

Cholinesterase Inhibitors

Key Terms

acetylcholine	Alzheimer's disease
alanine	dementia
aminotransferase	ginkgo biloba

Chapter Objectives

On completion of this chapter, the student will:

- Discuss the clinical manifestations of Alzheimer's disease.
- List the uses, general drug actions, general adverse reactions, contraindications, precautions, and interactions associated with the administration of the cholinesterase inhibitors.
- Discuss important preadministration and ongoing assessment activities the nurse should perform on the patient taking a cholinesterase inhibitor.
- List some nursing diagnoses particular to a patient taking a cholinesterase inhibitor.
- Discuss ways to promote an optimal response to therapy, how to manage common adverse reactions, and important points to keep in mind when educating patients about the use of the cholinesterase inhibitors.

Alzheimer's disease (AD) is a progressive deterioration of mental, physical, and cognitive abilities from which there is no recovery. About 2 million Americans have the disease. Almost 50% of individuals in nursing homes and almost half of all people older than 85 years experience the devastating effects of AD. Currently it is the fourth leading cause of death in adults. Specific pathologic changes occur in the cortex of the brain thought to be associated with deficiencies of one or more of the neurohormones, such as acetylcholine or norepinephrine.

Drugs that are used to treat AD do not cure the disease but are aimed at slowing the progression. These drugs are the cholinesterase inhibitors. Examples of the cholinesterase inhibitors include donepezil (Aricept), galantamine hydrobromide (Reminyl), rivastigmine tartrate (Exelon), and tacrine hydrochloride (Cognex). These drugs are used to treat mild to moderate **dementia** (decrease in cognitive functioning) of AD. Other drugs are used for symptomatic relief. For example, wandering, irritability, and aggression in people with AD are treated with the antipsychotics, such as risperidone and olanzapine (see Chap. 32). Other drugs, such as the antidepressants or antianxiety drugs, may be helpful in AD for symptoms of depression and anxiety.

Several herbal remedies are thought to be helpful in AD. **Ginkgo biloba** is a common herb that appears to increase blood flow to the brain and has antioxidant properties. The herb is available over the counter, but there are no standards in the United States to regulate its quality of effectiveness. No one should take this or any other herb for AD without first consulting with the primary care provider. When ginkgo biloba is used with other drugs, such as with warfarin or high doses of vitamin E, there is a risk for increased bleeding.

ACTIONS

Acetylcholine, a natural chemical in the brain, is required for memory and thinking. Individuals with AD slowly lose this chemical, and as the levels of the chemical decrease, the patient experiences problems with memory and thinking. The cholinesterase inhibitors act to increase the level of acetylcholine in the CNS by inhibiting its breakdown and slowing neuronal destruction. However, the disease is progressive, and although these drugs alter the progress of the disease, they do not cure the disease. The life span of a

SUMMARY DRUG TABLE CHOLINESTERASE INHIBITORS

GENERIC NAME	TRADE NAME*	USES	ADVERSE REACTIONS	DOSAGE RANGES
donepezil HCL <i>doe-nep'-ah-zill</i>	Aricept	Mild to moderate dementia of the Alzheimer type	Nausea, vomiting, diarrhea, muscle cramps, fatigue, anorexia, syncope	5–10 mg/d PO
galantamine hydrobromide <i>ga-lan'-ta-meen</i>	Reminyl	Mild to moderate dementia of the Alzheimer type	Nausea, vomiting, diarrhea, anorexia, weight loss, abdominal pain, headache, dizziness, lethargy, confusion	4 mg BID PO up to 24 mg/d
rivastigmine tartrate <i>riv-ah-stig'-meen</i>	Exelon, Exelon Oral Solution	Mild to moderate dementia of the Alzheimer type	Nausea, vomiting, diarrhea, dyspepsia, anorexia, abdominal pain, insomnia, fatigue, skin rash, dizziness, constipation, somnolence, tremor	1.5–12 mg/d BID PO
tacrine HCL <i>tay'-krin</i>	Cognex	Mild to moderate dementia of the Alzheimer type	Diarrhea, loss of appetite, clumsiness, nausea, vomiting, fainting, tachycardia, fever, hyper- or hypotension, skin rash, severe abdominal pain, hepatotoxicity	40–160 mg/d in 4 divided doses PO

*The term *generic* indicates the drug is available in generic form.

patient with AD is usually decreased, although a patient may live from 3 to 20 years after diagnosis.

USES

Cholinesterase inhibitors are used to treat the dementia associated with AD. The effectiveness of these drugs varies from individual to individual. The drugs may noticeably diminish the symptoms of AD, the symptoms could improve only slightly, or the symptoms could continue to progress (only at a slower rate).

Donepezil has the advantage of once-daily administration and appears to be better tolerated than tacrine. Tacrine is particularly harmful to the liver. The new drugs rivastigmine and galantamine, like the other two, are effective in treating mild-to-moderate dementia of AD.

ADVERSE REACTIONS

In most situations, adverse reactions of the cholinesterase inhibitors are mild and are most often experienced early in the treatment. When adverse reactions occur, they tend to disappear gradually as the body gets used to the treatment and generally will not last for more than several days. Adverse reactions of the cholinesterase inhibitors

include anorexia, nausea, vomiting, diarrhea, weight loss, abdominal pain, dizziness, and headache.

Tacrine is particularly damaging to the liver and can result in hepatotoxicity. Because tacrine is more likely to cause adverse reactions and drug interactions, it must be administered more frequently (4 times a day) and is rarely used in current therapy. Donepezil has fewer and milder side effects than tacrine. It is considered the agent of first choice. However, some patients may achieve a better response with one drug than another. Additional adverse reactions are listed in the Summary Drug Table: Cholinesterase Inhibitors.

CONTRAINDICATIONS

The cholinesterase inhibitors are contraindicated in patients with a hypersensitivity to the drugs and during pregnancy (Pregnancy Category B) and lactation.

PRECAUTIONS

These drugs are used cautiously in patients with renal or hepatic disease, bladder obstruction, seizure disorders, sick sinus syndrome, gastrointestinal bleeding, and asthma. Individuals with a history of ulcer disease may have a recurrence of the bleeding.

INTERACTIONS

When the cholinesterase inhibitors are administered with the anticholinergic drugs, there is a potential decrease in activity of the anticholinergic drug. There is an increased risk of toxicity of theophylline when the cholinesterase inhibitors are administered with tacrine. There is a synergistic effect when tacrine is administered with succinylcholine, cholinesterase inhibitors, or cholinergic agonists (eg, bethanechol).

Herbal Alert: Ginseng

Ginseng has been called the “king of herbs” because of its wide use and the benefits attributed to the herb. In early times in China, ginseng was valued as high as gold. Hundreds of ginseng products (eg, gum, teas, chewing gum, juices) are sold throughout the US. Ginseng is the fourth best selling herb in the US. The primary use of ginseng is to improve energy and mental performance. The benefits of ginseng include improving endurance during exercise, reducing fatigue, boosting stamina and reaction times, and increasing feelings of well-being.

Adverse reactions are rare, but sleeplessness, nervousness, and diarrhea have been reported in individuals taking large amounts of the herb. The herb should not be taken in combination with stimulants including those containing caffeine. Dosage is 200 to 500 mg/day of the standardized extract or 1 to 4 g of powdered root a day. Ginseng is contraindicated in individuals with high blood pressure and during pregnancy.

Herbal Alert: Ginkgo

Ginkgo is one of the oldest herbs in the world and has many beneficial effects. Ginkgo is taken to improve memory and brain function and to enhance circulation to the brain, heart, limbs, and eyes. Most of the research done on ginkgo has been done on standardized extract ginkgo. The recommended dose is 40 mg standardized extract ginkgo three times a day. The effects of ginkgo may not be seen until after 4 to 24 weeks of treatment. The most common adverse reactions include mild gastrointestinal discomfort, headache, and rash. Excessively large doses have been reported to cause diarrhea, nausea, vomiting, and restlessness. Ginkgo is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) because of the risk of a toxic reaction. Individuals taking anticoagulants should take ginkgo only on the advice of a primary care provider.

NURSING PROCESS

• The Patient Receiving a Cholinesterase Inhibitor for Mild-to-Moderate Dementia of Alzheimer's Disease

ASSESSMENT

Preadministration Assessment

A patient receiving a cholinesterase inhibitor may be treated in the hospital, nursing home, or in an outpatient setting. The patient's cognitive ability and functional

ability are assessed before and during therapy. The baseline or initial assessment depends on the stage of AD. The nurse assesses the patient for confusion, agitation, and impulsive behavior. Speech, ability to perform activities of daily living, and self-care ability also are assessed. These assessments will be used by the nurse in the ongoing assessment in monitoring the patient's improvement (if any) after taking the cholinesterase inhibitors. These drugs may slow the progression of the disease but are not a cure for AD.

Before starting therapy for the hospitalized patient, the nurse obtains a complete psychiatric and medical history. With AD, patients often are unable to give a reliable history of their illness. A family member or primary caregiver will be able to verify or give information needed for an accurate assessment. During the time the history is taken, the nurse observes the patient for any behavior patterns that appear to be deviations from normal. Examples of deviations include poor eye contact, failure to answer questions completely, inappropriate answers to questions, a monotone speech pattern, and inappropriate laughter, sadness, or crying. These patients are in varying stages of decline. Display 33-1 identifies the stages of AD and the associated clinical manifestations. The nurse documents the patient's cognitive ability using Display 33-1 as a guide.

Late dementia or the final phase of AD may last from a few months to several years while the patient becomes increasingly immobile and dysfunctional.

Physical assessments include obtaining blood pressure measurements on both arms with the patients in a sitting position, pulse, respiratory rate, and weight. The functional ability of the patient is also important.

DISPLAY 33-1 • Clinical Manifestations of Alzheimer's Disease

EARLY PHASE—MILD COGNITIVE DECLINE

- Increased forgetfulness
- Decreased performance in social settings
- Evidence of memory deficit when interviewed
- Mild to moderate anxiety

EARLY DEMENTIA PHASE—MODERATELY SEVERE COGNITIVE DECLINE

- Needs assistance for activities of daily living
- Unable to recall important aspects of current life
- Difficulty making choices (ie, what clothes to wear, what to eat)
- Able to recall major facts (ie, their name and family member's names)
- Need assistance for survival

LATE DEMENTIA PHASE—SEVERE COGNITIVE DECLINE

- Incontinent of urine
- No verbal ability
- No basic psychomotor skills
- Needs assistance when bathing, toileting, and feeding

The initial assessments of the outpatient are basically the same as those for the hospitalized patient. The nurse obtains a complete medical history and a history of the symptoms of AD from the patient (if possible), a family member, or the patient's hospital records. During the initial interview, the nurse observes the patient for what appear to be deviations from a normal behavior pattern. The nurse also should assess the patient's vital signs and body weight.

Ongoing Assessment

Ongoing assessment of patients taking the cholinesterase inhibitors includes both mental and physical assessments. Cognitive and functional abilities are assessed using Display 33-1 as a guide. Initial assessments will be compared with the ongoing assessments to monitor the patient's improvement (if any) after taking the cholinesterase inhibitors.

NURSING DIAGNOSES

Drug-specific nursing diagnoses are highlighted in the Nursing Diagnoses Checklist. Other nursing diagnoses applicable to these drugs are discussed in depth in Chapter 4.

PLANNING

The expected outcomes for the patient may include an optimal response to drug therapy, management of common adverse drug reactions, an absence of injury, and compliance with the prescribed therapeutic regimen.

IMPLEMENTATION

Promoting an Optimal Response to Therapy

The nurse develops a nursing care plan to meet the patient's individual needs. It is important to monitor vital signs at least daily. The nurse should report any significant change in the patient's vital signs to the primary health care provider.

Behavioral records should be written at periodic intervals (frequency depends on hospital or unit guidelines). An accurate description of the patient's behavior and cognitive ability aids the primary health care provider in planning therapy and thus becomes an

important part of nursing management. Patients with poor response to drug therapy may require dosage changes, discontinuation of the drug therapy, or the addition of other therapies to the treatment regimen. However, it is important for the nurse to know that response to these drugs may take several weeks. The symptoms that the patient is experiencing may get better or remain the same, or the patient may experience only a small response to therapy. It is important to remember that a treatment that slows the progression of symptoms in AD is a successful treatment.

Donepezil is administered orally once daily at bedtime. It can be taken with or without food. Galantamine is administered orally twice daily, preferably with morning and evening meals.

Rivastigmine is administered as a tablet or oral solution twice daily. When rivastigmine is administered as an oral solution, the nurse removes the oral dosing syringe provided in the protective container. The syringe provided is used to withdraw the prescribed amount. The dosage may be swallowed directly from the syringe or first mixed with a small glass of water, cold fruit juice, or soda.

Tacrine is administered orally 3 or 4 times a day, preferably on an empty stomach 1 hour before or 2 hours after meals. For best results the drug should be administered around the clock.

Monitoring and Managing Adverse Reactions

When taking the cholinesterase inhibitors, patients may experience nausea and vomiting. Although this can occur with all of the cholinesterase inhibitors, patients taking rivastigmine appear to have more problems with nausea and severe vomiting. Nausea and vomiting should be reported to the primary health care provider because the primary care provider may discontinue use of the drug and then restart the drug therapy at the lowest dose possible. Restarting therapy at the lower dose helps to reduce the nausea and vomiting.

Weight loss and eating problems related to the inability to swallow are two major problems in the late stage of AD. These problems coupled with the anorexia and nausea associated with administration of the cholinesterase inhibitors present a challenge for the nurse or the caregiver. Mealtime should be simple and calm. The patient should be offered a well-balanced diet with foods that are easy to chew and digest. Frequent, small meals may be tolerated better than three regular meals. Offering foods of different consistency and flavor is important in case the patient can handle one form better than another. Fluid intake of 6 to 8 glasses of water daily is encouraged to prevent dehydration. In later stages, the patient may be fed through a feeding syringe, or the caregiver can encourage chewing action by pressing gently on the bottom of the patient's chin and on the lips.

Nursing Diagnoses Checklist

- ✓ **Imbalanced Nutrition: Less than Body Requirements** related to adverse reactions (eg, anorexia, nausea)
- ✓ **Risk for Injury** related to an adverse drug reaction (eg, dizziness, syncope, clumsiness) or disease process
- ✓ **Impaired Physical Mobility** related to adverse drug reactions (eg, dizziness, syncope) or disease process

Physical decline and the adverse reactions of dizziness and syncope place the patient at risk for injury. The patient may require assistance by the nurse when ambulating. Assistive devices such as walkers or canes may reduce falls. To minimize the risk of injury, the patient's environment should be controlled and safe. Encouraging the use of bedrails, keeping the bed in low position, using night lights, and frequenting monitoring by the nurse or caregiver will reduce the risk of injury. The patient should wear an identification tag, such as a medical alert bracelet.

When administering tacrine, the nurse must monitor the patient for liver damage. This is best accomplished by monitoring **alanine aminotransferase (ALT)** levels. ALT is an enzyme found predominately in the liver. Disease or injury to the liver causes a release of this enzyme into the bloodstream, resulting in elevated ALT levels. In patients taking tacrine, ALT levels should be obtained weekly from at least week 4 to week 16 after the initiation of therapy. After week 16, transaminase levels are monitored every 3 months.

Nursing Alert

The nurse immediately reports any elevated alanine aminotransferase (ALT) level to the primary health care provider. The primary health care provider may want to continue monitoring the ALT level or discontinue use of the drug because of the danger of hepatotoxicity. However, abrupt discontinuation may cause a decline in cognitive functioning.

Within 6 weeks of the discontinuation of cholinesterase inhibitor therapy, individuals lose any benefit they have received from the drugs.

Educating the Patient and Family

The patient with AD may understand and comprehend the extent and severity of this disease early on in the disease process, but as cognitive abilities decrease, the nurse will focus on educating the family and major caregiver of the patient. Depending on the degree of cognitive decline, the nurse will discuss the drug regimen with the patient, family member, and/or caregiver. It is important for the nurse to accurately evaluate the patient's ability to assume responsibility for taking drugs at home. The administration of drugs to the patient with AD becomes a family responsibility if the outpatient appears to be unable to manage his or her own drug therapy.

The nurse explains any adverse reactions that may occur with a specific antipsychotic drug and encourages the caregiver or family members to contact the primary health care provider immediately if a serious drug reaction occurs.

The nurse includes the following points in a teaching plan for the patient or family member:

- Keep all appointments with the primary care provider or clinic because close monitoring of therapy is essential. Dose changes may be needed to achieve the best results.
- Report any unusual changes or physical effects to the primary health care provider.
- Take the drug exactly as directed. Do not increase, decrease, or omit a dose or discontinue use of this drug unless directed to do so by the primary health care provider.
- Do not drive or perform other hazardous tasks if drowsiness occurs. As soon as the diagnosis of AD is made, patients should not be permitted to drive.
- Do not take any nonprescription drug unless use of a specific drug has been approved by the primary health care provider.
- Inform physicians, dentists, and other medical personnel of therapy with this drug.
- Keep track of when the drug is taken. In the early stages of forgetfulness, a mark on the calendar each time the medicine is taken or use of a pill counter that holds the medicine for each day of the week may be used to help the patient remember to take the medication or if the medication has been taken for the day.
- Notify the primary care provider if the following adverse reactions are experienced for more than a few days: nausea, diarrhea, difficulty sleeping, vomiting, or loss of appetite.
- Immediately report the occurrence of the following adverse reactions: severe vomiting, dehydration, changes in neurologic functioning, or yellowing of the skin or eyes.
- Notify the primary health care provider if you have a history of ulcers, feel faint, experience severe stomach pains, vomit blood or material that resembles coffee grounds, or have bloody or black stools.
- Remember that these drugs do not cure AD but slow the mental and physical degeneration associated with the disease.
- Remember that during tacrine therapy the ALT level must be monitored at intervals prescribed by the primary health care provider.

EVALUATION

- The therapeutic effect is achieved.
- Adverse reactions are identified, reported to the primary health care provider, and managed successfully through appropriate nursing interventions.
- No evidence of injury is seen.
- The patient (if possible), family member, or caregiver demonstrates understanding of the drug regimen.

● Critical Thinking Exercises

1. A patient is prescribed tacrine (Cognex) for mild dementia related to AD. The nurse has a meeting with the patient and family. What patient assessments would you need to make before discussing the drug regimen with the patient? What would you include in a teaching plan for the patient and family?
2. A patient with AD is taking donepezil (Aricept). She attends an adult day care center during the day. She is not eating well and recently has lost 5 pounds. If you are the nurse at the center, what actions would you take and why would you take these particular actions?

● Review Questions

1. Adverse reactions that the nurse would assess for in a patient taking rivastigmine (Exelon) include _____.
 - A. occipital headache
 - B. vomiting
 - C. hyperactivity
 - D. hypoactivity
2. When administering tacrine (Cognex) to a patient with AD the nurse would expect which of the laboratory examinations most likely to be prescribed _____.
 - A. a complete blood count
 - B. cholesterol levels

- C. transaminase levels
- D. electrolytes

3. Which of the following nursing diagnoses would the nurse most likely place on the care plan of a patient with AD that is related to adverse reactions of the cholinesterase inhibitors?
 - A. Imbalanced nutrition
 - B. Confusion
 - C. Risk for suicide
 - D. Bowel incontinence
4. The nurse correctly administers donepezil (Aricept) _____.
 - A. three times daily around the clock.
 - B. twice daily 1 hour before meals or 2 hours after meals.
 - C. once daily in the morning.
 - D. once daily at bedtime.

● Medication Dosage Problems

1. Rivastigmine (Exelon) oral solution 6 mg PO is prescribed. The drug is available as an oral solution of 2 mg/mL. The nurse administers _____.
2. Galantamine (Reminyl) 4 mg PO is prescribed for a patient with AD. On hand are 8-mg tablets. The nurse administers _____.