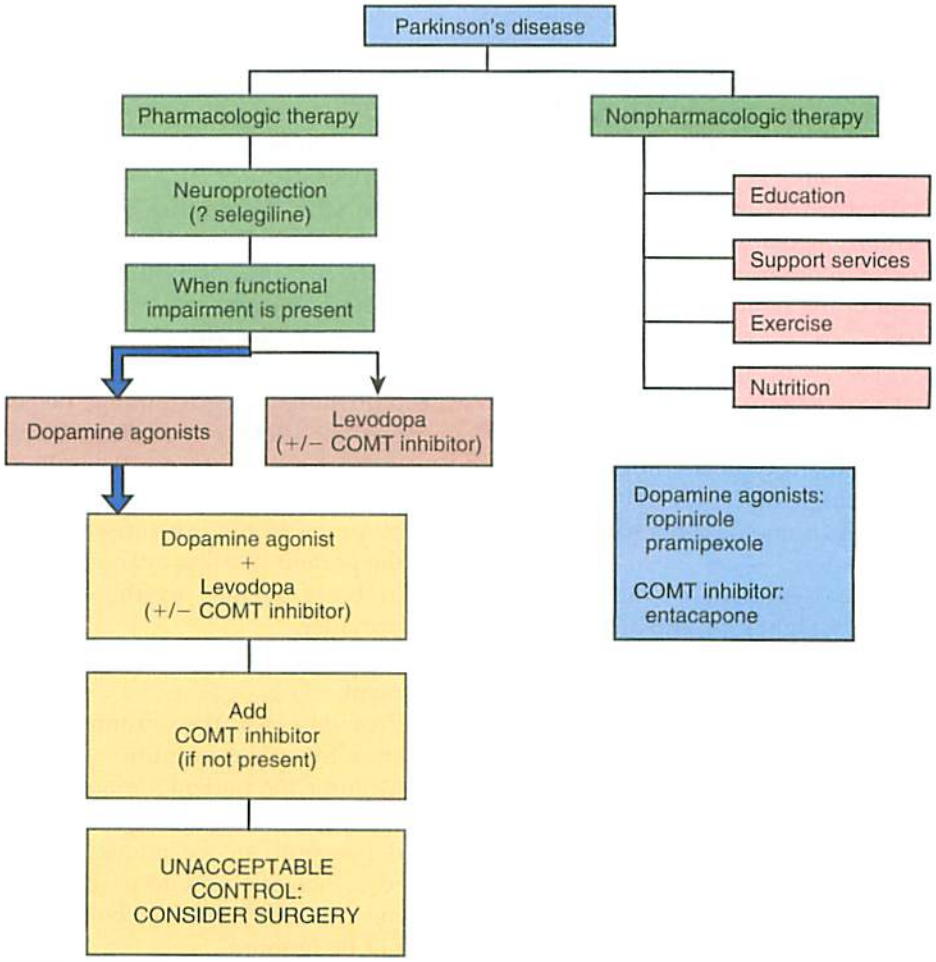

FIGURE 15-2 Management of Parkinson's disease. Consider neuroprotective therapy as soon as the diagnosis is made. When functional impairment starts, initiate a dopamine agonist; supplement this with levodopa when dopamine agonist monotherapy no longer provides satisfactory clinical control. Consider introducing supplemental levodopa in combination with a catechol-*O*-methyl transferase (COMT) inhibitor to extend levodopa's duration of action. Consider surgical intervention when parkinsonism cannot be satisfactorily controlled with medical therapies.

- Stage 2: Involvement of two limbs; early postural changes; some social withdrawal; possible depression
- Stage 3: Significant gait disturbances; moderate generalized disability
- Stage 4: Akinesia (i.e., an abnormal state of motor and psychic hypoactivity or muscle paralysis), rigidity, and severe disability; still able to walk or stand unassisted
- Stage 5: Unable to stand or walk or to perform all ADLs; wheelchair-bound or bedridden unless aided

Motor Function. Patients with Parkinson's disease progress through the following symptoms.

Tremor. ***Tremors*** are initially so minor that they are observed only by the patient. They occur primarily when the individual is at rest, but they are more noticeable during emotional turmoil or periods of increased concentration. The tremors are often observed in the hands and may involve the jaw, lips, and tongue. A "pill rolling" motion in the fingers and thumbs is characteristic. Tremors are usually reduced with voluntary movement. Emotional stress and fatigue may increase the frequency of tremors.

Assess the degree of tremor involvement and specific limitations in activities that are being affected by the tremors. Obtain a history of the progression of the symptoms from the patient.

Dyskinesia. ***Dyskinesia*** is the impairment of the individual's ability to perform voluntary movements. This symptom commonly starts in one arm or hand. It is usually most noticeable because the patient ceases to swing the arm on the affected side while walking.

As dyskinesia progresses, movement—especially in the small muscle groups—becomes slow and jerky. This motion is often referred to as *cogwheel rigidity.* Muscle soreness, fatigue, and pain are associated with the prolonged muscle contractibility. The patient develops a shuffling gait and may have difficulty with halting steps while walking (i.e., festination). When starting movement, there may be brief moments of immobility called *freezing.* Movements that were

formerly automatic, such as getting out of a chair or walking, require a concentrated effort.

In addition to the shuffling gait, the head and spine flex forward, and the shoulders become rounded and stooped. As mobility deteriorates, the steps quicken and become shorter. *Propulsive, uncontrolled movement* forward or backward is evident, and patient safety becomes a primary consideration. Obtain antislip pads for chairs and other positioning devices. Perform a safety check of the patient's environment to prevent accidents.

Bradykinesia. Bradykinesia is the extremely slow body movement that may eventually progress to *akinesia* (i.e., a lack of movement).

Facial Appearance. The patient typically appears to be expressionless, as if wearing a mask; the eyes are wide open and fixed in position. Some patients have almost total eyelid closure.

Nutrition. Complete an assessment of the person's dietary habits, any recent weight loss, and any difficulties with eating.

Salivation. As a result of excessive cholinergic activity, patients will salivate profusely. As the disease progresses, patients may be unable to swallow all secretions, and they will frequently drool. If the pharyngeal muscles are involved, the patient will have difficulty chewing and swallowing.

Psychological. The chronic nature of the disease and its associated physical impairment produce mood swings and serious depression. Patients commonly display a delayed reaction time. Dementia affects the intellectual capacity of about one third of patients.

Stress. Obtain a detailed history of the manner in which the patient has controlled his or her physical and mental stress.

Safety and Self-Care. Assess the level of assistance that is needed by the patient for mobility and for the performance of ADLs and self-care.

Family Resources. Determine what family resources are available as well as the closeness of the family during both daily and stress-producing events.

Implementation

- Implement planned interventions that are consistent with assessment data, and identify the individual needs of the patient.
- Monitor and record the patient's vital signs, especially blood pressure, during the course of therapy. Report significant changes in blood pressure; these are most likely to occur during periods of dosage adjustment. Emphasize measures to prevent orthostatic hypotension.
- Monitor for the degree of therapeutic response and adverse effects using forms provided by the clinical site to document changes in function.
- Monitor the patient's bowel function, and implement measures to prevent constipation (e.g., adequate fluid intake, bulk in diet, exercise, use of stool softeners).
- Support the patient's efforts to remain mobile. Provide a safe environment by removing clutter and throw rugs; use correct equipment and supportive devices.
- Minimize deformities by encouraging the patient to maintain an erect posture. Maintain joint mobility with the use of both active and passive range-of-motion exercises.
- Reinforce the principles that are taught for gait training.
- Nutritional needs must be carefully assessed, because dietary modifications will be required as the disease progresses. Be vigilant for difficulty with swallowing, and realize that the patient may be prone to the aspiration of food or water. Weigh the patient weekly; evaluate and report fluctuations in body weight to the dietitian or health care provider.
- Encourage self-maintenance and social involvement.
- Provide a restful environment, and attempt to keep stressors at a minimum.
- Monitor the patient's mood and affect, and be alert for signs of depression. Mood alterations and depression are secondary to disease progression (e.g., lack of ability to participate in sex, immobility, incontinence) and may be expected, but they should not be ignored.
- Provide for patient safety during ambulation and delivery of care.
- Stress that the effectiveness of medication therapy may take several weeks.
- Monitor behavioral changes on a consistent schedule that has been established within the clinical practice setting.

Patient Education

Nutrition. Teach the patient to drink at least six to eight glasses of water or fluid per day to maintain adequate hydration. Because constipation is often a problem, instruct the patient to include bulk in the diet and to use stool softeners as needed. As the disease progresses, the type and consistency of the foods eaten will need to be adjusted to meet the individual's needs. Because of fatigue and difficulty with eating, give assistance that is appropriate to the patient's degree of impairment. Do not rush the individual when he or she is eating, and cut foods into bite-sized pieces. Teach swallowing techniques to prevent aspiration. Plan six smaller meals daily rather than three larger meals.

Instruct the patient to weigh himself or herself weekly. Ask the patient to state the guidelines for weight loss or gain that should be reported to the health care provider.

Stress that vitamins should not be taken unless they have been prescribed by the health care provider. Pyridoxine (vitamin B_6) will reduce the therapeutic effect of levodopa.

Stress Management. Explain to the patient and caregivers about the importance of maintaining an environment that is as free from stress as possible. Explain that symptoms such as tremors are enhanced by anxiety.

Self-Reliance. Encourage patients to perform as many ADLs as they can. Parkinson's disease is a progressive disorder; explain to caregivers that it is important not to take over and that they should encourage patients' self-maintenance, continued social involvement, and participation in activities such as hobbies. Use adaptive devices to help the patient with dressing, and purchase clothing with easy closures or fasteners such as Velcro. As mobility diminishes, use a bath chair and handheld shower nozzle to help the patient maintain his or her cleanliness.

Exercise. Instruct the patient and caregiver about the importance of maintaining correct body alignment, walking as erect as possible, and practicing the gait training taught by the physical therapy department. Gait training is essential if the patient is to delay the onset of shuffling and gait propulsion. Patients should wear sturdy, supportive shoes and use a cane, walker, or other assistive device to maintain mobility. Exercises to maintain the strength of facial muscles and of the tongue help the patient to maintain speech clarity as well as the ability to swallow. Active and passive range-of-motion exercises of all joints help to minimize deformities. Explain that maintaining the exercise program can increase the patient's long-term well-being.

Mood Alterations. Explain to the patient and the caregiver that depression and mood alterations are secondary to disease progression (e.g., inability to participate in sex, immobility, incontinence) and are to be expected. Changes in mental outlook should be discussed with the health care provider.

Fostering Health Maintenance. Provide the patient and his or her significant others with important information contained in the specific drug monographs for the medicines that are prescribed, including the name of the medication; its dosage, route, and administration time; potential adverse effects; and drug-specific patient education. Stress the importance of nonpharmacologic interventions and the long-term effects that compliance with the treatment regimen can provide. Additional health teaching and nursing interventions for the adverse effects of these medications are described in the drug monographs that follow.

Provide information to the patient, family, and caregivers about resources, including the American Parkinson's Disease Association and the services and information available from this source. There are support groups for patients and families that can serve as caring environments for people with similar experiences and concerns. Respite care may also be available, which provides temporary services to the dependent older adult either at home or in an institutional setting to provide the family with relief from the demands of daily patient care.

Written Record. Enlist the patient's help with developing and maintaining a written record of monitoring parameters (e.g., degree of tremor relief, stability, changes in mobility and rigidity, sedation, constipation, drowsiness, mental alertness, deviations from the norm); see the Patient Self-Assessment Form for Antiparkinson Agents on the Evolve Web site. Complete the Premedication Data column for use as a baseline to track the patient's response to drug therapy. Ensure that the patient understands how to use the form, and instruct the patient to bring the completed form to follow-up visits. During follow-up visits, focus on issues that will foster adherence with the therapeutic interventions that have been prescribed.

DRUG CLASS: MONOAMINE OXIDASE INHIBITORS TYPE B

ACTIONS

Selegiline and rasagiline are potent monoamine oxidase inhibitors type B (MAOI-Bs) that reduce the metabolism of dopamine in the brain, thus allowing for greater dopaminergic activity. Although they are still under investigation, these agents may also be neuroprotective, which means that they may slow the rate of deterioration of the dopamine neurons with the use of other unknown mechanisms.

USES

Carbidopa-levodopa is the current combination of drugs of choice for the treatment of Parkinson's disease. Unfortunately, these agents lose effectiveness (i.e., the on–off phenomenon) and develop more adverse effects (i.e., dyskinesias) over time. It is often necessary to add other dopamine receptor agonists (e.g., pramipexole, ropinirole) or a COMT inhibitor (e.g., entacapone) to improve the patient's response and tolerance. The MAOI-Bs have similar adjunctive activity to carbidopa-levodopa for the treatment of Parkinson's disease. The combination of either MAOI-B with carbidopa-levodopa improves memory and motor speed, and it may also increase life expectancy.

These agents may also have a neuroprotective effect by interfering with the ongoing degeneration of striated dopaminergic neurons. They may be used early during the treatment of Parkinson's disease to slow the progression of symptoms and to delay the initiation of levodopa therapy. Selegiline was also recently approved for the treatment of depression (see p. 258).

Selegiline and rasagiline have different metabolic pathways and therefore somewhat different adverse effect profiles. Active metabolites of selegiline, when

swallowed, are amphetamines that cause cardiovascular and psychiatric adverse effects. The orally disintegrating tablet dosage form allows the drug to be absorbed from the buccal area in the mouth, thereby avoiding much of the formation of the active metabolites. Note the difference in strength between the tablets and the orally disintegrating tablets. A 10-mg tablet of selegiline is approximately equal in potency to a 1.25-mg orally disintegrating tablet of selegiline. Rasagiline is not metabolized to amphetamines, so cardiovascular and psychiatric adverse effects are minimal.

THERAPEUTIC OUTCOMES

The primary therapeutic outcomes sought from MAOI-Bs for the treatment of parkinsonism are as follows:

1. Slowing the development of symptoms and the progression of the disease
2. Establishing a balance of dopamine and acetylcholine in the basal ganglia of the brain by enhancing the delivery of dopamine to brain cells

Nursing Implications for Monoamine Oxidase Inhibitors Type B Therapy

Premedication Assessment

1. Perform a baseline assessment of parkinsonism with the use of the UPDRS.
2. Obtain a history of gastrointestinal (GI) symptoms.
3. Perform a baseline assessment of the patient's degree of alertness and orientation to name, place, and time before the initiation of therapy.
4. Check for any antihypertensive therapy that is currently prescribed. Monitor the patient's blood pressure daily in both the supine and standing positions. If antihypertensive medications are being taken, report this to the health care provider for possible dosage adjustment.
5. Check other medications prescribed; do not administer selegiline or rasagiline with meperidine. Other drug interactions are discussed later in this chapter.

Availability

See Table 15-1.

Dosage and Administration

The dosage must be adjusted according to the patient's response and tolerance.

Adult: PO: See Table 15-1. Selegiline orally disintegrating tablets should be taken in the morning before breakfast, without liquid. Patients should not attempt to push selegiline orally disintegrating tablets through the foil backing. Patients should peel back the backing of one or two blisters (as prescribed) with dry hands and gently remove the tablets. Patients should immediately place the orally disintegrating selegiline tablets on top of the tongue, where they will disintegrate in seconds. Patients should avoid ingesting food or liquids for 5 minutes both before and after taking orally disintegrating selegiline tablets.

After 2 to 3 days of treatment, the dosage of carbidopa-levodopa should start being titrated downward. Carbidopa-levodopa dosages may be able to be reduced by 10% to 30%.

Monitoring

Selegiline and rasagiline cause relatively few adverse effects. They may increase the adverse dopaminergic effects of levodopa (e.g., chorea, confusion, hallucinations), but these can be controlled by reducing the dosage of levodopa. Dosage reduction of the levodopa is usually the optimal treatment.

Common Adverse Effects

Gastrointestinal

Constipation, Stomach Upset. Most of these effects may be minimized by a temporary reduction in dosage,

Table 15-1 Monoamine Oxidase Inhibitors Type B

GENERIC NAME	BRAND NAME	AVAILABILITY	INITIAL DOSAGE (BY MOUTH)	MAXIMUM DAILY DOSAGE (mg)
rasagiline ⇄ *Do not confuse rasagiline with repaglinide, raloxifene, Risperdal, or risperidone.*	Azilect	Tablets: 0.5, 1 mg	Monotherapy: 1 mg once daily Adjunctive therapy: 0.5 mg once daily	1 1
selegiline ⇄ *Do not confuse selegiline with Serentil, sertraline, Serzone, or Salagen.*	Eldepryl ⇄ *Do not confuse Eldepryl with enalapril.* Zelapar	Tablets and capsules: 5 mg Tablets, orally disintegrating: 1.25 mg	Initial dose: 2.5 mg daily 1.25 mg dissolved on the tongue	5 mg twice daily 2.5

administration with food, and the use of stool softeners for constipation.

Serious Adverse Effects

Neurologic

Chorea, Confusion, Hallucinations. Selegiline may increase the adverse dopaminergic effects of levodopa. Make regularly scheduled subsequent evaluations of the patient's mental status, and compare findings. Report alterations. Provide patient safety, be emotionally supportive, and assure the patient that these adverse effects usually dissipate as tolerance develops over the next few weeks.

Cardiovascular

Orthostatic Hypotension. Monitor the patient's blood pressure daily in both the supine and standing positions. Anticipate the development of postural hypotension, and take measures to prevent such an occurrence. Teach the patient to rise slowly from a supine or sitting position, and encourage the patient to sit or lie down if feeling faint.

Drug Interactions

Levodopa. MAOI-Bs and levodopa have additive neurologic effects. These interactions may be beneficial, because they often allow for a reduction in the dose of the levodopa.

Meperidine, Tramadol, Methadone, Propoxyphene. Fatal drug interactions have been reported between MAOIs and these agents. Although these interactions have not been reported with selegiline or rasagiline, it is recommended that selegiline and rasagiline not be administered with any of these agents.

Dextromethorphan. Episodes of psychosis and bizarre behavior have been reported with selegiline and dextromethorphan. Do not administer these drugs concurrently.

Food. Patients should avoid foods and beverages with high tyramine content (e.g., Chianti wine, fava beans, cheeses), particularly if they are receiving selegiline in excess of 9 mg/day. Rare cases of hypertensive reactions have been reported.

Antihypertensive Agents. A dosage adjustment of the antihypertensive agent is often necessary in response to excessive orthostatic hypotension.

Ciprofloxacin. This antibiotic inhibits the metabolism of rasagiline, thus significantly raising rasagiline serum levels and potentially causing significant hypertension. Use the combination very cautiously. Reduce the dose of rasagiline by half to avoid complications.

Antidepressants (Tricyclic Antidepressants, Selective Serotonin Reuptake Inhibitors, Serotonin-Norepinephrine Reuptake Inhibitors, St. John's Wort). Use these drugs with extreme caution in conjunction with MAOI-B therapy. Although rare, there is a potential for serotonin syndrome, which is manifested by behavioral and mental status changes, diaphoresis, muscular rigidity, hypertension, syncope, and death. Many patients are receiving antidepressants for the treatment of depression that frequently accompanies parkinsonism. Closely monitor patients for symptoms.

Sympathomimetic Amines (Ephedrine, Pseudoephedrine, Phenylephrine). Cases of hypertensive crisis have rarely been reported among patients who are concurrently taking sympathomimetic amines and MAOI-Bs. Concurrent therapy is not recommended.

DRUG CLASS: DOPAMINE AGONISTS

apomorphine (ă-pō-MŌR-fēn)
⇄ *Do not confuse apomorphine with morphine.*
Apokyn (ă-PŌ-kĭn)

ACTIONS

Apomorphine is a nonergot dopamine agonist. It is thought to stimulate dopamine receptors in the brain, thereby temporarily restoring motor function. It is chemically related to morphine, but it does not have any opioid activity.

USES

As Parkinson's disease progresses, patients often experience episodes of lower responsiveness to levodopa, which causes periods of hypomobility (e.g., inability to rise from a chair, speak, or walk). Apomorphine is used to treat the hypomobility associated with the "wearing off" of dopamine agonists, either near the end of a dosage cycle or at unpredictable times (i.e., the "on–off" phenomenon).

THERAPEUTIC OUTCOMES

The primary therapeutic outcomes sought from apomorphine for the treatment of parkinsonism are improving motor and ADL scores and decreasing off time.

Nursing Implications for Apomorphine Therapy

Premedication Assessment

1. Perform a baseline assessment of parkinsonism with the use of the UPDRS.
2. Obtain a history of cardiovascular symptoms, including the baseline vital signs (e.g., blood pressure, heart rate).
3. Perform a baseline assessment of the patient's degree of mobility, alertness, and orientation to name, place, and time before initiating therapy. Ask specifically whether he or she may be taking any other sedating medicines. Make regularly scheduled subsequent evaluations of blood pressure, pulse, mental status, and mobility, and compare findings.

Availability

Subcutaneous: 10 mg/mL in 3-mL cartridges.

Dosage and Administration

Apomorphine is administered most commonly with the use of a manual, reusable, multidose injector pen that holds a 3-mL cartridge of medicine. To avoid potential confusion with the use of the pen and inadvertent overdose, it is recommended that the dose of the drug be identified in milliliters rather than in milligrams. The pen is adjustable in 0.02-mL increments. A training pamphlet that addresses the use of the injector pen is available for patient use.

Medication Safety Alert

DO NOT ADMINISTER APOMORPHINE INTRAVENOUSLY. This drug may crystallize in the vein and form a thrombus or embolism.

Adult: Subcutaneous: Initially, a test dose of 0.2 mL (2 mg) should be administered in the stomach area, upper leg, or upper arm. Both supine and standing blood pressures should be determined before administering the dose and again at 20, 40, and 60 minutes after administration. If significant orthostatic hypotension develops, therapy should be discontinued, and the patient should receive no further doses of apomorphine.

If the patient tolerates the 0.2-mL dose and responds, then the starting dose should be 0.2 mL used on a PRN basis to treat off events. If needed, the dose can be increased in 0.1-mL (1-mg) increments every few days on an outpatient basis. The maximum recommended dose is 0.6 mL (6 mg).

If a patient discontinues therapy for longer than 1 week and then wishes to go back to the use of apomorphine, therapy should be reinitiated at the starting dose of 0.2 mL, with gradual increases in dosage to optimal therapy.

Use of an Antiemetic. One of the pharmacologic actions of apomorphine is emesis. The antiemetic trimethobenzamide (Tigan) should be administered orally at a dosage of 300 mg three times daily for at least 3 days before the initial dose of apomorphine. It should be continued for at least the first 2 months of therapy. About 50% of patients are able to discontinue the antiemetic while continuing therapy with apomorphine. Do not use prochlorperazine (Compazine) or ondansetron (Zofran) as antiemetics. (See Drug Interactions on p. 233.)

Monitoring

Most adverse effects observed with apomorphine agents are direct extensions of their pharmacologic properties.

Common Adverse Effects

Gastrointestinal

Nausea, Vomiting. These effects can be reduced by premedicating the patient with trimethobenzamide and then slowly increasing the dosage.

Cardiovascular

Orthostatic Hypotension. Apomorphine commonly causes orthostatic hypotension, which is manifested by dizziness and weakness, particularly when therapy is initiated. Patients with Parkinson's disease are at risk for falling because of the underlying postural instability associated with the disease; apomorphine may increase the risk of falling by lowering blood pressure and altering mobility. Anticipate the development of postural hypotension, and provide assistance when necessary. Monitor the patient's blood pressure before and during apomorphine therapy in both the supine and standing positions. Teach patients to rise slowly from a supine or sitting position; encourage them to sit or lie down if feeling faint.

Serious Adverse Effects

Neurologic

Chewing Motions, Bobbing, Facial Grimacing, Rocking Movements. These involuntary movements (dyskinesias) occur in some patients, especially if they are also taking levodopa. A reduction in the dosage of the levodopa or apomorphine may be beneficial.

Sudden Sleep Events. Sleep episodes have been reported with the dopamine agonists (e.g., apomorphine, pergolide, pramipexole, ropinirole). These episodes are described as sleep attacks or sleep episodes that include daytime sleep. Some sleep events have been reported as sudden and irresistible; other sleep events have been preceded by sufficient warning to prevent accidents. Patients who are taking dopamine agonists should be informed about the possibility of daytime sleepiness and outright sleep attacks with these medicines and allowed to make their own decisions about driving on the basis of their past experiences with the medicines. The assessment of patients who are at risk for sleep attacks is possible with the Epworth Sleepiness Scale.

Psychological

Nightmares, Depression, Confusion, Hallucinations. Perform a baseline assessment of the patient's degree of alertness and orientation to name, place, and time before initiating therapy. Make regularly scheduled subsequent evaluations of mental status, and compare findings. Report alterations. Provide for patient safety during these episodes. Reducing the daily medication dosage may control these adverse effects.

Cardiovascular

Tachycardia, Palpitations. Take the patient's pulse at regularly scheduled intervals. Report for further evaluation.

Genitourinary

Penile Erection, Priapism. Apomorphine may cause penile erection and, rarely, priapism (i.e., prolonged, painful erection). Apomorphine has been overused because of its ability to induce erection and increase libido. Indications of abuse include frequent erections, atypical sexual behavior, heightened libido, dyskinesias, agitation, confusion, and depression.

Drug Interactions

Ondansetron (Zofran), Dolasetron (Anzemet), Granisetron (Kytril), Palonosetron (Aloxi), Alosetron (Lotronex). The use of serotonin antagonists with apomorphine is contraindicated. Profound hypotension and loss of consciousness have been reported.

Phenothiazines, Including Prochlorperazine (Compazine), Butyrophenones (e.g., Haloperidol), Thioxanthenes, Metoclopramide. These medicines are dopamine antagonists. They will block the dopaminergic effect of apomorphine, thereby aggravating parkinsonian symptoms.

Ethanol, Antihypertensive Agents, Vasodilators (e.g., Nitrates). The use of these agents concurrently with apomorphine significantly increases the frequency of orthostatic hypotension. Alcohol should be avoided when taking apomorphine. Dosage adjustment of the antihypertensive agent is often necessary because of excessive orthostatic hypotension.

carbidopa (kăr-bĭ-DŌ-pă)
levodopa (lē-vō-DŌ-pă)
Sinemet (SĪN-ĕ-mĕt)
⇄ *Do not confuse Sinemet with Senokot or Sinequan.*
Parcopa (păr-KŌ-pă)

ACTIONS

Dopamine, when administered orally, does not enter the brain. Levodopa *does* cross into the brain, where it is metabolized to dopamine and replaces the dopamine deficiency in the basal ganglia. Dopamine stimulates D_1, D_2, and D_3 dopamine receptors.

Sinemet and Parcopa are combination products of carbidopa and levodopa that are used for treating the symptoms of Parkinson's disease. Carbidopa is an enzyme inhibitor that reduces the metabolism of levodopa, thus allowing for a greater portion of the administered levodopa to reach the desired receptor sites in the basal ganglia. Carbidopa has no effect when it is used alone; it must be used in combination with levodopa.

USES

About 75% of patients with parkinsonism respond favorably to levodopa therapy. However, after a few years, the response diminishes and becomes more uneven, and it is accompanied by many more adverse effects. This loss of therapeutic effect reflects the progression of the underlying disease process.

Carbidopa is used to reduce the dose of levodopa required by approximately 75%. When administered with levodopa, carbidopa increases plasma levels and the plasma half-life of levodopa. Parcopa is a formulation that dissolves in the mouth, which reduces the incidence of choking as a result of attempting to swallow tablets.

THERAPEUTIC OUTCOMES

The primary therapeutic outcome sought from Sinemet for the treatment of parkinsonism is the establishment of a balance of dopamine and acetylcholine in the basal ganglia of the brain by enhancing the delivery of dopamine to brain cells.

Nursing Implications for Carbidopa-Levodopa Therapy

Premedication Assessment

1. Perform a baseline assessment of parkinsonism with the use of the UPDRS.
2. Obtain a history of GI and cardiovascular symptoms, including baseline vital signs (e.g., blood pressure, pulse).
3. Ask specifically about any symptoms of hallucinations, nightmares, dementia, or anxiety. Inquire about any urine testing that is being done.
4. All patients should be screened for the presence of angle-closure glaucoma before initiating therapy. Patients with open-angle glaucoma can safely use levodopa. Do not administer the medicine to people with a history of glaucoma unless it has been specifically approved by the patient's health care provider.
5. Review the medicines that have been prescribed that may require dose adjustments. Plan to perform focused assessments to detect responses to therapy that would need to be reported to the health care provider.

Availability

PO: Sinemet is a combination product that contains both carbidopa and levodopa. The combination product is available in ratios of 10/100, 25/100, and 25/250 mg of carbidopa and levodopa, respectively. There are also sustained-release products (Sinemet CR) that contain either 25/100 mg or 50/200 mg of carbidopa and levodopa, respectively.

Parcopa is a combination product that contains both carbidopa and levodopa. It is available as orally disintegrating tablets in ratios of 10/100, 25/100, and 25/250 mg of carbidopa and levodopa, respectively.

Dosage and Administration

Adult: PO: For patients who are not receiving levodopa initially, give Sinemet or Parcopa, 10/100 or 25/100 three times daily, increasing by one tablet every other day, until a dosage of six tablets daily is attained. As therapy progresses and patients show indications of needing more levodopa, substitute Sinemet 25/250, one tablet three or four times daily. Increase by one tablet every other day to a maximum of eight tablets daily. See the manufacturer's guidelines for switching a patient to the sustained-release form of Sinemet.

Administer this medication with food or milk to reduce gastric irritation. Therapy for at least 6 months may be necessary to determine this medication's full therapeutic benefits.

Monitoring

Levodopa causes many adverse effects, but most are dose related and reversible. Adverse effects vary greatly, depending on the stage of the disease.

Common Adverse Effects

Gastrointestinal

Nausea, Vomiting, Anorexia. These effects can be reduced by slowly increasing the dose, dividing the total daily dosage into four to six doses, and administering the medication with food or antacids.

Cardiovascular

Orthostatic Hypotension. Although the effects are generally mild, levodopa may cause some degree of orthostatic hypotension; this is manifested by dizziness and weakness, particularly when therapy is initiated. Tolerance usually develops after a few weeks of therapy. Monitor the patient's blood pressure daily in both the supine and standing positions. Anticipate the development of postural hypotension, and take measures to prevent such an occurrence. Teach patients to rise slowly from a supine or sitting position, and encourage them to sit or lie down if feeling faint.

Serious Adverse Effects

Neurologic

Chewing Motions, Bobbing, Facial Grimacing, Rocking Movements. These involuntary movements occur in about half of the patients who take levodopa for more than 6 months. A reduction in dosage may be beneficial.

Psychological

Nightmares, Depression, Confusion, Hallucinations. Perform a baseline assessment of the patient's degree of alertness and orientation to name, place, and time before initiating therapy. Make regularly scheduled subsequent evaluations of mental status, and compare findings. Report alterations. Provide for patient safety during these episodes. Reducing the daily dosage may control these adverse effects.

Cardiovascular

Tachycardia, Palpitations. Take the patient's pulse at regularly scheduled intervals. Report for further evaluation.

Drug Interactions

Sinemet may be used to treat parkinsonism in conjunction with dopamine agonists, COMT inhibitors, or anticholinergic agents. The dosages of all medications may need to be reduced as a result of combined therapy.

Monoamine Oxidase Inhibitors (Phenelzine, Tranylcypromine, Isocarboxazid, Selegiline). These MAOIs unpredictably exaggerate the effects of levodopa. They should be discontinued at least 14 days before the administration of levodopa.

Isoniazid. Use this drug with caution in conjunction with levodopa. Discontinue isoniazid if patients who are taking levodopa develop hypertension, flushing, palpitations, and tremor.

Pyridoxine. Pyridoxine (vitamin B_6) in oral doses of 5 to 10 mg may reduce the therapeutic and toxic effects of levodopa. Normal diets contain less than 1 mg of pyridoxine, so dietary restrictions are not necessary. However, the ingredients of multiple vitamins should be considered.

Diazepam, Chlordiazepoxide, Papaverine, Clonidine, Phenytoin. These agents appear to cause a deterioration of the therapeutic effects of levodopa. Use them with caution for patients with parkinsonism, and discontinue them if the patient's clinical status deteriorates.

Phenothiazines, Reserpine, Haloperidol, Risperidone, Metoclopramide. An adverse effect associated with these agents is a Parkinson's-like syndrome. Because this condition will nullify the therapeutic effects of levodopa, do not use the drugs concurrently.

Ephedrine, Epinephrine, Isoproterenol, Amphetamines. Levodopa may increase the therapeutic and toxic effects of these agents. Monitor the patient for tachycardia, dysrhythmias, and hypertension. Reduce the dosage of these agents if necessary.

Antihypertensive Agents. A dosage adjustment of the antihypertensive agent is frequently necessary in response to excessive orthostatic hypotension.

Anticholinergic Agonists (Benztropine, Diphenhydramine, Trihexyphenidyl). Although these agents are used to treat parkinsonism, they increase gastric deactivation and decrease the intestinal absorption of levodopa. The administration of doses of anticholinergic agents and levodopa should be separated by 2 hours or more.

Toilet Bowl Cleaners. The metabolites of levodopa react with toilet bowl cleaners to turn the urine red to black. This may also occur if the urine is exposed to air for long periods of time. Inform the patient that there is no cause for alarm.

pramipexole (pră-mĭ-PĔKS-ŏl)
Mirapex (MĪR-ă-pĕks)
Mirapex Er

⇄ *Do not confuse Mirapex with MiraLax.*

ACTIONS

Pramipexole is a nonergot dopamine agonist that stimulates D_2 and D_3 dopamine receptors.

USES

Pramipexole may be used alone to manage the early signs and symptoms of parkinsonism by improving ADLs as well as motor manifestations such as tremor, rigidity, bradykinesia, and postural stability. It may

also be used in combination with levodopa for advanced parkinsonism to manage similar signs and symptoms of the disease.

THERAPEUTIC OUTCOMES

The primary therapeutic outcomes sought from pramipexole for the treatment of parkinsonism are as follows:

1. Improved motor and ADL scores
2. Decreased off time
3. Reduced dosage of levodopa

Nursing Implications for Pramipexole Therapy

Premedication Assessment

1. Perform a baseline assessment of parkinsonism with the use of the UPDRS.
2. Obtain a history of GI and cardiovascular symptoms, including baseline vital signs (e.g., blood pressure, pulse).
3. Ask specifically about any symptoms of hallucinations, nightmares, dementia, or anxiety.

Availability

PO: tablets: 0.125-, 0.25-, 0.5-, 0.75-, 1-, and 1.5-mg; tablets, extended-release, 24 hour: 0.375-, 0.75-, 1.5-, 2.25-, 3-, 3.75-, and 4.5-mg.

Dosage and Administration

Adult: PO: Initially, give 0.125 mg three times daily for 1 week. If tolerated, increase the dosage to 0.25 mg three times daily the second week. If tolerated, increase by increments of 0.25 mg three times daily through the seventh week. The usual maintenance dosage is 0.5 to 1.5 mg three times daily, with or without levodopa therapy. When pramipexole is used with levodopa, consider reducing the levodopa dose.

Administer medication with food or milk to reduce gastric irritation.

If pramipexole is to be discontinued, the dosage should be gradually reduced over 1 week.

Monitoring

Pramipexole causes many adverse effects, but most are dose related and are reversible. Adverse effects vary greatly, depending on the stage of the disease and the concurrent use of other medicines.

Common Adverse Effects

Gastrointestinal

Nausea, Vomiting, Anorexia. These effects can be reduced by slowly increasing the dosage, dividing the total daily dose into three doses, and administering the medication with food.

Cardiovascular

Orthostatic Hypotension. Although it is generally mild, pramipexole may cause some degree of orthostatic hypotension; this is manifested by dizziness and weakness, particularly when therapy is being initiated. Tolerance usually develops after a few weeks of therapy. Monitor the patient's blood pressure daily in both the supine and standing positions. Anticipate the development of postural hypotension, and take measures to prevent such an occurrence. Teach patients to rise slowly from a supine or sitting position, and encourage them to sit or lie down if feeling faint.

Serious Adverse Effects

Neurologic

Chewing Motions, Bobbing, Facial Grimacing, Rocking Movements. These involuntary movements occur in some patients, especially if they are also taking levodopa. A reduction in dosage of the levodopa may be beneficial.

Sudden Sleep Events. Sleep episodes have been reported with the dopamine agonists (e.g., pramipexole, ropinirole). These episodes are described as "sleep attacks" or "sleep episodes," and they may include daytime sleep. Some sleep events have been reported as sudden and irresistible; other sleep events have been preceded by sufficient warning to prevent accidents. Patients who are taking dopamine agonists should be informed about the possibility of daytime sleepiness and outright sleep attacks with these medicines and be allowed to make their own decisions about driving on the basis of their past experiences with the medicines. The assessment of patients who are at risk for sleep attacks is possible with the Epworth Sleepiness Scale.

Psychological

Nightmares, Depression, Confusion, Hallucinations. Perform a baseline assessment of the patient's degree of alertness and orientation to name, place, and time before initiating therapy. Make regularly scheduled subsequent evaluations of mental status, and compare findings. Report alterations. Provide for patient safety during these episodes. Reducing the daily dosage may control these adverse effects.

Cardiovascular

Tachycardia, Palpitations. Take the pulse at regularly scheduled intervals. Report for further evaluation.

Drug Interactions

Cimetidine, Ranitidine, Diltiazem, Verapamil, Quinidine, Triamterene. These agents inhibit the urinary excretion of pramipexole. A dose reduction of pramipexole is often required to prevent toxic effects.

Dopamine Antagonists. Dopamine antagonists include phenothiazines, butyrophenones, thioxanthenes, and metoclopramide. As dopamine antagonists, these agents will diminish the effectiveness of pramipexole, which is a dopaminergic agonist.

Antihypertensive Agents. A dosage adjustment of the antihypertensive agent is often necessary in response to excessive orthostatic hypotension.

ropinirole (rō-PĪN-ĭ-rōl)
⇄ *Do not confuse ropinirole with raloxifene or risperidone.*
Requip (RĒ-kwĭp)
Requip XL
⇄ *Do not confuse Requip with Risperdal.*

ACTIONS

Ropinirole is a nonergot dopamine agonist that stimulates D_2 and D_3 dopamine receptors.

USES

Ropinirole may be used alone to manage the early signs and symptoms of parkinsonism by improving ADLs as well as motor manifestations such as tremor, rigidity, bradykinesia, and postural stability. It may also be used in combination with levodopa for advanced parkinsonism to manage similar signs and symptoms of the disease and to reduce the degree of on–off symptoms that are often associated with the long-term use of levodopa.

THERAPEUTIC OUTCOMES

The primary therapeutic outcomes sought from ropinirole for the treatment of parkinsonism are as follows:

1. Improved motor and ADL scores
2. Decreased off time
3. Reduced dosage of levodopa

Nursing Implications for Ropinirole Therapy

Premedication Assessment

1. Perform a baseline assessment of parkinsonism with the use of the UPDRS.
2. Obtain a history of GI and cardiovascular symptoms, including baseline vital signs (e.g., blood pressure, pulse).
3. Ask specifically about any symptoms of hallucinations, nightmares, dementia, or anxiety.

Availability

PO: tablets: 0.25-, 0.5-, 1-, 2-, and 3-mg; tablets, extended-release, 24 hour: 2-, 4-, 6-, 8-, and 12-mg.

Dosage and Administration

Adult: *PO:* Initially, give 0.25 mg three times daily for 1 week. If tolerated, increase to 0.5 mg three times daily the second week. If tolerated, increase to 0.75 mg three times daily for the third week and then to 1 mg three times daily through the fourth week. If necessary, the daily dosage may be increased by 1.5 mg/day on a weekly basis up to a daily dosage of 9 mg/day. Dosages may be further adjusted at weekly intervals up to a total dosage of 24 mg/day.

Administer medication with food or milk to reduce gastric irritation.

When ropinirole is used with levodopa, consider reducing the levodopa. If ropinirole is to be discontinued, the dosage should be gradually reduced over the course of 1 week.

Monitoring

Ropinirole causes many adverse effects, but most are dose related and are reversible. Adverse effects vary greatly, depending on the stage of the disease and the concurrent use of other medicines.

Common Adverse Effects

Gastrointestinal

Nausea, Vomiting, Anorexia. These effects can be reduced by slowly increasing the dosage, dividing the total daily dose into three doses, and administering the medication with food.

Cardiovascular

Orthostatic Hypotension. Although it is generally mild, ropinirole may cause some degree of orthostatic hypotension; this is manifested by dizziness and weakness, particularly when therapy is being initiated. Tolerance usually develops after a few weeks of therapy.

Monitor the patient's blood pressure daily in both the supine and standing positions. Anticipate the development of postural hypotension, and take measures to prevent such an occurrence. Teach patients to rise slowly from a supine or sitting position, and encourage them to sit or lie down if feeling faint.

Serious Adverse Effects

Neurologic

Chewing Motions, Bobbing, Facial Grimacing, Rocking Movements. These involuntary movements occur in some patients, especially if they are also taking levodopa. Reducing the dosage of levodopa may be beneficial.

Sudden Sleep Events. Sleep episodes have been reported with the dopamine agonists (e.g., pergolide, pramipexole, ropinirole). These episodes are described as "sleep attacks" or "sleep episodes," and they include daytime sleep. Some sleep events have been reported as sudden and irresistible, whereas other sleep events have been preceded by sufficient warning to prevent accidents. Patients who are taking dopamine agonists should be informed about the possibility of daytime sleepiness and outright sleep attacks with these medicines and be allowed to make their own decisions about driving on the basis of their past experiences with the medicines. The assessment of patients who are at risk for sleep attacks is possible with the Epworth Sleepiness Scale.

Psychological

Nightmares, Depression, Confusion, Hallucinations. Perform a baseline assessment of the patient's degree of alertness and orientation to name, place, and time before initiating therapy. Make regularly scheduled subsequent evaluations of mental status, and compare findings. Report alterations. Provide patient safety during these episodes. Reducing the daily dosage may control these adverse effects.

Cardiovascular

Tachycardia and Palpitations. Take the pulse at regularly scheduled intervals. Report for further evaluation.

▪ Drug Interactions

Ciprofloxacin. This antibiotic inhibits the metabolism of ropinirole. A dosage reduction of ropinirole is often required to prevent toxic effects.

Estrogens (Primarily Ethinyl Estradiol). Estrogen inhibits ropinirole excretion. If estrogen therapy is started or stopped during treatment with ropinirole, it may be necessary to adjust the dosage of ropinirole.

Dopamine Antagonists. Dopamine antagonists include phenothiazines, butyrophenones, thioxanthenes, and metoclopramide. As dopamine antagonists, these agents will diminish the effectiveness of ropinirole, which is a dopaminergic agonist.

Antihypertensive Agents. A dosage adjustment of the antihypertensive agent is often necessary in response to excessive orthostatic hypotension.

DRUG CLASS: CATECHOL-O-METHYLTRANSFERASE INHIBITORS

entacapone (ĕn-TĂK-ă-pōn)
Comtan (CŎM-tăn)
Entacapone/levodopa/carbidopa
Stalevo (stă-LĒ-vō)

ACTIONS

Entacapone is a potent COMT inhibitor that reduces the destruction of dopamine in the peripheral tissues, thereby allowing significantly more dopamine to reach the brain to eliminate the symptoms of parkinsonism.

USES

Carbidopa-levodopa is the current drug combination of choice for the longer-term treatment of Parkinson's disease. Unfortunately, these agents lose effectiveness (i.e., the on-off phenomenon) and result in the development of more adverse effects (i.e., dyskinesias) over time. Adding entacapone inhibits the metabolism of dopamine, which results in the more constant dopaminergic stimulation in the brain. This stimulation reduces motor fluctuations, increases on time, reduces off time, and often results in a reduction in the dosage of levodopa. Entacapone should always be administered with carbidopa-levodopa. Entacapone has no antiparkinsonian effect when it is used alone. Stalevo is a combination product that contains levodopa, carbidopa, and entacapone.

THERAPEUTIC OUTCOMES

The primary therapeutic outcomes sought from entacapone for the treatment of parkinsonism are as follows:

1. Reduced motor fluctuations
2. Increased on time and reduced off time
3. Reduced total daily dosage of carbidopa-levodopa

❖ Nursing Implications for Entacapone Therapy

▪ Premedication Assessment

1. Perform a baseline assessment of parkinsonism with the use of the UPDRS.
2. Obtain a history of bowel patterns and any ongoing GI symptoms.
3. Perform a baseline assessment of the patient's degree of alertness and orientation to name, place, and time before initiating therapy.
4. Check for any antihypertensive therapy that is currently prescribed. Monitor the patient's blood pressure daily in both the supine and standing positions. If antihypertensive medications are being taken, report this to the health care provider for possible dosage adjustment.
5. Check the patient's hepatic function before the initiation of therapy and periodically throughout the course of administration.

▪ Availability

PO: Comtan: 200-mg tablets; Stalevo 50: 12.5 mg carbidopa, 50 mg levodopa, and 200 mg entacapone; Stalevo 100: 25 mg carbidopa, 100 mg levodopa, and 200 mg entacapone; Stalevo 150: 37.5 mg carbidopa, 150 mg levodopa, and 200 mg entacapone.

▪ Dosage and Administration

Dosage must be adjusted in accordance with the patient's response and tolerance.

Adult: PO: Initially, give one 200-mg tablet with each carbidopa-levodopa dose to a maximum of eight times daily (1600 mg of entacapone). The dosage of carbidopa-levodopa will need to be reduced, particularly if the levodopa dose is higher than 600 mg/day and if the patient has moderate or severe dyskinesias before the entacapone is started.

▪ Monitoring

Entacapone may increase the adverse dopaminergic effects of levodopa (e.g., chorea, confusion, hallucinations), but these can be controlled by reducing the dosage of levodopa.

Common Adverse Effects

Gastrointestinal

Diarrhea. Diarrhea of usually mild to moderate severity may develop 1 to 12 weeks after the initiation of therapy, especially when higher doses are used. These effects may be minimized by a temporary reduction in dosage.

Neurologic

Sedative Effects. Patients may complain of drowsiness and lethargy, especially during the initiation of therapy.

People should not drive or operate complex machinery or perform duties for which they must remain mentally alert until they have gained enough experience with entacapone to know whether it affects their mental or motor performance.

Genitourinary

Urine Discoloration. Patients should be advised that entacapone may change the color of their urine to a brownish orange but that this is harmless and there is no cause for alarm.

Serious Adverse Effects

Neurologic

Neurologic Effects. Entacapone may increase the adverse dopaminergic effects of levodopa, such as chorea, confusion, and hallucinations. Make regularly scheduled subsequent evaluations of mental status, and compare findings. Report alterations. A reduction of the carbidopa-levodopa dosage may be required to alleviate these effects. Provide for patient safety, be emotionally supportive, and assure the patient that these effects usually dissipate as tolerance to the drug develops over the subsequent few weeks.

Cardiovascular

Orthostatic Hypotension. Monitor the patient's blood pressure daily in both the supine and standing positions. Anticipate the development of postural hypotension, and take measures to prevent such an occurrence. Teach the patient to rise slowly from a supine or sitting position, and encourage the patient to sit or lie down if feeling faint.

Drug Interactions

Levodopa. Entacapone and levodopa have additive neurologic effects. This interaction may be beneficial, because it often allows for a reduction in the dosage of the levodopa.

Antihypertensive Agents. A dosage adjustment of the antihypertensive agent is often necessary in response to excessive orthostatic hypotension.

Apomorphine, Isoproterenol, Epinephrine, Levarterenol, Dopamine, Dobutamine, Methyldopa. These agents are metabolized by COMT. The concurrent administration of entacapone with these agents may prolong their duration of activity. Monitor the patient's blood pressure and heart rate.

DRUG CLASS: ANTICHOLINERGIC AGENTS

ACTIONS

Parkinsonism is induced by the imbalance of neurotransmitters in the basal ganglia of the brain. The primary imbalance appears to be a deficiency of dopamine, which results in a relative excess of the cholinergic neurotransmitter acetylcholine. Anticholinergic agents are thus used to reduce the hyperstimulation that is caused by excessive acetylcholine.

USES

The anticholinergic agents reduce the severity of the tremor and drooling that are associated with parkinsonism. Anticholinergic agents are more useful for patients with minimal symptoms and no cognitive impairment. Combination therapy with levodopa and anticholinergic agents is also successful for controlling symptoms of the disease more completely in about half of patients who are already stabilized on levodopa therapy. Anticholinergic agents have little effect on rigidity, bradykinesia, or postural abnormalities. If anticholinergic therapy is to be discontinued, it should be done so gradually to avoid withdrawal effects and the acute exacerbation of parkinsonian symptoms, even for patients in whom there appears to have been no clinical response.

THERAPEUTIC OUTCOMES

The primary therapeutic outcome sought from anticholinergic agents for the treatment of parkinsonism is a reduction in the severity of the tremor and drooling that are caused by a relative excess of acetylcholine in the basal ganglia.

Nursing Implications for Anticholinergic Agent Therapy

Premedication Assessment

1. Perform a baseline assessment of parkinsonism with the use of the UPDRS.
2. Obtain baseline data related to patterns of urinary and bowel elimination.
3. Perform a baseline assessment of the patient's degree of alertness and orientation to name, place, and time before initiating therapy.
4. Take the patient's blood pressure in both the supine and standing positions. Record the pulse rate, rhythm, and regularity.
5. All patients should be screened for the presence of angle-closure glaucoma before the initiation of therapy. Anticholinergic agents may precipitate an acute attack of angle-closure glaucoma. Patients with open-angle glaucoma can safely use anticholinergic agents. Monitor intraocular pressure regularly.

Availability

See Table 15-2.

Dosage and Administration

Adult: PO: See Table 15-2. Administer medication with food or milk to reduce gastric irritation.

Monitoring

Most adverse effects that are observed with anticholinergic agents are direct extensions of the pharmacologic properties of these drugs.

Table 15-2 Anticholinergic Agents

GENERIC NAME	BRAND NAME	AVAILABILITY	INITIAL DOSE (BY MOUTH)	MAXIMUM DAILY DOSAGE (mg)
benztropine mesylate ⇄ *Do not confuse benztropine with benzonatate.*	Cogentin, Apo-Benztropine 🍁	Tablets: 0.5, 1, 2 mg Injection ❗: 1 mg/mL in 2-mL ampules	0.5-1 mg at bedtime	6
diphenhydramine hydrochloride ⇄ *Do not confuse diphenhydramine with dicyclomine or dipyridamole.*	Benadryl Allerdryl ❗ ⇄ *Do not confuse Benadryl with benazepril or Bentyl.*	Tablets: 12.5, 25, 50 mg Capsules: 25, 50 mg Strips, orally disintegrating: 25, 50 mg Elixir: 12.5 mg/5 mL Syrup: 12.5 mg/5 mL Injection ❗: 50 mg/mL in 1-, 10-mL vials; 1 mL cartridges	25-50 mg three or four times daily	400
orphenadrine citrate	Banflex, Norflex ⇄ *Do not confuse Norflex with Keflex, norfloxacin, Noroxin, or Norvasc.*	Tablets: sustained-release, 12 hour: 100 mg Injection: 30 mg/mL in 2-mL vials	50 mg three times daily	150-250
trihexyphenidyl hydrochloride	Trihexy, Trihexyphen 🍁	Tablets: 2, 5 mg Elixir: 2 mg/5 mL	1-2 mg daily	12-15

🍁 Available in Canada.

Common Adverse Effects

Gastrointestinal

Constipation, Dryness of the Mucosa of the Mouth, Throat, and Nose. These symptoms are the anticholinergic effects that are produced by these agents. Patients who are taking these medications should be monitored for the development of these adverse effects. Milder adverse effects (e.g., dry mouth) may subside with continued treatment.

Dryness of the mucosa may be relieved by sucking hard candy or ice chips or by chewing gum. Give stool softeners as prescribed. Encourage adequate fluid intake, foods that provide sufficient bulk, and exercise as tolerated.

Genitourinary

Urinary Retention. If patients develop urinary hesitancy, assess them for bladder distention. Report to the health care provider for further evaluation. These symptoms are the anticholinergic effects produced by these agents. Patients who are taking these medications should be monitored for the development of these adverse effects.

Sensory

Blurred Vision. This symptom may subside with continued treatment. Provide for patient safety.

Serious Adverse Effects

Psychological

Nightmares, Depression, Confusion, Hallucinations. Make regularly scheduled subsequent evaluations of mental status, and compare findings. Report the development of alterations. Provide patient safety during these episodes. Reducing the daily dosage may control these adverse effects.

Cardiovascular

Orthostatic Hypotension. Although this condition is infrequent and generally mild, all anticholinergic agents may cause some degree of orthostatic hypotension, which is manifested by dizziness and weakness, particularly when therapy is being initiated.

Monitor the patient's blood pressure daily in both the supine and standing positions. Anticipate the development of postural hypotension, and take measures to prevent such an occurrence. Teach the patient to rise slowly from a supine or sitting position, and encourage the patient to sit or lie down if feeling faint.

Palpitations, Dysrhythmias. Report for further evaluation.

Drug Interactions

Amantadine, Tricyclic Antidepressants, Phenothiazines. These agents may enhance the anticholinergic adverse effects. Confusion and hallucinations are characteristic of excessive anticholinergic activity. A dosage reduction may be required.

Levodopa. Large doses of anticholinergic agents may slow gastric emptying and inhibit the absorption of levodopa. An increase in the dosage of levodopa may be required.

Get Ready for the NCLEX® Examination!

Key Points

- Parkinson's disease is a progressive neurologic disorder that is caused by the deterioration of dopamine-producing cells in the portion of the brain that is responsible for the maintenance of posture and muscle tone and the regulation of voluntary smooth muscle.
- Normally, a balance exists between dopamine, which is an inhibitory neurotransmitter, and acetylcholine, which is an excitatory neurotransmitter. The symptoms associated with Parkinson's disease develop because of a relative excess of acetylcholine in the brain.
- The goal of treatment is to restore dopamine neurotransmitter function to as close to normal as possible and to relieve the symptoms that are caused by excessive acetylcholine.
- Therapy must be individualized, but selegiline therapy is often started first to slow the development of symptoms. As selegiline becomes less effective, levodopa is started, with or without selegiline.
- Dopamine agonists (e.g., ropinirole, pramipexole) may be added to directly stimulate dopamine receptors.
- Entacapone may be added to levodopa therapy to reduce the metabolism of levodopa, thus prolonging its action.
- Anticholinergic agents may be added at any time to reduce the effects of the "excessive" acetylcholine.
- The nonpharmacologic treatment (e.g., diet, exercise, physical therapy) of Parkinson's disease is equally as important as medication for maintaining the long-term well-being of the patient.

Additional Learning Resources

SG Go to your Study Guide for additional Review Questions for the NCLEX® Examination, Critical Thinking Clinical Situations, and other learning activities to help you master this chapter's content.

Evolve Go to your Evolve Web site (http://evolve.elsevier.com/Clayton) for the following FREE learning resources:

- Animations
- Appendices
- Drug dosage calculators
- Drugs@FDA (a catalog of FDA-approved drug products)
- Gold Standard Patient Teaching Handouts in English and Spanish
- Interactive Drug Flashcards
- Interactive Review Questions for the NCLEX® Examination and more!

Review Questions for the NCLEX® Examination

1. What is the primary purpose of selegiline (Eldepryl) therapy during the early treatment of Parkinson's disease?
   1. Reducing excessive acetylcholine stimulation
   2. Increasing dopamine in the basal ganglia
   3. Slowing symptom progression and delaying the initiation of levodopa therapy
   4. Reducing the metabolism of levodopa, thereby making more available

2. Possible adverse effects of carbidopa-levodopa therapy for a patient with Parkinson's disease include: *(Select all that apply.)*
   1. "on-off" fluctuations.
   2. sudden sleep events.
   3. orthostatic hypotension.
   4. involuntary movements such as chewing and bobbing.
   5. depression.

3. How is carbidopa used for the treatment of Parkinson's disease? *(Select all that apply.)*
   1. As successful monotherapy
   2. In conjunction with levodopa to block peripheral conversion to dopamine
   3. To decrease the incidence of gastrointestinal adverse effects associated with levodopa
   4. To slow disease progression
   5. As a parenteral supplement

4. What does essential patient education for an individual who is receiving levodopa (Larodopa) include?
   1. Assessing vitamins being taken daily
   2. Limiting the daily intake of fluids
   3. Taking medication with food or milk
   4. Providing monthly gait training

5. Drugs classified as anticholinergic agents are used to treat Parkinson's disease because they:
   1. decrease the amount of dopamine available.
   2. increase the amount of acetylcholine available.
   3. decrease the amount of acetylcholine available.
   4. increase the amount of dopamine available.