Medications for Alzheimer's & Other Dementias: Benefits & Side Effects

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Our Speaker

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Medications for Alzheimer's Disease and Other Dementias: Benefits and Side Effects

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Outline

- FDA approved medications
  - ✓ Benefits
  - ✓ Side effects
- Treating associated conditions (behavioral disturbances, sleep problems, depression, anxiety, etc.)
- Other important considerations: falls, polypharmacy

Foreword

Before starting and considering therapy, ask "Why and how?" and "What do we want treatment to accomplish?"

- ✓ Improve cognitive function
- ✓ Alleviate related symptoms (e.g. psychiatric, behavioral, etc.)
- ✓ Address comorbidities

But what about those drug-related adverse reactions?

Key words: ***balance*** risks and benefits, ***individualize*** and ***optimize***

Cognitive impairment: what options do we have?

Class	Drug	Formulation	FDA Approved Indication
Cholinesterase Inhibitors (ChEI)	Donepezil*	Tablet (5, 10, or 23 mg) Orally disintegrating tablet (5, 10 mg)	Alzheimer's dementia, mild to moderate and moderate to severe
	Rivastigmine	Capsule (1.5, 3, 4.5, 6 mg) Oral solution (2 mg/mL) Transdermal patch	Alzheimer's dementia, mild to moderate Parkinson's dementia, mild to moderate
	Galantamine	Tablet (4, 8, 12 mg) ER^ capsules (8, 16, 24 mg) Oral solution (4 mg/mL)	Alzheimer dementia, mild to moderate
NMDA receptor antagonist**	Memantine*	Tablet (5, 10 mg) ER capsule (7, 14, 21, 28 mg) Solution (2mg/mL)	Alzheimer dementia, moderate to severe

*donepezil and memantine available in combination
**NMDA: Noncompetitive N-methyl-D-aspartate
^ER: extended release

Cholinesterase inhibitors: donepezil

- **Mild to moderate AD**: 5 or 10 mg once daily
  Note: A dose of 10 mg once daily can be administered once patients have been on a daily dose of 5 mg for 4 to 6 weeks
- **Moderate to severe AD**: 10 or 23 mg once daily
  Note: A dose of 23 mg* once daily can be administered once patients have been on a dose of 10 mg once daily for at least 3 months
  *Should not be split, crushed or chewed because this may increase its rate of absorption

Additional considerations:
- ✓ Should be taken in the evening, just prior to retiring
- ✓ Can be taken with or without food
- ✓ Available in combination with memantine

Cholinesterase inhibitors: rivastigmine (oral)

Alzheimer's disease:
- ✓ Initiate treatment with 1.5 mg BID
- ✓ Can increase dose, if tolerated, to 3 mg and further to 4.5 mg and 6 mg BID with a minimum of 2 weeks at each dose

Parkinson's disease dementia (the only ChEI approved for Parkinson's)
- ✓ Initiate treatment with 1.5 mg BID
- ✓ Can increase dose, if tolerated, to 3 mg and further to 4.5 mg and 6 mg BID with a minimum of 4 weeks at each dose

- Should be taken with meals in divided doses in the morning and evening
- Oral solution and capsules may be interchanged at equal doses

Cholinesterase inhibitors: rivastigmine patch

Advantage: better tolerability (reduces nausea)

Formulation:
- ✓ 4.6 mg/24 hours: 5 cm^2 size containing 9 mg rivastigmine
- ✓ 9.5 mg/24 hours: 10 cm^2 size containing 18 mg rivastigmine

Administration:
- ✓ Initial dose: one patch 4.6 mg/24 hours once daily
- ✓ Maintenance dose: one patch 9.5 mg/24 hours once daily
- ✓ A minimum of 4 weeks of treatment and good tolerability with the previous dose should be observed before increasing the dose

Cholinesterase inhibitors: galantamine

- **Tablets and oral solution**: start with 4 mg BID; can increase to initial maintenance dosage of 8 mg BID after a minimum of 4 weeks (max. dose: 12 mg BID after a minimum of 4 weeks at 8 mg BID)
- **ER capsule**: start with 8 mg/day in the morning; can increase to initial maintenance dose of 16 mg/day after a minimum of 4 weeks (max. dose: 24 mg/day after a minimum of 4 weeks at 16 mg/day)

Additional considerations:

- ✓ **Conversion from tablets and oral solution to ER capsule** should occur at the same daily dosage with the last dose of tablets/oral solution taken in evening and starting ER once daily treatment the next morning
- ✓ Take with meals and ensure adequate fluid intake during treatment
- ✓ Renal or hepatic impairment require dose adjustment

Cholinesterase inhibitors

- Benefits are small, but measurable
  - ➢ Symptom progression delayed by 4 to 9 months
- Long half-life: may benefit noncompliant patients
- Consider discontinuation:
  - ➢ Lack of efficacy
  - ➢ Adverse drug reactions

Rabins PV. Practice guideline for the treatment of patients with Alzheimer's disease and other dementias, in Guideline watch. Washington, DC: APA Press; 2014. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/alzheimerwatch.pdf
Winslow BT, et al. Treatment of Alzheimer disease. Am Fam Physic 2011;83(12):1403-12.

Cholinesterase inhibitors: side effects

Cholinesterase inhibitors

- Gastrointestinal: Nausea, vomiting, diarrhea, anorexia, increased stomach acid
  - ➢ Donepezil: Lowest rates of nausea, vomiting and anorexia
- Central Nervous System: sedation or insomnia, vivid/disturbing dreams
- Cardio-vascular: bradycardia, syncope
- Other: muscle cramps

Caution:

- Patients with cardiac conduction problems or history of ulcer
- May exacerbate asthma, COPD, or sleep disturbance

Additional considerations:

- Cholinergic side effects tend to fade within 1 week of initiation
- GI side effects may be lessened with transdermal preparations
- Attention to concomitant use of anticholinergic medications

Memantine

- Initial dose is 5 mg once daily; can increase dose in 5 mg increments to a maintenance dose of 10 mg BID (20 mg total). A minimum of 1 week of treatment with the previous dose should be observed before increasing the dose.
- Renal impairment: reduce dose (severe renal impairment: 5 mg BID)
- May be taken with or without food
- Available in combination with donepezil (better tolerability compared to ChEI)-available as ER capsules (7/14/21/28 mg memantine + 10 mg donepezil)

Side effects:

- Typically well tolerated
- Mild confusion, dizziness, headache, sedation, constipation

Should you consider supplements?

- ✓ No evidence of beneficial effect
- ✓ Not approved/evaluated for safety by the FDA
- ✓ Purity is unknown
- ✓ Possible interactions with prescription medications

Additional considerations for treatment

- Neuropsychiatric and behavioral symptoms (agitation, aggression, psychosis)
  - ✓ ≥ 80% of patients with AD will experience agitation
  - ✓ ~ 40% of patients with AD experience aggression
- Sleep disturbances
- Depression
- Falls
- Polypharmacy

Behavioral disturbances

It is important to understand the behavior- ask:

- ✓ What triggered the behavior?
  - ➢ Assess for pain, infection (UTI), delirium
  - ➢ Assess medications (anything new added?)
- ✓ What type of behavior does the patient exhibit?
- ✓ What are the consequences? To whom? The patient or others?

DeMers S, et al. Med Clin NA. 2014; 98:1145–1168.
Reus VI, et al. Am J Psychiatry 2016;173:543-6.
Sink K. et al. JAMA 2005;293(5):596–608.

Behavioral disturbances: medications to avoid

Medication class	Examples
Anticholinergics	Diphenhydramine, promethazine, oxybutynin
Antidopaminergics	Metoclopramide, chlorpromazine, bupropion
Sedative/hypnotics	Benzodiazepines: diazepam, clonazepam Barbiturates: secobarbital, phenobarbital Hypnotics: zolpidem, zaleplon, ramelteon
Antipsychotics*	Haloperidol, quetiapine, olanzapine, ziprasidone
Opioids	Hydrocodone, oxycodone, morphine
Other centrally acting agents	Relaxants: tizanidine, cyclobenzaprine, baclofen Dopaminergic: carbidopa/levodopa, selegiline Stimulants: amphetamine, methylphenidate

*All antipsychotics carry a black box warning about increased risk of mortality in elderly patients, The modest symptom benefit of antipsychotics in Alzheimer disease is offset by adverse effects, including further cognitive impairment

Concerns with use of psychotropics in dementia

Typical adverse effects

- Anticholinergic effects
- Somnolence and altered cognition
- Falls
- Hypotension
- Dystonias

Serious adverse effects

- Sudden death, stroke
- Pneumonia and hospitalizations
- Parkinsonism and tardive dyskinesia
- Neuroleptic malignant syndrome and serotonin syndrome

Other effects

- Weight gain, diabetes, metabolic syndrome
- Bone marrow suppression
- Infections
- Seizures
- Hormonal disturbances
- Altered thermoregulation
- Cataracts

Chahine LM, et al. The elderly safety imperative and antipsychotic usage. Harv Rev Psychiatry 2010;18:158-172.

Important to remember:

- ✓ Antipsychotics are NOT approved for dementia-related psychosis
  - If considered, the use of antipsychotics in dementia patients should be reassessed frequently, and periodic attempts to withdraw or reduce the dose should be made
- ✓ Benzodiazepines may be considered on an as-needed basis for patients in whom anxiety is prominent or when sedation is needed for a particular medical or dental procedure
  - Benzodiazepines carry significant risk of over sedation, delirium, and disinhibition, and may worsen behaviors that caregivers are trying to prevent

Rabins PV. Practice guideline for the treatment of patients with Alzheimer's disease and other dementias, in Guideline watch. Washington, DC: APA Press; 2014.
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By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29.

Behavioral disturbances: what else to consider?

- Look for reasons behind each behavior
- Don't take the behavior personally- try to distance the person and the behavior
- Monitor personal comfort and create a calm environment
- Avoid being confrontational/arguing about facts, redirect the person's attention
- Allow adequate rest between stimulating events
- Acknowledge requests and respond to them
- Be creative and get engaged (use humor, music, or art)
- Sensory practices
- Psychosocial practices
- Structured care protocols

https://www.alz.org/alzheimers-dementia/treatments/treatments-for-behavior
K. Scales et al. Evidence-Based Nonpharmacological Practices to Address Behavioral and Psychological Symptoms of Dementia *The Gerontologist*, Volume 58, Issue suppl_1, February 2018, Pages S88–S102.

Sleep hygiene

- Maintain regular times for meals and for going to bed and getting up
- Seek morning sunlight exposure
- Encourage regular daily exercise, but no later than four hours before bedtime
- Avoid alcohol, caffeine and nicotine
- Treat any pain
- If the person is taking a ChEI, avoid giving the medicine before bed
- Make sure the bedroom temperature is comfortable
- Provide nightlights and security objects
- If the person awakens, discourage staying in bed while awake; use the bed only for sleep; discourage watching television during periods of wakefulness

https://www.alz.org/alzheimers-dementia/treatments/for-sleep-changes
DC. Moga, M. Roberts, GA. Jicha. Dementia. In Geriatrics issue of *Primary Care: Clinics in Office Practice*, edited by Dr. Demetra Antimisiaris. Elsevier Clinics/Continuity. 2017; 44(3): 439–456.

Treating sleep disturbances

- ✓ "begin low and go slow"
- ✓ Assess the balance between risks and benefits
  - ➢ falls and fractures
  - ➢ confusion
  - ➢ decline in the ability to care for oneself
- ✓ If sleep medications are used, an attempt should be made to discontinue them after a regular sleep pattern has been established

https://www.alz.org/alzheimers-dementia/treatments/for-sleep-changes
DC. Moga, M. Roberts, GA. Jicha. Dementia. In Geriatrics issue of *Primary Care: Clinics in Office Practice*, edited by Dr. Demetra Antimisiaris. Elsevier Clinics/Continuity. 2017; 44(3): 439–456.

Treating sleep disturbances

- Melatonin- definitive benefit has yet to be proved, but safer
- **Avoid**: diphenhydramine and other over-the-counter sleep aids (anticholinergic properties)
- Options (**only after assessing risks and benefits!!!**):
  - ➢ Patients treated for other neuropsychiatric conditions may benefit from the use of a sedating medication close to bedtime (eg, mirtazapine for depression or a second-generation antipsychotic, such as olanzapine or quetiapine, for psychosis)
  - ➢ Low doses of trazodone at bedtime or a small dose of zolpidem or zaleplon
  - ➢ Clonazepam - rapid eye movement sleep behavior disturbance in dementia with Lewy bodies and Parkinson dementia

https://www.alz.org/alzheimers-dementia/treatments/for-sleep-changes
DC. Moga, M. Roberts, GA. Jicha. Dementia. In Geriatrics issue of *Primary Care: Clinics in Office Practice*, edited by Dr. Demetra Antimisiaris. Elsevier Clinics/Continuity. 2017; 44(3): 439–456.

Treating depression

- Always consider non-pharmacological treatment first (similar to treating behavioral disturbances)
  - ➢ Support groups
  - ➢ Predictable daily routine
  - ➢ Identify routines and places that are enjoyable
  - ➢ Physical activity
  - ➢ Celebrate small successes
  - ➢ Show love and consideration
- If medications are deemed necessary, selective serotonin reuptake inhibitors (SSRIs) have a lower risk than some other antidepressants of causing interactions with other medications

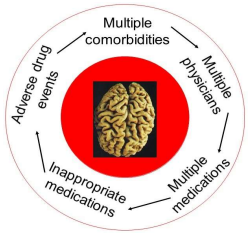
!!! Assess risks and benefits first

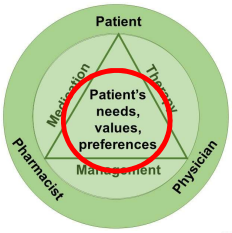
https://www.alz.org/help-support/caregiving/stages-behaviors/depression
DC. Moga, M. Roberts, GA. Jicha. Dementia. In Geriatrics issue of *Primary Care: Clinics in Office Practice*, edited by Dr. Demetra Antimisiaris. Elsevier Clinics/Continuity. 2017; 44(3): 439–456.

Medications and the risk of falling

- Falls are a common problem and can lead to serious consequences.
- Environmental modifications (lowering beds, removing loose rugs, installing night lights, and rearranging furniture) can reduce fall risk
- Additionally, gait disturbances should be addressed, and physical therapy may be appropriate for muscle strengthening and balance retraining
- An important risk factor are **medications:**
  - Antipsychotics
  - Anxiolytics
  - Sedatives and hypnotics
  - Antidepressants
  - Polypharmacy

F. Fernando et al. Risk Factors Associated with Falls in Older Adults with Dementia: A Systematic Review. Physiother Can. 2017; 69(2): 161–170.
DC Moga et al. Dementia. In Geriatrics issue of *Primary Care. Clinics in Office Practice*, edited by Dr. Demetra Antimisiaris. Elsevier Clinics/Continuity. 2017; 44(3): 439–456.





Resources

24/7 Nationwide Helpline: 800.272.3900

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Education Programs
Information & Referrals

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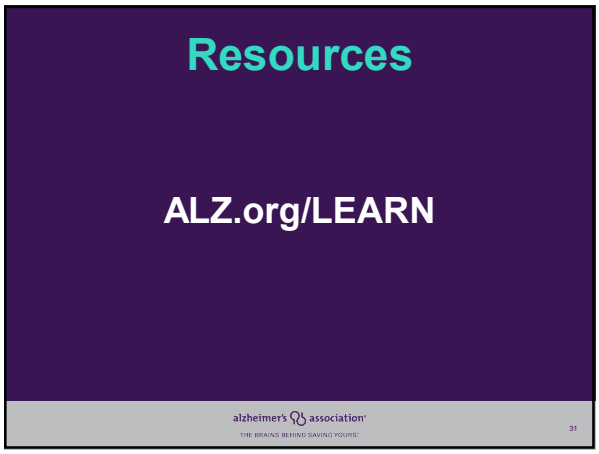
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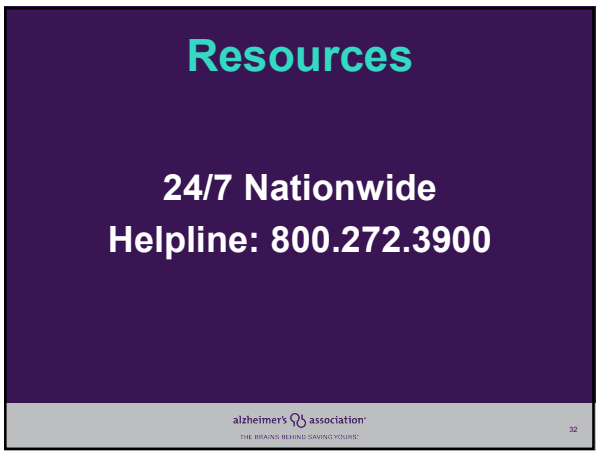
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