Best practices for the (de)prescribing of medications used to treat dementia

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Conflicts of Interest

• No conflicts of interest related to this presentation
Objectives

• Discuss medications used to treat dementia
• Review best practices for when to stop using FDA medications for dementia
Dementia

- **DSM-IV**
  - Multiple cognitive deficits
    - Memory loss must be present
    - One or more other deficit (aphasia, apraxia, agnosia, executive functions)
  - Decline from a prior level of function
  - Deficits do not occur exclusively in the presence of delirium

- **DSM-V**
  - Memory loss not necessary
  - Major (dementia) vs. minor cognitive impairment

Subtypes:

- Frontotemporal Lobar Degeneration
- Parkinson’s Related Dementia
- Traumatic Brain Injury
- Creutzfeldt Jacob Disease
- Vascular Disease
- HIV

Alzheimer’s Disease
Alzheimer’s Disease (AD)

• AD accounts for 60-70% of dementia cases worldwide

• In the United States, 2018
  – 5.4 million Americans of all ages have AD
    • 5.2 million ≥65 years old
    • 200,000 ≤65 years old
  – 1 in 9 people (11%) aged ≥65 have AD

*World Health Organization, http://www.who.int/mediacentre/factsheets
Alzheimer’s Disease

• Insidious development of recent memory loss
• Forgetting details of recent events
• Difficulty learning and retaining new information
• Aphasia is frequent early in course (word-finding difficulties)
• Visuospatial (getting lost, constructional apraxia)
• Executive dysfunction (problem solving, multi-tasking, judgment)
• Impaired behaviors during advanced disease course
Pharmacotherapy for Cognitive and Functional Symptoms

- The goal of current FDA approved pharmacologic therapies:
  - To delay the progression of symptoms of neurocognitive and physical decline
    - One analysis estimated that these effects would be similar to preventing a two-months-per-year decline in a typical patient with AD
    - For every 12 patients treated, one would benefit by achieving minimal improvement and one would develop a treatment-related adverse effect
<table>
<thead>
<tr>
<th>Drug</th>
<th>Class/Indication</th>
<th>Mechanism of Action</th>
<th>Common Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil (Aricept)</td>
<td>Cholinesterase Inhibitor</td>
<td>Prevents Ach breakdown</td>
<td>Nausea, vomiting, diarrhea, vivid dreams, weight loss, bradycardia, syncope, urinary retention</td>
</tr>
<tr>
<td>Galantamine (Razadyne)</td>
<td>Cholinesterase Inhibitor</td>
<td>Prevents Ach breakdown and stimulates nicotinic Ach release</td>
<td>Nausea, vomiting, diarrhea, vivid dreams, weight loss, bradycardia, syncope, urinary retention</td>
</tr>
<tr>
<td>Rivastigmine (Exelon)</td>
<td>Cholinesterase Inhibitor</td>
<td>Prevents Ach and butyrylcholine breakdown</td>
<td>Nausea, vomiting, diarrhea, anorexia, weight loss, muscle weakness, bradycardia, syncope</td>
</tr>
<tr>
<td>Memantine (Namenda)</td>
<td>NMDA antagonist</td>
<td>Blocks toxic effect from excess glutamate and regulates glutamate action</td>
<td>Dizziness, headache, diarrhea, constipation, confusion</td>
</tr>
<tr>
<td>Donepezil/Memantine XR (Namzaric)</td>
<td>Combination donepezil/memantine</td>
<td>Prevents Ach breakdown and reduces glutamate toxicity</td>
<td>Headache, diarrhea, dizziness, constipation, anorexia, vomiting, bradycardia, syncope</td>
</tr>
</tbody>
</table>
Pharmacotherapy for Cognitive and Functional Symptoms
Two main classes of medications:

• Cholinesterase Inhibitors (CI)
  • Considered symptomatic treatment and are not believed to be neuroprotective or to alter the underlying disease trajectory

• NMDA Antagonist (NA)
  • No effect on the rate of nursing home placement
  • No effect on behavior or activities of daily living
  • A small reduction in agitation was seen in patients taking memantine
  • Adding memantine to a CI was not associated with a statistically significant improvement compared with placebo
Guide for Deprescribing Cholinesterase Inhibitors and Memantine

- Cognition +/- function significantly worsened over the past 6 months (or less, as per individual)
  - Sustained decline at a greater rate than previous after exclusion of other causes
- No benefit seen during treatment
  - No improvement / No stabilization / No decreased rate of decline
- Severe/End-stage dementia
  - Dependence in most ADL’s
  - Inability to respond to their environment +/- limited life expectancy

*Deprescribing.org
Implementation of Deprescribing

• Discuss monitoring plan with the individual/family/caregiver
  • Honor values and preferences and reference goals of care
  • Deprescribing is a trial

• Conduct close periodic monitoring
  • Assess for changes in cognition / function / neuropsychiatric symptoms

• Taper and consider other causes for any change in condition
  • Halve dose every 4 weeks to lowest available dose
  • Consider timing of emergence of symptoms after dose reduction
    • Less than one week or 2-6 weeks after dose reduction, consider restarting

*Deprescribing.org
Surveillance of recent evidence

• There is a growing body of evidence showing a limited efficacy of antidementia medications at keeping patients longer in the community

• According to research published online in *JAMA Network Open*, the time to skilled nursing facility (SNF) admission does not differ across approved medications used to treat Alzheimer disease (AD)
Some 2019 statistics

• Among Medicare beneficiaries who were newly diagnosed with Alzheimer’s disease and who initiated any antidementia medication
  • 26.6% were admitted into a skilled nursing facility during follow-up
  • 22.7% experienced at least one cardiovascular event during follow-up
  • Bradycardia and syncope were the most frequently experienced cardiovascular events (9.0% and 13.0%, respectively)
  • There is limited evidence about efficacy of antidementia medications, especially as Alzheimer’s disease progress into the moderate and severe stages

Cost Analysis

CVS Retail Prices

• Namzaric (all strengths): $493.01 for 30 capsules
  • Sanford center patient: copay for Namzaric was $377 per month
  • $5,916/year
• Memantine 10 mg: $95.81 for 60 tabs
  • $1,150/year
• Donepezil 10 mg: $55.95 for 30 tabs
  • $671/year
• Galantamine 16 mg ER: $51.83 for 30 caps
  • $622/year
• Rivastigmine 13.3 mg/24 hours: $125.66 for 30 patch
  • $1,507.92/year
Cost Analysis continued

Home care: home health aide $21/hour
Home care: homemaker $19/hour
Adult day services $70/day

Source: MetLife 2011 Market Survey of Long-Term Care Costs
Special thanks to the EJC Foundation for their support of the Sanford Center Geriatric Specialty Clinic.

Sanford Center for Aging
775-784-4774
https://med.unr.edu/aging
References

• 1. UCLA Geriatric Medicine Board Review Course 2016, *Pharmacologic treatment across dementia syndromes*, Kremen, Sarah A., M.D., Clinical Physician of Neurology, David Geffen School of Medicine at UCLA

• 2. Up-to-date
Case Report: Mrs. L

• 95 y.o. female with severe dementia, hypertension, hypothyroidism, vitamin D deficiency and insomnia
  • November 2018: Outpatient neurologist started patient on Donepezil/Namenda. No cognitive screening tests performed, no follow up appointment scheduled.
  • Dec 2018/Jan 2019: Community SNF stay for PT
  • March 27, 2019: Establishes care from community to VA with chief complaint of “wants to get all meds from the VA now.”
  • March 29, 2019: Presents to VA ED with increased confusion, inability to walk, urinary incontinence
  • April 2019: Admitted to long term care for inability to care for self
Case Report: Mrs. L continued

• Interdisciplinary Geriatric Assessment upon admission to long term care unit resulted in shared recommendation from provider and pharmacist to discontinue Donepezil/Namenda
  • Husband of patient: “Absolutely NOT! Her memory will get even worse than it already is!!”
  • Intervention: Palliative Care Consult for Goals of Care meeting
  • Husband expresses his deepest fear: “That someday she won’t recognize me.”
    • Validation of thoughts, fears and emotions
    • Agrees to gradual dose reduction over 1 month
    • Acknowledges no change in condition from week to week
    • Donepezil/Namenda discontinued
Lessons from Mrs. L

• 1. Was the chosen medication initiated correctly?
• 2. Did the medication achieve any specific outcome?
• 3. Why was the patient’s husband so hesitant to discontinue the medication?
• 4. What are the implications for discontinuing a medication that never achieved the desired clinical outcome?
• 5. What factors should be taken into consideration when discontinuing a medicine?