

Medications for Dementia

CE for Pharmacy Technicians

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Disclosure Statement

- I do not have anything to disclose.



Objectives

- Provide an over-view of medications used to treat dementia
 - Definitions of disease state
 - Drug classes
 - Doses of medication
 - Side effects
 - Any necessary monitoring

Upon conclusion of the program, the participant should be able to:

- Define dementia
- Recognize usual dosing regimens for cholinesterase inhibitors and memantine
- Recognize common side effects for cholinesterase inhibitors and memantine
- Describe medications used to help control mood or behavior problems in dementia

What is dementia?

- Dementia describes a group of symptoms affecting memory, thinking, and social abilities severely enough to interfere with daily functioning.
- Dementia generally involves memory loss, but it can have many causes.
- Memory loss alone does not mean you have dementia.

Criteria for Dementia

- Significant cognitive impairment in at least one of the following cognitive domains:
 - Learning and memory
 - Language
 - Executive function
 - Complex attention
 - Perceptual-motor function
 - Social Cognition

Criteria for Dementia

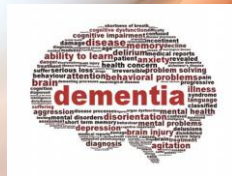
- Impairment must be acquired and represent a significant decline from a previous level of functioning.
- Cognitive deficits must interfere with independence in everyday activities.
- Disturbances are not occurring exclusively during the course of delirium.
- Disturbances are not better accounted for by another mental disorder (i.e. depression, schizophrenia)
- In the case of neurodegenerative dementias (Alzheimer's disease), the disturbances are of insidious onset and progressive, based on evidence from the history or serial mental-status exams.

Types of Dementia

- Alzheimer's disease (**most common type = 60-80% of cases**)
- Vascular dementia
- Dementia with Lewy bodies (DLB)
- Mixed dementia
- Parkinson's disease
- Frontotemporal dementia
- Huntington's disease
- Creutzfeldt-Jakob disease
- Normal pressure hydrocephalus
- Wernicke-Korsakoff Syndrome

Dementia is not just memory loss!

- May have difficulty with one or more of the following:
 - Retaining new information
 - Handling complex tasks
 - Reasoning
 - Spatial ability and orientation
 - Language
 - Behavior



Mini Mental Status Exam (MMSE)

- Most widely used cognitive test for dementia in the US
- Takes ~ 7 minutes to complete
- Tests a broad range of cognitive functions
 - Orientation
 - Recall
 - Attention
 - Calculation
 - Language manipulation
 - Constructional praxis

Mini Mental Status Exam (MMSE)

Risk Factors

- Age – biggest risk factor
- Family history
- Others
 - High blood pressure
 - Smoking
 - Diabetes
 - Lifestyle

Medications for Dementia

- Cholinesterase inhibitors
 - Donepezil (Aricept)
 - Rivastigmine (Exelon)
 - Galantamine (Razadyne)
- N-methyl-D-aspartate (NMDA) receptor antagonist
 - Memantine (Namenda)
- Combination product
 - Donepezil/memantine (Namzaric)



Medications for Dementia

Drug name	Brand name	Approved For
1. donepezil	Aricept	All stages
2. galantamine	Razadyne	Mild-to-moderate
3. memantine	Namenda	Moderate-to-severe
4. rivastigmine	Exelon	All stages
5. donepezil and memantine	Namzaric	Moderate-to-severe

Cholinesterase inhibitors

- Used to help treat symptoms related to:
 - Memory
 - Thinking
 - Language
 - Judgement
 - Thought processes



Cholinesterase inhibitors

- Prevent the breakdown of acetylcholine (a chemical messenger important for learning and memory).
- Delay worsening of symptoms for 6 to 12 months, on average, for about 50% of the patients who take them.
- Generally well tolerated.

Cholinesterase inhibitors

- Most common side effects include:
 - Nausea
 - Vomiting
 - Loss of appetite
 - Increased frequency of bowel movements

Cholinesterase inhibitors

- FDA approved to treat all stages of Alzheimer's
 - Donepezil (Aricept)
- FDA approved to treat mild to moderate Alzheimer's
 - Rivastigmine (Exelon)
 - Severe – transdermal patch
 - Galantamine (Razadyne)

Cholinesterase inhibitors

- Donepezil dosing
 - Mild-to-moderate: initial 5mg daily, may increase to 10mg daily after 4 to 6 weeks.
 - Moderate-to-severe: initial 5mg daily, may increase to 10mg daily after 4 to 6 weeks. May increase further to 23mg daily after at least 3 months.
 - Effective dose range is **10 to 23mg daily**.

Cholinesterase inhibitors

- Rivastigmine dosing
 - Mild-to-moderate/Oral: initial 1.5mg twice a day, may increase by 3mg daily (1.5mg/dose) every 2 weeks based on tolerability – **MAX 6mg twice a day**.
 - Mild-to-moderate/Patch: initial 4.6mg/24 hour patch once daily, if well tolerated may titrate every 4 weeks to 9.5mg/24 hour patch, then to 13.3mg/24 hour patch – **MAX 13.3mg/24 hours**.
 - Severe/Patch: initial 4.6mg/24 hour patch once daily and titrate as above– **MAX 13.3mg/24 hours**.

Cholinesterase inhibitors

- Galantamine dosing
 - Mild-to-moderate:
 - Immediate release: Initial 4mg twice a day for 4 weeks, may increase to 8mg twice a day after 4 weeks if tolerated, and again to 12mg twice a day if tolerated after 4 weeks.
 - Extended release: Initial 8mg daily for 4 weeks, if tolerated increase to 16mg daily for 4 weeks, and if tolerated increase to 24mg daily.
 - Range is **16 to 24mg daily** (dose may be divided if immediate release formulation is used).

NMDA Receptor Antagonist

- Regulates the activity of glutamate, an important neurotransmitter in the brain involved in learning and memory.
- Thought to be neuroprotective.

NMDA Receptor Antagonist

- Most common side effects (1-10%) include:
 - High or low blood pressure
 - Dizziness, confusion, headache, anxiety, depression, drowsiness, hallucination, pain, aggressive behavior, fatigue
 - Weight gain
 - Diarrhea, constipation, vomiting, abdominal pain

NMDA Receptor Antagonist

- FDA approved for moderate to severe Alzheimer's disease.
 - Memantine (Namenda)
 - Immediate release
 - Extended release
 - Combination product with donepezil

NMDA Receptor Antagonist

- Memantine dosing
 - **Immediate release**
 - Initial: 5mg daily. Increase by 5mg daily to a target dose of 20mg daily (wait at least 1 week between dose changes). Doses greater than 5mg should be divided twice a day.
 - Suggested titration: 5 mg daily for ≥ 1 week; 5 mg twice daily for ≥ 1 week; 15 mg daily given in 5 mg and 10 mg separate doses for ≥ 1 week; then **10 mg twice daily**

NMDA Receptor Antagonist

- Memantine dosing
 - **Extended release**
 - Initial: 7mg daily. Increase by 7mg daily to a **target maximum dose of 28mg daily** (wait at least 1 week between dose changes).

Combination tablet

- Donepezil/memantine (Namzaric)
 - Moderate-to-severe Alzheimer's dementia
- Patients stabilized on donepezil 10 mg once daily and not currently on memantine:
 - Initial: Memantine extended release (ER) 7 mg/donepezil 10 mg once daily in the evening. Increase dose in increments of memantine ER 7 mg at intervals of ≥ 1 week to maintenance dose of memantine ER 28 mg/donepezil 10 mg once daily based on patient response and tolerability.
 - **Maximum dose: memantine ER 28 mg/ donepezil 10 mg once daily.**

Combination tablet

- Patients stabilized on memantine (10 mg twice daily or 28 mg ER once daily) and donepezil 10 mg:
 - Initial: Memantine ER 28 mg/donepezil 10 mg once daily in the evening. Initiate combination therapy the day after the last dose of memantine and donepezil administered separately.
 - **Maximum dose: memantine ER 28 mg/ donepezil 10 mg once daily.**

Other Medications

- Antioxidant therapy
 - Vitamin E
 - Selegiline
- Estrogen replacement
- Anti-inflammatory drugs
- Ginkgo biloba
- Statins
- Dietary Supplements
 - Vitamin B
 - Omega-3 fatty acids



Management Issues

- Behavioral disturbance
- Nutrition
- Rehabilitation
 - Cognitive rehabilitation
 - Exercise programs
 - Occupational therapy
- Patient referral
- Risk factor control
- Alcohol
- Safety and societal issues
- Survival

Behavioral Disturbance

- Neuropsychiatric symptoms in Alzheimer disease and other types of dementia are extremely common, and often much more troubling than amnesic symptoms.
- One or more of these symptoms are observed in 61-92% of patients with dementia; the prevalence increases with disease severity.
- Agitation
- Aggression
- Delusions
- Hallucinations
- Wandering
- Depression
- Apathy
- Disinhibition
- Sleep disturbances

Behavioral Disturbance

- Agitation and other behavioral abnormalities can arise from a variety of underlying causes in patients with dementia, and identifying the genesis of the abnormal behavior is critical to effective management.
- In many patients, behavioral changes herald a new infection or medication toxicity.
- In others, agitation is driven by pain, fear, confusion, or poor sleep.
- *As with physical symptoms such as shortness of breath, **no single approach or medication can be expected to treat the symptom of agitation without regard to the underlying cause.***

Behavioral Disturbance

- Evaluation of new or worsening symptoms
 - Search for an underlying cause
 - Delirium
 - Medication side effects
 - Other precipitating factors
 - Pain assessment

Behavioral Disturbance

- Antidepressants can be used to help improve mood and irritability:
 - Citalopram (Celexa)
 - Fluoxetine (Prozac)
 - Paroxetine (Paxil)
 - Sertraline (Zoloft)
 - Trazodone (Desyrel)
- Anxiolytics are used for anxiety, restlessness, verbally disruptive behavior and resistance:
 - Lorazepam (Ativan)
 - Oxazepam (Serax)

Behavioral Disturbance

- Antipsychotics for hallucinations, delusions, aggression, agitation, hostility and uncooperativeness:
 - Aripiprazole (Ablify)
 - Clozapine (Clozaril)
 - Haloperidol (Haldol)
 - Olanzapine (Zyprexa)
 - Quetiapine (Seroquel)
 - Risperidone (Risperdal)
 - Ziprasidone (Geodon)

Management Issues

- Environmental, behavioral, and other non-pharmacologic therapies can be effective in this population and, when appropriate, are preferred over medications, which have a high rate of adverse effects.
- Pain is an important source of behavioral disturbances in patients with dementia.
- A trial of selective serotonin reuptake inhibitors (SSRIs) is suggested for the treatment of depression in Alzheimer's disease.
- Antipsychotic agents have limited efficacy and are associated with increased mortality in patients with dementia.

Management Issues

- Physical restraints are rarely indicated in the care of patients with dementia and should be used only for patients who pose an imminent risk of physical harm to themselves or others.
- Sleep disturbances are common in patients with dementia. Non-pharmacologic strategies, including maintenance of good sleep hygiene, maximizing morning natural light, and daily exercise, are generally preferred to pharmacotherapy.
- Because of the risk of side effects with long-term use, benzodiazepines should be reserved for acute stressful episodes.

Summary

- Current medications cannot stop the progression of dementia, but they can help to lessen or stabilize symptoms for a limited time.
- Two main classes are used to treat dementia:
 - Cholinesterase inhibitors
 - N-methyl-D-aspartate (NMDA) receptor antagonist
- Behavioral disturbances are very common.
- Non-pharmacologic strategies should be utilized.

Test Your Knowledge

Dementia describes a group of symptoms affecting _____, _____, and _____ severely enough to interfere with daily functioning.

- Language, memory, and planning
- Thinking, memory, and social abilities
- Orientation, thinking, and language
- Concentration, social abilities, and memory

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Test Your Knowledge

John Doe has been using the rivastigmine patch for several months, but recently his family has noticed his memory is getting even worse. His new prescription for rivastigmine patches is written for 17.9mg/24 hours. You should:

- Fill the rx as is, he has been using the patch for at least 12 weeks.
- Fill the rx as is, he is declining and needs a higher dose.
- Call the provider/office to verify the dose.
- Tell the caregiver who is dropping off the rx there is nothing you can do for them.

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Test Your Knowledge

Common side effects of cholinesterase inhibitors include:

- A. Dizziness, headache, fatigue
- B. Suicidal thoughts, seizures, stroke
- C. Low blood pressure, dizziness, difficulty breathing
- D. Increased frequency of bowel movements, nausea, vomiting

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Test Your Knowledge

True or False:

Antipsychotics, such as quetiapine, should be used routinely to help control behavioral issues in people with dementia.

Test Your Knowledge

True or **False**:

Antipsychotics, such as quetiapine, should be used routinely to help control behavioral issues in people with dementia.

Sources

- Up To Date: <https://www.uptodate.com>
- Micromedex: <http://www.micromedexsolutions.com/>
- Alzheimer's Association: www.alz.org

Questions?



