Practical Issues Related to Medication Use in Dementia

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Disclosure Statement
I, Kevin Schleich, PharmD, BCACP do not have any financial interests or relationships with any manufacturers of products or providers of services I might be discussing in my presentation.

I have no financial relationships with any of the companies supporting this educational event.

I will not discuss any pharmaceuticals, medical procedures, or devices that are investigational or unapproved for use by the FDA.

Objectives
• Briefly review the background and prevalence of dementia in the United States
• Understand the importance of a thorough medication review, and appropriate steps involved when conducting a medication review
• Discuss methods to help patients with dementia improve medication adherence
• Address goals of therapy for chronic disease states as they relate to patients with dementia

Background

<table>
<thead>
<tr>
<th>Cause of Dementia</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s</td>
<td>Most common cause (60-80% of cases)</td>
</tr>
<tr>
<td></td>
<td>Progressive accumulation of beta amyloid plaques in brain</td>
</tr>
<tr>
<td>Vascular</td>
<td>Accounts for ~20% of dementia cases</td>
</tr>
<tr>
<td></td>
<td>Impaired judgment/ability to make decisions</td>
</tr>
<tr>
<td>Lewy body</td>
<td>Manifests as deep affective, visuohallucinatory, and gait imbalance, significant memory impairment may be absent</td>
</tr>
<tr>
<td></td>
<td>Often co-exists with Alzheimer’s dementia</td>
</tr>
<tr>
<td>Frontotemporal lobar degeneration</td>
<td>Alpha-synuclein inclusions (&quot;loss of filter&quot;)</td>
</tr>
<tr>
<td></td>
<td>Memory typically intact in early stages</td>
</tr>
<tr>
<td>Mixed</td>
<td>Halftab abnormalities of more than one cause</td>
</tr>
<tr>
<td></td>
<td>Most commonly Alzheimer’s combined with vascular dementia</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>Restlessness, rigidity, tremor, gait abnormalities</td>
</tr>
<tr>
<td></td>
<td>Other results in accumulation of Lewy bodies</td>
</tr>
<tr>
<td>Normal pressure hydrocephalus</td>
<td>Accounts for &lt;5% of dementia cases</td>
</tr>
<tr>
<td></td>
<td>May be corrected with shunt to drain excess cerebral fluid</td>
</tr>
<tr>
<td>Creutzfeldt-Jakob disease</td>
<td>Extremely rare</td>
</tr>
</tbody>
</table>

Epidemiology

• Difficult to ascertain a good approximation of people living with dementia
• Most statistics focus on Alzheimer’s dementia
• Estimated that 35.6 million people worldwide were living with dementia as of 2010
• That number is expected to at least double every 20 years
Predicted Impact

Treating Patients with Dementia

“FIRST, DO NO HARM”

“IN ELDERLY PATIENTS, PRESCRIBERS SHOULD ALWAYS CONSIDER THE POSSIBILITY THAT A NEW SYMPTOM IS DUE TO DRUG THERAPY”

5-Step Medication Review

Meet Our Patient

• MF is an 80-year-old female who reluctantly moved back to Iowa City to be closer to her family after her husband passed away within the past year. She was formally diagnosed with cognitive impairment in 2013, but her family believes her cognition has acutely worsened over the past 3 months. Additionally, she fell once in the past month. Her past medical history is significant for:
  • Cognitive impairment
  • Hypertension
  • Hypothyroidism
  • Insomnia
  • Depression/Anxiety
  • Parkinsonism
  • Osteoarthritis
  • Chronic back pain
  • Diarrhea/GI pain
  • Hysterectomy (1982)
  • Cataract removal (2013)
**Patient Info**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen 500 mg as needed</td>
<td>OA Pain</td>
</tr>
<tr>
<td>Hydrocodone/APAP 10/325 mg as needed</td>
<td>OA Pain</td>
</tr>
<tr>
<td>Meloxicam 7.5 mg daily</td>
<td>OA Pain</td>
</tr>
<tr>
<td>Alprazolam 0.5 mg three times daily</td>
<td>Depression/Insomnia</td>
</tr>
<tr>
<td>Amiodarone 500 mg twice daily</td>
<td>Parkinson's</td>
</tr>
<tr>
<td>Amlodipine 10 mg daily</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Levothyroxine 75 mcg daily</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Potassium Chloride 20 meq daily</td>
<td>Hypokalemia</td>
</tr>
<tr>
<td>Donepezil 10 mg daily</td>
<td>Cognitive Impairment</td>
</tr>
</tbody>
</table>

BP: 148/84 mmHg  
P: 80 bpm  
Calcium: 10.2 mg/dL  
Hemoglobin A1c: 5.6%  
TSH: 2.53 mIU/L

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**Medication Review**

1) **Does each medication have a legitimate indication?**

- Acetaminophen → OA Pain
- Hydrocodone/APAP → OA Pain
- Meloxicam → OA Pain
- Alprazolam → Depression/Insomnia
- Amantadine → Parkinson's
- Amlodipine → Hypertension
- Levothyroxine → Hypothyroidism
- Donepezil → Cognitive Impairment
- Potassium → Hypokalemia

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**Safety of Medications?**

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**AGS Beers Criteria**

- The Beers Criteria is a consensus-based list of **potentially** inappropriate medications for older adults.
- Most recently published in 2015, adhering to the IOM's challenge of developing evidence-based guidelines.
- 20-page document with nine reader-friendly tables:

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**AGS Beers Criteria**
### Medication Review

#### 2) Is each medication safe for a geriatric patient?
- Acetaminophen
- Hydrocodone/APAP
- Meloxicam
- Alprazolam
- Amantadine
- Amlodipine
- Levothyroxine
- Potassium
- Donepezil

#### 3) Is each medication effective for the indication?
- **Acetaminophen**: unsure, still having occasional pain
- **Hydrocodone/APAP**: unsure, still having occasional pain
- **Meloxicam**: unsure, still having occasional pain
- **Alprazolam**: very happy with the effect on her tremor. She had previously been on carbidopa/levodopa without benefit
- **Amantadine**: very happy with the effect on her tremor. She had previously been on carbidopa/levodopa without benefit
- **Amlodipine**: yes, blood pressure 148/84 mmHg in clinic, lower at home per her report
- **Levothyroxine**: yes, TSH is 2.53 mIU/L and she is not having any symptoms of hypo- or hyperthyroidism
- **Potassium**: yes, but closer to being hyperkalemic at 4.9 mEq/L
- **Donepezil**: family believes it was helping until the most recent 3 months

#### 4) Is each medication being tolerated by the patient?
- **Acetaminophen**: no adverse effects, does not drink EtOH
- **Hydrocodone/APAP**: had a fall, problems with memory recently
- **Meloxicam**: treated for hypertension
- **Alprazolam**: had a fall, problems with memory recently
- **Amantadine**: diarrhea and GI upset
- **Amlodipine**: no lower extremity edema, denies dizziness/lightheadedness
- **Levothyroxine**: no signs/symptoms of hypo/hyperthyroidism
- **Potassium**: GI upset
- **Donepezil**: GI upset

#### 5) Are any indications being undertreated?
- **Depression**: very tearful in clinic
  - previously on venlafaxine and mirtazapine with questionable efficacy
- **Osteoarthritis pain**: still complaining of relatively constant pain

<table>
<thead>
<tr>
<th>No Indication</th>
<th>Potentially Unsafe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium?</td>
<td>Hydrocodone/APAP</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
</tr>
<tr>
<td></td>
<td>Alprazolam</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Not Effective</th>
<th>Not Tolerated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Hydrocodone/APAP</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>Meloxicam</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Amlodipine</td>
</tr>
<tr>
<td>Potassium</td>
<td>Alprazolam</td>
</tr>
<tr>
<td>Donepezil?</td>
<td>Potassium</td>
</tr>
</tbody>
</table>
Our Plan

• **Discontinue:**
  - Hydrocodone/APAP → safety, tolerability, and unsure efficacy
  - Meloxicam → safety, tolerability, and unsure efficacy
  - Potassium → no indication and tolerability
  - Alprazolam → safety, tolerability, and unsure efficacy

• **Change:**
  - Acetaminophen to 1000 mg three times daily

• **Start:**
  - Sertraline 25 mg daily for depression/anxiety
    - Would not go back to venlafaxine due to questionable efficacy, and potential to increase blood pressure
  - Start lidocaine patches every 12 hours

Follow-Up

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen 1000 mg three times daily</td>
<td>OA Pain</td>
</tr>
<tr>
<td>Lidocaine patch every 12 hours</td>
<td>OA Pain</td>
</tr>
<tr>
<td>Amantadine 100 mg twice daily</td>
<td>Parkinson's</td>
</tr>
<tr>
<td>Amlodipine 10 mg daily</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Levothyroxine 75 mcg daily</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Donepezil 20 mg daily</td>
<td>Cognitive Impairment</td>
</tr>
<tr>
<td>Sertraline 25 mg daily</td>
<td>Depression/Insomnia</td>
</tr>
</tbody>
</table>

- Decreased number of medications from 9 to 7
- Follow-up potassium in 2 weeks was 3.9 mEq/L
- Ended up increasing the sertraline to 50 mg daily in 6 weeks
- Family felt her mind was “less cloudy” and they reported no more falls

The Problem

• As patients age, most have some impairment in:
  - Dexterity
  - Mobility
  - Hearing
  - Vision
  - Each of these alone can be a barrier to medication adherence. When added to progressing dementia, adherence becomes increasingly more problematic.

• As dementia worsens, the ability to plan accordingly, organize complex plans, and execute meticulous tasks diminishes

• Non-adherence to medications has been shown to:
  - Worsen therapeutic outcomes
  - Increase medical interventions
  - Increase incidence of adverse effects
  - Increase hospitalizations

Medication Adherence

Improving Adherence

Simplifying Medication Regimens

- Complete a comprehensive medication review
- Utilize combination medications if appropriate
- Switch to extended-release formulations if appropriate
- Exploit personal habits to help improve adherence
Simplifying Medication Regimens

• LZ is a 76-year-old female with a PMH significant for hypertension, type 2 diabetes mellitus, and mild cognitive impairment. Her current medication regimen is listed below:

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochlorothiazide</td>
<td>HTN</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>HTN</td>
</tr>
<tr>
<td>Metformin</td>
<td>Type 2 DM</td>
</tr>
<tr>
<td>Glipizide</td>
<td>Type 2 DM</td>
</tr>
<tr>
<td>Donepezil</td>
<td>Cognitive impairment</td>
</tr>
</tbody>
</table>

Medication Adherence

Advantages
- Cheap ($3-$10)
- Easy to use
- Large variation allows for differing complexities of medication regimen
  - Single dose, single day
  - 4 x dosing, weekly
- Easy to change regimen

Disadvantages
- Requires adequate cognition to set up pill box
- Requires assistance from family, friend, nursing services to set up in absence of adequate cognition
- No system to actually remind patient to take doses
- No feedback with missed doses

Automated Devices

Advantages
- Offer both monitored and stand-alone options; ability to lock
- Alert for patient to take meds
- Monitored options allow for text, phone, or e-mail notifications of missed doses to designated person
- Can coordinate with pharmacies

Disadvantages
- EXPENSIVE
  - $400-$2000 for the machine
  - Often monthly fees for monitoring
  - Can be very difficult to set up and fill on weekly or monthly basis
Medication Adherence

1. Evaluate the patient’s cognition to help determine their ability to manage their medications
   a) Montreal Cognitive Assessment (MOCA)

2. Assess family/community support available for patients unable to manage their own medications
   a) Competent/willing family
   b) In-home nursing services
   c) Pharmacy services

3. Determine the best plan to maximize medication adherence

Principles of Chronic Disease States in Elderly

1. Establish goals of care with patient and family members

2. Achieve acceptable goals without causing undue treatment burden

3. Continuously assess therapy for safety, efficacy, and tolerability

4. Be willing to de-escalate therapy
   “Hope is not a plan.”
   — Dr. Atul Gawande

Neurological

**Depression/Anxiety**
- Most common mental disorder in geriatric patients
  - Estimated that ~40% of patients with Alzheimer’s dementia have depression
- Geriatric depression scale helps screen patients in clinic
- Treatment revolves around SSRIs
  - Sertraline: favorite (start with low dose, and titrate slowly)
  - Paroxetine: too short half-life
  - Fluoxetine: too long half-life
  - Citalopram: associated with prolonged QT-interval
- Mirtazapine: helpful for depression, insomnia, appetite stimulation

**Insomnia**
- Many patients with dementia have trouble with insomnia
- No prescription medications work very well, and all have potential for serious adverse effects
  - **Sleep Hygiene**
    - Increase physical activity throughout the day
    - Avoid naps
    - Only use bedroom for sleep
    - Limit caffeine/alcohol intake

**Potential Medication Trials**
- Melatonin 3 mg
- Trazodone 50-200 mg
- Mirtazapine 7.5 mg
- Nortriptyline 10 mg

**Medications to AVOID**
- Diphenhydramine (all OTC “PM” medications)
- Zolpidem
- Benzodiazepines
**Endocrine**

**Type 2 Diabetes Mellitus**
- Most important part of tight glycemic control in adults is to avoid long-term complications.
- Patients of advanced age with numerous comorbid conditions will have different goals of care.

**Cardiovascular**

**Atrial Fibrillation**
- Still utilize the CHADS2 or CHA2DS2-VASc scores to stratify embolic risk for elderly patients with atrial fibrillation.
- Equally important to use validated bleed-risk scores to predict the risk of complications associated with anticoagulants:
  - HAS-BLED
  - mOARI

**Hypertension**
- Goal BP: <150/90 mmHg.
- Always assess for overtreatment:
  - Dizziness
  - Lightheadedness
  - Falls
- Choose agents carefully to not exacerbate common conditions in elderly:
  - Amlodipine: lower extremity edema
  - Diuretics: dehydration
  - Beta-blockers: orthostatic hypotension

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**Diabetes Care**

- May consider newer agents:
  - DPP-4 inhibitors: once daily, oral
    - Sitagliptin (Januvia®), Linagliptin (Tradjenta®), alogliptin (Nesina®), saxagliptin (Onglyza®)
  - GLP-1 agonists: available as once weekly injections
    - Extended-release exenatide (Bydureon®)
    - Albiglutide (Taniona®)
    - Dulaglutide (Trulicity®)
  - If insulin is necessary, basal insulin much safer than bolus insulin.

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**Table:**

<table>
<thead>
<tr>
<th>Pro</th>
<th>Warfarin (Coumadin®)</th>
<th>Dabigatran (Pradaxa®)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Requires monitoring</td>
<td>Requires monitoring</td>
</tr>
<tr>
<td></td>
<td>Not user-friendly</td>
<td>Not user-friendly</td>
</tr>
<tr>
<td></td>
<td>Stable interruption</td>
<td>Stable interruption</td>
</tr>
<tr>
<td></td>
<td>No quality monitoring</td>
<td>No quality monitoring</td>
</tr>
<tr>
<td></td>
<td>No routine monitoring</td>
<td>No routine monitoring</td>
</tr>
<tr>
<td></td>
<td>No routine monitoring</td>
<td>No routine monitoring</td>
</tr>
</tbody>
</table>

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**Figure:**

- Dabigatran
- Edoxaban
- Apixaban

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**Type 2 Diabetes Mellitus**
- With increased hemoglobin A1C goals, comes increased blood glucose goals:
  - ~100-150 mg/dl fasting
  - < 200-250 mg/dl pre-prandial
- Utilize medications with convenient dosing and low risk of hypoglycemic events:
  - Metformin H. daily: be cognizant of renal function

<table>
<thead>
<tr>
<th>Renal function (mL/min)</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 45</td>
<td>No need to adjust to metformin</td>
</tr>
<tr>
<td>30 – 45</td>
<td>Max dose of 500 mg/daily</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Discontinue metformin</td>
</tr>
</tbody>
</table>

- Sulfonylureas: AVOID glyburide
  - Glipizide (available XL) or glibizide once daily preferred
Cardiovascular
ASCVD Risk (Hyperlipidemia)

• Treating with statins for primary prevention is looking to reduce 10-year ASCVD risk

• Utilizing a medication to potentially prevent an event over 10 years may not be practical in a patient with dementia

• Statins have loosely/potentially inaccurately been associated with dementia
  • Most recent literature leans toward statins neither causing, nor playing a significant role in preventing dementia

Goals of Treatment

1. Establish goals of care with patient and family members
2. Achieve acceptable goals without causing undue treatment burden
   a) Preventing stroke by treating atrial fibrillation
   b) Minimizing 10-year cardiovascular risk with statins
3. Continuously assess therapy for safety, efficacy, and tolerability
   a) CHADS2 score = 1 vs. HAS-BLED score = 5
4. Be willing to de-escalate therapy

Summary

• Dementia is currently affecting more than 35 million people worldwide, with expectations that number will double every 20 years

• It is essential to complete a thorough medication review for patients with dementia

• Adherence to complex medication regimens is unlikely in patients with dementia, therefore simplification is necessary

• Be familiar with your patients’ goals of therapy, and tailor their treatment to best accomplish those goals

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Thank you.