Cardiovascular

Orthostatic Hypotension. Although orthostatic hypotension occurs infrequently and is generally mild, all anticholinergic agents may cause some degree of this condition, which is manifested by dizziness and weakness, particularly when therapy is 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 it. 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 feels faint.

Palpitations, Dysrhythmias. Contact the health care provider for further evaluation.

Drug Interactions

Amantadine, Tricyclic Antidepressants, Phenothiazines. These agents may potentiate anticholinergic adverse effects. Confusion and hallucinations are characteristic of excessive anticholinergic activity.

Get Ready for the NCLEX® Examination!

Key Points

- The nervous system is one of two primary regulators of body homeostasis and defense. The CNS is composed of the brain and the spinal cord.
- The efferent nervous system is subdivided into the motor nervous system, which controls skeletal muscle, and the autonomic nervous system, which regulates smooth muscle and heart muscle and which controls secretions from certain glands.
- Nerve impulses are passed between neurons and from neurons to end organs by neurotransmitters. The main neurotransmitters of the autonomic nervous system are acetylcholine and norepinephrine. Nerve endings that liberate acetylcholine are called *cholinergic fibers;* those that secrete norepinephrine are called *adrenergic fibers.*
- The CNS is composed of systems of different types of neurons that secrete separate neurotransmitters, such as acetylcholine, norepinephrine, epinephrine, dopamine, serotonin, and gamma-aminobutyric acid.
- The control of neurotransmitters is a primary way to alleviate the symptoms that are associated with many diseases. As shown in Table 13-1, the administration of one type of autonomic nervous system drug can affect several organ systems, and adverse effects can be numerous. Therefore, the use of these drugs requires the monitoring of more than just the symptoms for which the medicine was prescribed.

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 prescriber orders phenytoin (Dilantin) suspension, 150 mg q8h.

   Available: Dilantin suspension, 125 mg/5 mL
   Calculate the correct dose to the nearest whole number: Give _____ mL every _____ hours.

2. Which data in the patient's history and physical examination cause the nurse to question a preoperative medication order for atropine sulfate and morphine before administration?

   1. Excessive oral secretions
   2. Bradycardia
   3. Increased gastric motility
   4. Prostatic enlargement

3. A patient who has recently been prescribed a beta-adrenergic blocking drug presents to the emergency department with a serious adverse effect. Which adverse effect is the patient likely exhibiting?

   1. Hypertension
   2. Angina pectoris
   3. Bronchoconstriction
   4. Cardiac dysrhythmias

4. A nurse was assessing a patient who presented to the clinic with complaints of dizziness and weakness after starting amitriptyline for sleep. The nurse knows that over-the-counter medications may increase therapeutic effects and even cause toxic effects. Which medication that the patient reports taking would be the most concerning?

   1. Thyroid medications
   2. Aspirin
   3. Cold remedies
   4. Vitamin supplements

5. A patient with closed-angle glaucoma can safely receive drugs from which classification? *(select all that apply.)*

   1. Beta-adrenergic receptor blockers
   2. Anticholinergic agents
   3. Cholinergic agents
   4. Alpha-adrenergic receptor blockers
   5. Dopaminergic agents

chapter

14

Drugs Used for Sleep

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Objectives

1. Differentiate among the terms *sedative* and *hypnotic*; *initial*, *intermittent*, and *terminal insomnia*; and *rebound sleep* and *paradoxical excitement*.
2. Identify alterations found in the sleep pattern when hypnotics are discontinued.
3. Cite nursing interventions that can be implemented as an alternative to administering a sedative-hypnotic medication.
4. Compare the effects of barbiturates and benzodiazepines on the central nervous system.
5. Identify the antidote drug used for the management of benzodiazepine overdose.
6. Identify laboratory tests that should be monitored when benzodiazepines or barbiturates are administered for an extended period.

Key Terms

rapid eye movement (REM) sleep (p. 212)
insomnia (ĭn-SŎM-nē-ă) (p. 213)
hypnotic (hĭp-NŎT-ĭk) (p. 213)
sedative (SĔD-ă-tĭv) (p. 213)
rebound sleep (RĒ-bŏwnd SLĒP) (p. 213)

SLEEP AND SLEEP PATTERN DISTURBANCE

Sleep is a state of unconsciousness from which a patient can be aroused by an appropriate stimulus. It is a naturally occurring phenomenon that occupies about one third of an adult's life.

Adequate sleep that progresses through the normal stages is important to maintain body function, including psychiatric equilibrium and the strengthening of the immune system to ward off disease. A normal sleep duration of 7 to 8 hours per night is thought to be optimal for good health. Studies also show that a reduced amount of sleep is associated with overweight and obesity as well as the development of metabolic syndrome (see Chapter 21). Obesity itself is also detrimental to healthy sleep patterns, and it can contribute to the development of sleep apnea. Other studies show a strong connection between a shortened duration of sleep and cardiovascular disease. Individuals who sleep less than 5 hours per night have a threefold increased risk of heart attacks. The National Health Interview Survey also demonstrates a close relationship between symptoms of insomnia and common adverse physical and mental health conditions, including obesity, diabetes mellitus, hypertension, heart failure, anxiety, and depression. *Healthy People 2020* has as one of its objectives the promotion of sleep health, which includes promoting optimal sleep durations and reducing the prevalence and impact of sleep disorders.

Natural sleep rhythmically progresses through phases that provide both physical and mental rest. On the basis of brain-wave activity, muscle activity, and eye movement, normal sleep can be divided into two phases: non–rapid eye movement (NREM) sleep and ***rapid eye movement (REM) sleep***. The NREM phase can be further divided into four stages, each of which is characterized by a specific set of brain-wave activities. Stage 1 is a transition phase between wakefulness and sleep that lasts only a few minutes. Some people experience it as wakefulness, whereas others feel it as drowsiness. Approximately 2% to 5% of sleep is stage 1 sleep. Stage 2 sleep comprises about 50% of normal sleep time. People often experience a drifting or floating sensation, and, if they are awakened during this stage, they will often deny being asleep, responding, "I was just resting my eyes." Stages 1 and 2 are light sleep periods from which a person is easily aroused. Stage 3 is a transition from the lighter to deeper sleep state of stage 4. Stage 4 sleep is dreamless, very restful, and associated with a 10% to 30% decrease in blood pressure, respiratory rate, and basal metabolic rate. Stage 4 sleep is also referred to as *delta sleep* on the basis of the pattern of brain waves that are observed during this stage. Stage 4 sleep comprises 10% to 15% of sleep time in young, healthy adults. Stage 4 sleep diminishes in length as people age, and many people who are more than 75 years old do not demonstrate any stage 4 sleep patterns. Older adults also take longer to cycle through the relaxation stages of NREM sleep, with an increased frequency and duration of awakenings.

During a normal night of sleep, a person will rhythmically cycle from wakefulness through stages 1, 2, 3, and 4; he or she will then go back to stage 3, then to stage 2, and then to REM sleep over the course of about 90 minutes. The early episodes of REM sleep last only a few minutes. However, as sleep progresses, the

amount of REM sleep increases, with REM periods becoming longer and more intense around 5 AM. This type of sleep represents 20% to 25% of sleep time, and it is characterized by REM, dreaming, increased heart rate, irregular breathing, the secretion of stomach acids, and some muscular activity. REM sleep appears to be an important time for the subconscious mind to release anxiety and tension and reestablish a psychiatric equilibrium.

Insomnia is the most common sleep disorder known; 95% of all adults experience insomnia at least once during their lives, and up to 35% of adults will have insomnia during a given year. The term ***insomnia*** is defined as the inability to sleep. In general, insomnia is not a disease but rather a symptom of physical or mental stress. It is usually mild and lasts only a few nights. Common causes are changes in lifestyle or environment (e.g., hospitalization), pain, illness, the excess consumption of products that contain caffeine (e.g., coffee, energy drinks) or alcohol, eating large or rich meals shortly before bedtime, and stress. *Initial insomnia* is the inability to fall asleep when desired, *intermittent insomnia* is the inability to stay asleep, and *terminal insomnia* is characterized by early awakening with the inability to fall asleep again. Insomnia is also classified in accordance with its duration. A sleep disturbance that lasts only a few nights is considered to be *transient insomnia*. A sleep disturbance that lasts less than 3 weeks is referred to as *short-term insomnia*, and it is usually associated with travel across time zones, illness, or anxiety (e.g., job-related changes, financial stress, examinations, emotional relationships). Chronic insomnia requires at least 1 month of sleep disturbance before the individual is diagnosed with a sleep disorder. About 10% of adults and up to 20% of older people report having chronic insomnia. Women report suffering from insomnia twice as frequently as men. A higher incidence of insomnia is reported by older adults, the unemployed, those of lower socioeconomic status, and the recently separated or widowed. As many as 40% of patients with chronic insomnia also suffer from psychiatric disorders (e.g., anxiety, depression, substance abuse). People with chronic insomnia often develop fatigue or drowsiness that interferes with daytime functioning and employment responsibilities.

SEDATIVE-HYPNOTIC THERAPY

Drugs that are used in conjunction with altered patterns of sleep are known as *sedative-hypnotic agents*. A ***hypnotic*** is a drug that produces sleep; a ***sedative*** quiets the patient and gives him or her a feeling of relaxation and rest, but this is not necessarily accompanied by sleep. A good hypnotic should provide the following actions within a short period of time: the onset of restful, natural sleep; a duration of action that allows a patient to awaken at the usual time; a natural awakening with no "hangover" effects; and no danger of habit formation. Unfortunately, the ideal hypnotic is not available; however, for short-term use, benzodiazepines and three benzodiazepine receptor agonists—zolpidem, zaleplon, and eszopiclone—are available. The most commonly used sedative-hypnotic agents increase total sleeping time, especially the time spent in stage 2 sleep (i.e., light sleep); however, they also decrease the number of REM periods and the total time spent in REM sleep. REM sleep is needed to help maintain a mental balance during daytime activities. When REM sleep is decreased, there is a strong physiologic tendency to make it up. Compensatory REM sleep or ***rebound sleep*** seems to occur even when hypnotic agents are used for only 3 or 4 days. After the chronic administration of sedative-hypnotic agents, REM rebound may be severe and accompanied by restlessness and vivid nightmares. Depending on the frequency of hypnotic administration, normal sleep patterns may not be restored for weeks. The effects of REM rebound may enhance an individual's chronic use of and dependence on these agents to avoid the unpleasant consequences of rebound sleep. Because of this, a vicious cycle occurs as the normal physiologic need for sleep is not met and the body attempts to compensate.

Because sedative-hypnotic agents have many adverse effects, especially with long-term use, medications that are recognized for other primary uses are being used by health care providers for the treatment of insomnia. Antidepressants such as amitriptyline, trazodone, and mirtazapine are prescribed in lower dosages for their sedative effects to assist patients with getting to sleep (see Chapter 17). Anticonvulsants that are used in this way include gabapentin and topiramate (see Chapter 19). Antipsychotic agents such as quetiapine and olanzapine are prescribed for patients with psychoses who also have insomnia (see Chapter 18). However, it is important to note that no extensive studies have been completed regarding the use of these antidepressants, antipsychotics, and anticonvulsants for insomnia, so their long-term effects are unknown, and their use for treating chronic insomnia cannot be recommended.

ACTIONS

Sedatives, which are used to produce relaxation and rest, and hypnotics, which are used to produce sleep, are not always different drugs. Their effects may depend on the dosage and the condition of the patient. A small dose of a drug may act as a sedative, whereas a larger dose of the same drug may act as a hypnotic and produce sleep.

The sedative-hypnotic medications may be classified into three groups: barbiturates; benzodiazepines; and nonbarbiturate, nonbenzodiazepine sedative-hypnotic medications.

USES

The primary uses of sedative-hypnotic medications are as follows: (1) to improve sleep patterns for the temporary treatment of insomnia; and (2) to decrease the level of anxiety and increase relaxation or sleep before diagnostic or operative procedures.

❖ Nursing Implications for Sedative-Hypnotic Therapy

▪ Assessment

Central Nervous System Function. Since sedative-hypnotic drugs depress overall central nervous system (CNS) function, identify the patient's level of alertness and orientation as well as his or her ability to perform various motor functions.

Vital Signs. Obtain the patient's current blood pressure, pulse, and respiration rates before initiating drug therapy.

Sleep Pattern. Assess the patient's usual pattern of sleep, and obtain information about the pattern of sleep disruption (e.g., difficulty falling asleep, inability to remain sleep the entire night, awakening during the early morning hours and unable to return to a restful sleep).

Ask about the amount of sleep (i.e., number of hours) that the patient considers normal and how his or her insomnia is managed at home. Does the patient have a regular time to go to bed and wake up? If the patient is taking medications, determine the drug, dosage, and frequency of administration and whether this may be contributing to sleeplessness. (Medicines that may induce or aggravate insomnia include theophylline, caffeine, pseudoephedrine, ephedrine, nicotine, levodopa, corticosteroids, and selective serotonin reuptake inhibitor antidepressants.)

Patients with persistent insomnia should be carefully monitored for the number of naps taken during the day. Investigate the type of activities that the patient performs immediately before going to bed.

Anxiety Level. Assess the patient's exhibited degree of anxiety. Is it really a sedative-hypnotic medication that the patient needs, or does the patient just need someone to listen to him or her? Ask about the stressors that the patient has been experiencing in his or her personal and work environments.

Environmental Control. Obtain data related to possible disturbances present in the individual's sleeping environment that may interfere with sleep (e.g., room temperature, lights, noise, traffic, restlessness, a snoring partner).

Nutritional Needs. Obtain a dietary history to identify sources of caffeinated products that may act as stimulants.

Alcohol Intake. Although alcohol causes sedation, it disrupts sleep patterns and may cause early-morning awakening.

Exercise. Obtain data related to the patient's usual degree of physical activity and at what times during the day he or she is most active.

Respiratory Status. People with respiratory disorders and those who snore heavily may have low respiratory reserves and should not receive hypnotic agents because of their potential to cause respiratory depression.

▪ Implementation

Vital Signs. Obtain the patient's vital signs periodically as the situation indicates.

Preoperative Medication. Give the patient preoperative medications at the specified time.

Monitoring Effects. When a medication is administered, carefully assess the patient at regular intervals for the drug's therapeutic and adverse effects.

As-Needed Medications (PRN). If giving the patient PRN medications, assess the record for the effectiveness of previously administered therapy. It is sometimes necessary to repeat a medication if an order permits doing so. This is done at the nurse's discretion on the basis of the evaluation of a particular patient's needs.

Patient Education

Promote Good Sleep Hygiene

Bedtime. Encourage the patient to choose a standard time to go to bed to help the body to establish a rhythm and routine.

Nutrition. Teach the patient appropriate nutrition information concerning the FDA's recommendations of MyPlate, adequate fluid intake, and vitamin use. Communicate the information at the educational level of the patient.

Avoid Heavy Meals During the Evening. Alcohol and caffeine consumption should be reduced or discontinued, especially within several hours of bedtime. Introduce the patient to decaffeinated or herbal products that can be substituted for caffeinated foods. Help the patient to avoid products that contain caffeine, such as coffee, tea, energy drinks, soft drinks, and chocolate. Limit the total daily intake of these items, and provide the patient with warm milk and crackers as a bedtime snack. Protein foods and dairy products contain an amino acid that synthesizes serotonin, which is a neurotransmitter that has been found to increase sleep time and decrease the time required to fall asleep.

For insomnia, suggest that the patient drink warm milk about 30 minutes before going to bed.

Personal Comfort. Position the patient for maximum comfort, provide a back rub, encourage the patient to empty the bladder, and be certain that the bedding is clean and dry. Take time to meet the patient's individual needs and to calm his or her fears. Foster a trusting relationship.

Environmental Control. Tell the patient to sleep in the proper environment, such as a quiet, darkened room

free from distractions and to avoid using the bedroom or watching television, preparing work for the following day, eating, and paying bills. Provide adequate ventilation, subdued lighting, and the correct room temperature, and control of traffic in and out of the patient's room.

For safety, instruct the patient to leave a nightlight on and not smoke in bed after taking medication.

Activity and Exercise. Suggest the inclusion of exercise in the patient's daily activities so that the patient obtains sufficient exercise and is tired enough to sleep. For some individuals, plan a quiet "unwinding" time before retiring for the night. For children, assist with sleep by providing a warm bath and structure prior to bedtime. Try a bedtime story that is pleasant and soothing (rather than one that may cause anxiety or fear).

Stress Management

- Explore personal and work stressors that could have a bearing on the patient's insomnia. Some stressors may exist in the work environment; therefore, the involvement of the occupational health nurse, along with a thorough exploration of work factors, may be appropriate. Stress produced within the dynamics of the family may require professional counseling.
- Teach the patient relaxation techniques and personal comfort measures (e.g., a warm bath) to relieve stress. Playing soft music may also promote relaxation.
- Make referrals for the mastery of biofeedback, meditation, or other techniques to reduce stress levels.
- Encourage the patient to openly express feelings about his or her stress and insomnia. The adjustment to this situation involves working through great personal fears, frustrations, hostilities, and resentments.
- Explore the coping mechanisms that the person uses in response to stress, and identify methods of channeling these toward positive realistic goals and alternatives to the use of medication.

Fostering Health Maintenance. Throughout the course of treatment, discuss medication information and how it will benefit the patient. Stress the importance of nonpharmacologic interventions and the long-term effects that compliance with the treatment regimen can provide.

Provide the patient or the patient's significant others with important information that is contained in the specific drug monographs for the medicines prescribed. Additional health teaching and nursing interventions for the common adverse effects and serious adverse effects that require contact with the health care provider are described in the following drug monographs (e.g., barbiturates, benzodiazepines, miscellaneous sedative-hypnotic medications).

Written Record. Enlist the patient's help with developing and maintaining a written record of monitoring parameters (e.g., extent and frequency of insomnia); see the Patient Self-Assessment Form for Sleeping Medication 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 these follow-up visits, focus on issues that will foster the patient's adherence with the therapeutic interventions that have been prescribed.

DRUG THERAPY FOR SLEEP DISTURBANCE

DRUG CLASS: BARBITURATES

The first barbiturate went on the market as a sedative-hypnotic product in 1903. It became so successful that chemists identified some 2500 compounds, of which more than 50 went on to be distributed commercially. Barbiturates became such a mainstay of therapy that fewer than a dozen other sedative-hypnotic agents were successfully marketed through 1960. The release of the first benzodiazepine—chlordiazepoxide—in 1961 started the decline in the use of barbiturates. However, several barbiturate compounds are still prescribed (Table 14-1).

ACTIONS

Barbiturates can reversibly depress the activity of all excitable tissues. The CNS is particularly sensitive, but the degree of depression—ranging from mild sedation to deep coma and death—depends on the dose, the route of administration, the degree of tolerance from any previous use, the degree of excitability of the CNS at the time of administration, and the condition of the patient. When used for hypnosis, barbiturates suppress REM and the sleep patterns of stages 3 and 4. Because barbiturates have long half-lives, residual daytime sedation is a common adverse effect.

USES

Barbiturates are now rarely used for sedation and hypnosis, but when they are used, therapy should be limited to 2 weeks, because tolerance to sedation and hypnosis develops during this time. The ultra–short-acting agents (e.g., methohexital, thiopental) may be administered intravenously as general anesthetics. Short-acting barbiturates (e.g., pentobarbital, secobarbital) are used for sedation before diagnostic procedures; intermediate-acting barbiturates (e.g., amobarbital, butalbital) are used as sedative-hypnotic agents; and long-acting barbiturates (e.g., mephobarbital, phenobarbital) are used primarily as anticonvulsant drugs.

Table 14-1 Barbiturates

GENERIC NAME	BRAND NAME	AVAILABILITY	ADULT ORAL DOSAGE	COMMENTS
amobarbital ❗	—	Injection: 500-mg vials	Sedation: 30-50 mg IM two or three times daily Hypnosis: 65-200 mg IM 30 min before bedtime	Intermediate-acting; schedule II; used primarily as a sedative before anesthesia or during labor
butabarbital	Butisol	Tablets: 30, 50 mg Elixir: 30 mg/5 mL	Sedation: 15-30 mg three or four times daily Hypnosis: 50-100 mg at bedtime	Intermediate-acting; schedule III; elixir contains 7.5% alcohol; used primarily as a daytime sedative and a bedtime hypnotic
mephobarbital	Mebaral	Tablets: 32, 50, 100 mg	Sedation: 32-100 mg three or four times daily Anticonvulsant: 400-600 mg daily	Long-acting; schedule IV; used primarily as an anticonvulsant; may also be used as a daytime sedative
pentobarbital ❗	Nembutal	Injection: 50 mg/mL	Hypnosis: 150-200 mg IM at bedtime Sedation: 2-6 mg/kg IV (maximum, 100 mg)	Short-acting; schedule II; used primarily as a preanesthetic sedative for pediatric patients
phenobarbital ❗	Luminal, Solfoton	Tablets: 15, 16, 30, 60, 97.2, 100 mg Elixir: 20 mg/5 mL Injection: 20, 60, 65, 130 mg/mL	Sedation: 8-30 mg two or three times daily Hypnosis: 100-200 mg Anticonvulsant: 60-100 mg two or three times daily	Long-acting; schedule IV; currently used most commonly as an anticonvulsant; may also be used as a daytime sedative, preanesthetic, or hypnotic agent; also available for use IM and IV; elixir contains 13.5% alcohol
secobarbital	Seconal	Capsules: 100 mg	Hypnosis: 100 mg at bedtime	Short-acting; schedule II; used primarily as a daytime sedative or a bedtime hypnotic; therapy not recommended for more than 14 days

❗ High-alert medication.

Nursing Implications of Barbiturate Therapy

Premedication Assessment

1. Seek information from the patient regarding any prior use of sedative-hypnotic medications.
2. Obtain information related to the patient's baseline neurologic function (e.g., degree of alertness).
3. Obtain the vital signs (e.g., blood pressure, pulse, respirations, pain rating using a scale of 0 to 10).

Availability

See Table 14-1.

Dosage and Administration

See Table 14-1. Rapidly discontinuing barbiturates after the long-term use of high dosages may result in symptoms that are similar to those of alcohol withdrawal. These may vary from weakness and anxiety to delirium and grand mal seizures. Treatment consists of cautious and gradual withdrawal over the course of 2 to 4 weeks.

Monitoring

General adverse effects of barbiturates include drowsiness, lethargy, headache, muscle or joint pain, and mental depression.

Common Adverse Effects

Neurologic

Hangover, Sedation, Lethargy, Diminished Alertness. Patients may complain of "morning hangover," blurred vision, and transient hypotension on arising. The hangover feeling commonly occurs after the administration of hypnotic doses of long-acting barbiturates. Patients may display a dulled affect, a subtle distortion of mood, and impaired coordination. Explain to the patient the need to first rise to a sitting position, equilibrate, and then stand. Assistance with ambulation may be required. If the hangover effect becomes troublesome, there should be a reduction in the dosage, a

change in the medication, or both. People who work around machinery, drive a car, pour and give medicines, or perform other duties for which they must remain mentally alert should not take these medications while working.

Serious Adverse Effects

Psychological

Excessive Use or Abuse. The habitual use of barbiturates may result in physical dependence. Discuss the case with the physician, and make plans to cooperatively approach the gradual withdrawal of the medications being abused. Help the patient to recognize the abuse problem. Identify the patient's underlying needs, and plan for the more appropriate management of those needs. Provide for the emotional support of the individual; display an accepting attitude, and be kind but firm.

Paradoxical Response. Older patients and those who are in severe pain may respond paradoxically to barbiturates by demonstrating excitement, euphoria, restlessness, and confusion. Provide supportive physical care and safety during these responses. Assess the level of the patient's excitement, and deal calmly with the individual. During periods of excitement, protect the patient from harm, and provide for the physical channeling of energy (e.g., walking). Seek a change in the patient's medication order.

Hypersensitivity. Reactions to barbiturates are infrequent, but they may be serious. Report symptoms of hives, pruritus, rash, high fever, or the inflammation of the mucous membranes for evaluation by a health care provider. Withhold further barbiturate administration until the health care provider's approval has been granted.

Blood Dyscrasias. Blood dyscrasias are rare; however, laboratory studies (e.g., red and white blood cell counts, differential counts, platelets) should be scheduled when symptoms warrant. Stress the importance of the patient returning for this laboratory work. Monitor the patient for the development of sore throat, fever, purpura, jaundice, or excessive and progressive weakness.

Drug Interactions

Antihistamines, Alcohol, Analgesics, Anesthetics, Tranquilizers, Valproic Acid, Monoamine Oxidase Inhibitors, and Other Sedative-Hypnotics. These agents increase the toxic effects of barbiturates. Monitor the patient for excessive sedation, and reduce the dosage of the barbiturate, if necessary.

Phenytoin. The effects of barbiturates on phenytoin are variable. Serum levels may be ordered, and a change in phenytoin dosage may be required. Observe patients for increased seizure activity and for signs of phenytoin toxicity (e.g., nystagmus, sedation, lethargy).

Reduced Effects. Barbiturates reduce the effects of the following medicines:

- *Warfarin:* Monitor the patient's prothrombin time, and increase the dosage of warfarin, if necessary.
- *Estrogens:* This drug interaction may be critical in patients who are receiving oral contraceptives that contain estrogen. If patients develop spotting and breakthrough bleeding, a change in oral contraceptives and the use of alternative forms of contraception should be considered.
- *Corticosteroids, beta-adrenergic blockers, metronidazole, doxycycline, antidepressants, quinidine, and chlorpromazine:* The patient should be monitored for signs of increased activity of the illness for which the medication was prescribed. Dosage increases may be necessary, or the barbiturate may have to be discontinued.

DRUG CLASS: BENZODIAZEPINES

Benzodiazepines have been extremely successful products from both the therapeutic and safety standpoints. A major advantage of these drugs as compared with the barbiturate and other nonbarbiturate sedative-hypnotic agents is the wide safety margin between the therapeutic and lethal doses. Intentional and unintentional overdoses well above the normal therapeutic doses are well tolerated and not fatal.

More than 2000 benzodiazepine derivatives have been identified, and more than 100 have been tested for sedative-hypnotic or other activity. Although there are many similarities among the benzodiazepines, they are difficult to characterize as a class. Some benzodiazepines are effective anticonvulsants, others serve as antianxiety and muscle-relaxant agents, and others are used as sedative-hypnotic drugs.

ACTIONS

It is thought that the benzodiazepines have similar mechanisms of action as CNS depressants but that individual drugs within the benzodiazepine family act more selectively at specific sites, thereby allowing for a variety of uses (e.g., sedative-hypnotic effects, muscle relaxation, antianxiety effects, anticonvulsant action). Those drugs that are used as sedative-hypnotic agents bind to receptors that stimulate the release of gamma-aminobutyric acid, an inhibitory neurotransmitter in the CNS, thereby initiating sleep and increasing total sleep time. They increase stage 2 sleep while decreasing stage 3 and 4 sleep and, to a lesser extent, REM sleep.

USES

Benzodiazepines are the most commonly used type of sedative-hypnotic drugs. Estazolam, flurazepam, quazepam, temazepam, and triazolam are the benzodiazepines that have been marketed for hypnosis. Triazolam, which is a shorter-acting hypnotic, as well as estazolam and temazepam, which are intermediate-acting hypnotic agents, do not contain

active metabolites and therefore do not accumulate as readily after several days of dosing. Flurazepam and quazepam have long half-lives and active metabolites, thus making patients much more susceptible to hangovers the day after use.

When benzodiazepine therapy is started, patients experience deep and refreshing sleep. However, benzodiazepine-induced sleep varies from normal sleep in that there is less REM sleep involved. With the chronic administration of benzodiazepines, the amount of REM sleep gradually increases as tolerance develops to the REM-suppressant effects of the drugs. When benzodiazepines are discontinued, a rebound increase in REM sleep may occur despite the patient's tolerance. During the rebound period, the number of dreams stays about the same, but many of the dreams are reported to be bizarre. After long-term use of most benzodiazepines, there is also a rebound in insomnia. Consequently, it is important to use these agents only for short courses (i.e., usually no more than 4 weeks) of therapy.

The short-acting benzodiazepines (e.g., midazolam) are used parenterally as preoperative sedatives and intravenously for conscious sedation before short diagnostic procedures or for the induction of general anesthesia. Midazolam has a more rapid onset of action than diazepam and a much shorter duration. It also produces a greater degree of amnesia and a shorter duration of action as compared with diazepam, again making it beneficial for short diagnostic and operative procedures. Lorazepam is used as an antianxiety agent in general, but it is particularly useful before diagnostic procedures when a longer duration of action is required; a parenteral dosage form is available. It also has no active metabolites that may prolong sedation.

Flumazenil (Romazicon) is an antidote that is administered intravenously for the complete or partial reversal of the effects of benzodiazepines that are used as general anesthetics or during diagnostic or therapeutic procedures. Flumazenil is also used for the management of an intentional or accidental overdose of benzodiazepines.

THERAPEUTIC OUTCOMES

The primary therapeutic outcomes sought from benzodiazepine therapy are as follows:

1. To produce mild sedation
2. For short-term use, to produce sleep
3. Preoperative sedation with amnesia

Nursing Implications for Benzodiazepines

Premedication Assessment

1. Record the patient's baseline vital signs (e.g., blood pressure, pulse, respirations); measure the patient's blood pressure in both sitting and lying positions.
2. Check for a history of blood dyscrasias or hepatic disease, and determine whether patient is in the first trimester of pregnancy.
3. Assess the patient's level of pain.

Availability

See Table 14-2.

Dosage and Administration

See Table 14-2. The habitual use of benzodiazepines may result in physical and psychological dependence. The rapid discontinuance of benzodiazepines after long-term use may result in symptoms that are similar to those of alcohol withdrawal, such as weakness, anxiety, delirium, and grand mal seizures. These symptoms may not appear for several days after discontinuation. Treatment consists of the gradual withdrawal of benzodiazepines over the course of 2 to 4 weeks.

Pregnancy and Lactation. It is generally recommended that benzodiazepines not be administered during at least the first trimester of pregnancy. There may be an increased incidence of birth defects if these drugs are taken, because these agents readily cross the placenta and enter the fetal circulation.

Mothers who are breastfeeding should not receive benzodiazepines regularly. These agents readily cross into breast milk and exert a pharmacologic effect on the infant.

Monitoring

Common Adverse Effects

Neurologic

Drowsiness, Hangover, Sedation, Lethargy, Decreased Level of Alertness. Patients may complain of "morning hangover" and blurred vision. If the hangover effect continues and becomes troublesome, there should be a reduction in the drug dosage, a change in the medication, or both. People who work around machinery, drive a car, pour and give medications, or perform other duties for which they must remain mentally alert should not take these medications while working.

Cardiovascular

Transient Hypotension When Arising. Explain to the patient the need for arising first to a sitting position, equilibrating, and then standing. Assistance with ambulation may be required.

Serious Adverse Effects

Psychological

Confusion, Agitation, Hallucinations, Amnesia. All benzodiazepines have the potential to cause these symptoms, particularly in older patients who have been taking higher doses or taking the drugs for prolonged periods. Discuss the case with the physician, and make plans to approach the gradual reduction of the medication cooperatively to prevent withdrawal symptoms and rebound insomnia.

Table 14-2 Benzodiazepines Used for Sedation and Hypnosis

GENERIC NAME	BRAND NAME	AVAILABILITY	ADULT ORAL DOSAGE	COMMENTS
estazolam	—	Tablets: 1, 2 mg	Hypnosis: 1-2 mg at bedtime	Intermediate-acting; schedule IV; used to treat insomnia; tapering therapy recommended to reduce rebound insomnia; minimal morning hangover
flurazepam	Flurazepam, Novoflupam 🍁	Capsules: 15, 30 mg	Hypnosis: 15-30 mg at bedtime	Long-acting; schedule IV; used for short-term treatment of insomnia for up to 4 wk; morning hangover may be significant; rebound insomnia and rapid eye movement sleep occur less frequently
lorazepam ❗ ⇄ *Do not confuse lorazepam with loperamide.*	Ativan, Novo-Lorazem 🍁 ⇄ *Do not confuse Ativan with Ambien or Atarax.*	Tablets: 0.5, 1, 2 mg Oral solution: 2 mg/mL Injection: 2 mg and 4 mg/mL in 1-, 10-mL vials; 2, 4 mg/mL in prefilled syringes	Hypnosis: 2-4 mg at bedtime	Used primarily to treat insomnia but may also be used for preoperative anxiety, status epilepticus; administration IM and IV also available
midazolam	Apo-Midazolam 🍁	Syrup: 2 mg/mL Injection: 1, 5 mg/mL in 1-, 2-, 5-, 10-mL vials; 2 mg/2 mL in prefilled syringes	Preoperatively: 0.07-0.08 mg/kg IM 1 hr before surgery Induction of anesthesia: 0.2-0.3 mg/kg IV Conscious sedation: 0.5-2 mg IV slowly over 2 min; repeat every 2-3 min as needed	Short-acting; schedule IV; causes amnesia in most patients; lower dosages for patients more than 55 yr old Onset: IM, 15 min; IV, 3-5 min Duration: IM, 30-60 min; IV, 2-6 hr
quazepam	Doral	Tablets: 15 mg	Hypnosis: 7.5-15 mg at bedtime	Long-acting; schedule IV; used to treat insomnia; tapering therapy recommended to reduce rebound insomnia; morning hangover may be significant
temazepam	Restoril ⇄ *Do not confuse Restoril with Remeron, Risperdal, or Vistaril.* Nu-Temazepam 🍁	Capsules: 7.5, 15, 22.5, 30 mg	Hypnosis: 15-30 mg at bedtime	Intermediate-acting; schedule IV; used to treat insomnia; minimal if any morning hangover; rebound insomnia may occur
triazolam	Halcion ⇄ *Do not confuse Halcion with Haldol.* Gen-Triazolam 🍁	Tablets: 0.125, 0.25 mg	Hypnosis: 0.125-0.5 mg at bedtime	Short-acting; schedule IV; used to treat insomnia but tends to lose effectiveness within 2 wk; tapering therapy recommended to reduce rebound insomnia; rapid onset of action; no morning hangover

🍁 Available in Canada.
❗ High-alert medication.

Excessive Use or Abuse. The habitual use of benzodiazepines may result in physical dependence. Discuss the case with the prescriber, and make plans to cooperatively approach the gradual withdrawal of the medications that are being abused. Assist the patient with recognizing the abuse problem. Identify the patient's underlying needs, and plan for the more appropriate management of those needs. Provide for the emotional support of the individual, and display an accepting attitude. Be kind but firm.

Blood Dyscrasias. Routine laboratory studies (e.g., red and white blood cell counts, differential and platelet counts) should be scheduled. Stress that the patient should return for these tests. Monitor the patient for the development of a sore throat, fever, purpura, jaundice, or excessive and progressive weakness.

Hepatotoxicity. The symptoms of hepatotoxicity are anorexia, nausea, vomiting, jaundice, hepatomegaly, splenomegaly, and abnormal liver function tests (e.g., elevated levels of bilirubin, aspartate aminotransferase [AST], alanine aminotransferase [ALT], gamma-glutamyltransferase [GGT], and alkaline phosphatase; increased prothrombin time).

Drug Interactions

Antihistamines, Alcohol, Analgesics, Anesthetics, Tranquilizers, Narcotics, Cimetidine, Disulfiram, Isoniazid, Rifampin, Erythromycin, Other Sedative-Hypnotics. All of these agents increase the toxic effects of these drugs.

Smoking. Smoking enhances the metabolism of benzodiazepines. Larger doses may be necessary to maintain sedative effects in patients who smoke.

DRUG CLASS: NONBARBITURATE, NONBENZODIAZEPINE SEDATIVE-HYPNOTIC AGENTS

ACTIONS

The nonbarbiturate, nonbenzodiazepine sedative-hypnotic drugs are listed in Table 14-3. They represent a variety of chemical classes, all of which cause CNS depression. These include the histamine-1 blockers (i.e., antihistamines); melatonin, which is a hormone secreted from the pineal gland (see Chapter 48); a melatonin-receptor stimulant; and valerian, which is an herbal medicine (see Chapter 48). The newest class of agents is the benzodiazepine receptor agonists. All of these drugs have somewhat variable effects on REM sleep, tolerance development, rebound REM sleep, and insomnia.

USES

Antihistamines—particularly diphenhydramine and doxylamine—have sedative properties that may be used for the short-term treatment of mild insomnia. These drugs are common ingredients in over-the-counter sleep aids. Tolerance develops after only a few nights of use; thus, increasing the dose actually causes a more restless and irregular sleep pattern. Doxylamine has a longer half-life of approximately 10 hours, which frequently causes a morning hangover.

Melatonin is available over the count as a sleep aid. It appears to be particularly useful for patients who have been traveling through time zones and who are suffering from jet lag. Because this medicine is classified as a dietary supplement and thus is not regulated by the U.S. Food and Drug Administration, there may be inconsistencies with regard to its potency.

Ramelteon is a melatonin-receptor stimulant, and it is the first member of this class to be approved by the U.S. Food and Drug Administration. It is used to treat patients with insomnia who have difficulty falling asleep.

Valerian, which is an herbal medicine, has been used for hundreds of years as a mild sedative. Its mechanism of action is unknown, but it may inhibit the enzyme that metabolizes gamma-aminobutyric acid GABA, thereby prolonging the inhibitory neurotransmitter's duration of action. Like melatonin, valerian is classified as a dietary supplement, and thus it is not regulated by the U.S. Food and Drug Administration. There may be differences in the strength and potency of this substance among distributors.

As a result of their effect on sleep patterns and REM sleep, the use of benzodiazepines is diminishing in favor of the newer benzodiazepine receptor agonists such as zaleplon, zolpidem, and eszopiclone, which bind to different gamma-aminobutyric acid GABA receptors in the CNS. In contrast with benzodiazepines and barbiturates, zaleplon, zolpidem, and eszopiclone have less effect on sleep stages 3 and 4 and REM sleep. These agents are used as hypnotics to produce sleep. The recommended period of use for these benzodiazepine receptor agonists is 7 to 10 days, with reevaluation of the patient occurring if use exceeds 2 to 3 weeks. Daytime drowsiness is generally not a problem with these agents because of their short half-lives, although it is more likely with eszopiclone. The return of insomnia has been reported after the discontinuation of these drugs. Zaleplon has a short onset of action and a duration of 2 to 4 hours. It is used clinically for people who have difficulty getting to sleep and for those who awaken in the middle of the night. Zolpidem has a similar onset of action but a duration of 3 to 5 hours. It is more effective for helping patients get to sleep and for prolonging sleep duration without causing a morning hangover.

Eszopiclone is the newest of these agents. Its onset of action is somewhat slower than that of the other two agents, but its duration of action is 5 to 8 hours, thus making it more effective for patients who wake up during the night or early morning. It has been reported to cause morning hangover, especially among older patients and with higher doses.

Table 14-3 Nonbarbiturate, Nonbenzodiazepine Sedative-Hypnotic Agents

GENERIC NAME	BRAND NAME	AVAILABILITY	ADULT ORAL DOSAGE	COMMENTS
chloral hydrate ❗	Somnote PMS-Chloral Hydrate 🍁	Capsules: 500 mg Syrup: 500 mg/5 mL	Sedation: 250 mg three times daily after meals Hypnosis: 500 mg to 1 g 15-30 min before bedtime	The original "Mickey Finn"; schedule IV; used primarily as a bedtime hypnotic but also as a preoperative sedative because it does not depress respirations or the cough reflex; may cause nausea; administer with a full glass of water; do not chew capsules; see Drug Interactions on p. 222
dexmedetomidine ❗	Precedex	Infusion: 100 mcg/mL in 2-mL vials	Intravenous sedation: 1 mcg/kg over 10 min followed by the infusion of 0.2-0.7 mcg/kg/hr with the use of a controlled-infusion device	For the sedation of initially intubated and mechanically-ventilated patients in the intensive care setting; infusion should not continue for more than 24 hr
diphenhydramine ⇄ *Do not confuse diphenhydramine with dicyclomine or dipyridamole.*	Benadryl ⇄ *Do not confuse Benadryl with benazepril or Bentyl.* Simply Sleep 🍁	Tablets: 12.5, 25, 50 mg Capsules: 25, 50 mg Liquid: 12.5 mg/5 mL	Sedation: 25-50 mg at bedtime	Over-the-counter availability; used for mild insomnia for up to 1 wk; tolerance develops, and increased dosage causes more adverse effects with no additional efficacy
doxylamine	Unisom	Tablets: 25 mg	Sedation: 25 mg at bedtime	Over-the-counter availability; morning hangover may be significant; see diphenhydramine on p. 220
eszopiclone	Lunesta	Tablets: 1, 2, 3 mg	Hypnosis: 2-3 mg	Onset within 45 min; duration 5-8 hr Older adult patients should start with 1 mg; see Drug Interactions on p. 222
melatonin	—	—	—	See Chapter 48, p. 824
ramelteon ⇄ *Do not confuse ramelteon with Remeron, Remegel, Reminyl, or Renagel.*	Rozerem ⇄ *Do not confuse Rozerem with Remeron, Remegel, Reminyl, or Renagel.*	Tablets: 8 mg	Hypnosis: 8 mg within 30 min of bedtime	Do not take with or immediately after a high-fat meal
valerian ⇄ *Do not confuse valerian with Valium.*	—	—	—	See Chapter 48, p. 821
zaleplon ⇄ *Do not confuse zaleplon with zolpidem.*	Sonata ⇄ *Do not confuse Sonata with Soma.*	Capsules: 5, 10 mg	Hypnosis: 10 mg at bedtime	Schedule IV; short-acting; onset within 30 min, duration 2-4 hr; older adults or low-weight patients should start with 5 mg
zolpidem ⇄ *Do not confuse zolpidem with zaleplon.*	Ambien ⇄ *Do not confuse Ambien with Ativan or Atarax.* Ambien CR Edluar Zolpimist	Tablets: 5, 10 mg Tablets, controlled-release: 6.25, 12.5 mg Tablets, sublingual: 5, 10 mg Oral spray: 5 mg/actuation	Hypnosis: 10 mg at bedtime Hypnosis: 12.5 mg at bedtime	Schedule IV; short-acting; onset within 30 min, duration 3-5 hr; older adult patients should start with 5-mg immediate-release tablets or 6.25-mg controlled-release tablets; place a sublingual tablet under tongue, where it will disintegrate in seconds; do not chew, break, or split the tablet; sublingual tablets and oral spray should not be administered with or immediately after a meal

🍁 Available in Canada.
❗ High-alert medication.

Chloral hydrate is one of the oldest manufactured sedative-hypnotic agents. Its use for the treatment of insomnia has been replaced by benzodiazepines and the newer nonbarbiturate, nonbenzodiazepines, but it is still used as a sedative for diagnostic procedures.

THERAPEUTIC OUTCOMES

The primary therapeutic outcomes sought from miscellaneous sedative-hypnotic agents are as follows:

1. To produce mild sedation
2. For short-term use to produce sleep

Nursing Implications of Miscellaneous Sedative-Hypnotic Agents

Premedication Assessment

1. Record the patient's baseline vital signs (i.e., blood pressure, pulse, and respirations); measure the patient's blood pressure with him or her in both sitting and lying positions.
2. Check for the patient's history of blood dyscrasias or hepatic disease.
3. Assess the patient's level of pain using a scale of 0 to 10.

Availability

See Table 14-3.

Dosage and Administration

See Table 14-3. The habitual use of sedative-hypnotic agents may result in physical dependence. Rapid discontinuance after long-term use may result in symptoms that are similar to those of alcohol withdrawal, such as weakness, anxiety, delirium, and generalized seizures. Treatment consists of gradual withdrawal over the course of 2 to 4 weeks.

Zaleplon, zolpidem, and eszopiclone have a very rapid onset of action. These agents should be taken only immediately before going to bed or after the patient has gone to bed and then has difficulty falling asleep.

Monitoring

General Adverse Effects. General adverse effects include drowsiness, lethargy, headache, muscle or joint pain, and mental depression. Some people experience transient restlessness and anxiety before falling asleep. Morning hangover commonly occurs after the administration of hypnotic doses of chloral hydrate, doxylamine, and the long-acting benzodiazepines quazepam and flurazepam, and it is also being reported with eszopiclone. Patients may display dulled affect, subtle distortion of mood, and impaired coordination.

Common Adverse Effects

Neurologic

Hangover, Sedation, Lethargy, Decreased Level of Alertness. Patients may complain of morning hangover, blurred vision, and transient hypotension upon arising. Explain to the patient the need for first rising to a sitting position, equilibrating, and then standing. Assistance with ambulation may be required. If the hangover effect becomes troublesome, the dosage should be reduced, the medication should be changed, or both. People who work around machinery, drive a car, pour and give medications, or perform other duties for which they must remain mentally alert should not take these medications while working.

Cardiovascular

Transient Hypotension When Arising. Explain to the patient the need for first rising to a sitting position, equilibrating, and then standing. Assistance with ambulation may be required.

Psychological

Restlessness, Anxiety. These adverse effects are usually mild and do not warrant discontinuing the medication. Encourage the patient to try to relax and to let the sedative effect take over. Older patients and those in severe pain may respond paradoxically with excitement, euphoria, restlessness, and confusion. Safety measures such as the maintenance of bed rest, side rails, and observation should be used during this period. Pain medications may also be administered, if indicated.

Drug Interactions

Antihistamines, Alcohol, Analgesics, Anesthetics, Tranquilizers, Narcotics, Cimetidine, Disulfiram, Isoniazid, Rifampin, Erythromycin, Ketoconazole, Other Sedative-Hypnotics. All these agents increase the toxic effects of all sedative-hypnotic agents.

Fluvoxamine. Fluvoxamine specifically inhibits the metabolism of ramelteon, thus causing excessive sedation. Patients who are receiving fluvoxamine, a serotonin reuptake inhibitor that can be used as an antidepressant, should not take ramelteon.

Rifampin. Rifampin significantly enhances the metabolism of eszopiclone and ramelteon, thereby reducing the therapeutic effect. Consider the use of zolpidem instead.

Warfarin. Chloral hydrate may enhance the anticoagulant effects of warfarin. Observe patients for petechiae, ecchymoses, nosebleeds, bleeding gums, dark tarry stools, and bright red or coffee-ground emesis. Monitor patients' prothrombin time, and reduce the dosage of warfarin, if necessary.

Food. The presence of food—particularly food with a high fat content—slows the absorption of zolpidem, zaleplon, eszopiclone, and ramelteon by slowing the onset of action. For a faster onset of action, do not administer these drugs with or immediately after a meal.

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.

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-ŪR-jĭk) (p. 226)
tremors (TRĒ-mŭrz) (p. 227)
dyskinesia (dĭs-kĭ-NĒ-zhă) (p. 227)
propulsive, uncontrolled movement (prō-PŬL-sĭv ŭn-kŏn-TRŌLD MŪV-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.