

PALLIATIVE PEARLS

BY ENCLARA PHARMACIA

Discontinuing Dementia Medications Case April 2017

Patient Case

MJ is an 86 year-old female with a primary diagnosis of Alzheimer's disease and history of anemia, cystitis, depression, Type II DM, HTN, TIA and osteoarthritis. Amoxicillin and sulfa are listed as allergies, however, her reaction to these medications is not documented. MJ was readmitted to hospice today after being off service for 8 months. She lives at home with her daughter who is the primary caregiver.

Current medications:

- Acetaminophen 1000mg PO three times daily for pain
- Acetaminophen 650mg PR every 4 hours for mild pain or fever
- Aricept® 10mg PO daily for memory
- Aspirin 81mg chewable by mouth daily for clot prevention
- Bisacodyl 10mg PR daily as needed for constipation
- Calcium w/ Vit D 600mg-400units PO twice daily for supplementation
- Carbamazepine 100mg chewable PO twice daily for seizures
- Escitalopram 20mg PO daily for depression
- Miralax® powder 17gm PO daily for constipation
- Glimepiride 2mg PO twice daily for diabetes
- Haloperidol 2mg/mL concentrate – 1mg PO every 6 hours as needed for agitation
- Lantus® inject 9 units subcut every night at bedtime for diabetes
- Lidocaine 5% patch – Apply 2 patches daily to painful area
- Lorazepam 0.5mg PO every morning and afternoon and every 2 hours as needed for anx/agit
- Melatonin 10mg PO every night at bedtime as needed for sleep
- Namenda® 10mg PO twice daily for memory
- Nitrofurantoin 100mg PO every night at bedtime for UTI prevention
- Valsartan-HCTZ 160mg-25mg PO daily for the blood pressure

The pharmacist reviewing the readmission notes that MJ has been taking all of her medications prior to readmission and tolerating them without known side effects. In addition to dementia, the hospice medical director noted the following conditions related to the terminal prognosis: TIA, HTN, and depression. Currently, MJ has no unresolved signs or symptoms, including pain. The pharmacist recommends discontinuation of the calcium supplement, Aricept and Namenda and advises the nurse case manager regarding the 3 gram per day maximum limit for acetaminophen. The nurse will discuss these recommendations with the hospice team, but notes it will be difficult to stop the Aricept and Namenda because the patient's family is "not ready for this". What information can the pharmacist

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provide to support the nurse in discussing Aricept and Namenda discontinuation with the hospice team and caregiver?

How does Aricept (donepezil) and Namenda (memantine) work in patients with Alzheimer's disease?^{1,2}

Alzheimer's disease is the most common form of dementia in the elderly affecting memory, thinking, and behavior. It is characterized by plaques, tangles, and decreased acetylcholine in the brain. Two drug classes are indicated for the treatment of dementia associated with Alzheimer's disease: (1) Cholinesterase inhibitors (ChEIs) (i.e., donepezil (Aricept[®]), galantamine (Razadyne[®]), and rivastigmine (Exelon[®]) and (2) N-methyl-D-aspartate (NMDA) receptor antagonist memantine (Namenda[®]). Namzaric[®] is an extended-release form containing both donepezil and memantine.

The ChEIs inhibit acetylcholinesterase (AChE), the enzyme responsible for the degradation of acetylcholine, thereby improving the availability of acetylcholine in the brain. Memantine works by slowing intracellular calcium accumulation and helps to prevent further nerve damage, which is thought to prevent excitatory amino acid neurotoxicity without interfering with the physiological actions of glutamate required for memory and learning.

Is there literature to support the use of dementia medications in patients on hospice?

Evaluation of randomized controlled trials (RCTs) suggest that donepezil and memantine lead to some improvements in patients' global cognition, functional communication, and some behavioral symptoms (agitation and aggression) in patients with moderate to severe dementia.³

The effectiveness of donepezil is less evident when patients reach a severe stage of dementia when cognitive and functional abilities and social interactions are very limited. Along with some benefit in behavioral symptoms, reports of cognitive and global benefits of donepezil in mild to moderate dementia stages are primarily described as "showing less worsening" compared to placebo. Memantine may have greater benefit in patients with a high prevalence of behavioral and psychological symptoms (delusions, hallucinations, and agitation) for those with more advanced disease, although evidence for end stage disease is lacking. However, studies have demonstrated that there is no additional benefit in adding memantine to donepezil versus memantine alone.³

What are the potential risks and burdens of dementia medications in end-stage dementia?

- Adverse effects such as anorexia, diarrhea, nausea, and vomiting (ChEIs)
- Potential drug-drug interactions
- Increased risk of bradycardia and syncope (ChEIs)
- Burdens and risks associated with taking oral medications when swallowing ability and appetite are decreased
- Memantine dose should be adjusted or stopped in patients with severe renal insufficiency
- High cost (average 15-day supply of one prescription of tabs or caps costs \$100-\$250)

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What are some considerations for discontinuing dementia medications?

The following rationale can be used in the decision-making process to support the discontinuation of anti-dementia drugs as an appropriate intervention:

- The patient or caregiver (designated health care proxy) chooses to stop treatment
- The patient refuses to take the medication
- The patient does not adhere to the medication regimen, such that continuation would be useless
- There is no response to therapy after a reasonable trial
- The potential benefit of treatment is no longer clinically significant in terms of the overall disease severity/stage:
 - The Functional Assessment Staging Tool (FAST) can be used to identify patients with dementia in the late-stage of dementia. A FAST score \geq stage 7A along with one or more specific dementia-related co-morbidities (e.g., aspiration, urinary tract infection, sepsis, multiple stage 3-4 ulcers, persistent fever, weight loss $>$ 10% within 6 months) may be an indicator of a 6 months or less prognosis.
 - Mini-Mental State Examination (MMSE) - score \leq 10 out of possible 30 points.
 - Global Deterioration Scale (GDS) – stage 7
- The patient experiences intolerable side effects.
 - ChEIs – nausea, vomiting, diarrhea, anorexia, weight loss, abdominal pain, muscle cramps, tremor, dizziness, and headache
 - NMDA antagonists - dizziness, confusion, constipation, and increased blood pressure

How should I approach discontinuing dementia medications with patient's family/caregiver?

- Recognize that it may be difficult for family members to discontinue medications that their loved one has been taking for a long time. Ask what concerns or questions that they might have.
- Help family members to understand that you are prioritizing the medications that are most important right now based upon their loved one's condition and needs.
- Ask the family what symptom(s) improved when their loved one was first placed on the medication. Do they think that it is still helping?
- Recommend a gradual dose taper, carefully observing for any changes in behavior or symptoms. Reassure that you will restart the medication or discuss alternate approaches to managing symptoms if they recur.
- Highlight possible adverse effects associated with dementia medications, including insomnia, nausea and weight loss that may improve once the medications are stopped.

SAMPLE SCRIPT FOR USE WITH FAMILY MEMBERS:

"Your mother's dementia medication is most likely no longer contributing to her comfort and may be causing unwanted side effects such as nausea and poor appetite. These medications also increase the burden of taking her pills each day. For these reasons, I suggest that we slowly decrease these medications over the next few weeks while we carefully observe for any changes. Are you OK with that?"

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What is the recommended discontinuation process?

- Begin discontinuation with only one medication at a time (often patients are taking ChEI and an NMDA antagonist together)
- Taper the drug by decreasing the dose by half for two weeks and then stop. Assess for any reappearance of behavioral or psychological symptoms. If they recur, restart the medication at the effective dose.
- Once the first drug (such as donepezil) is tapered, begin tapering any other remaining ChEIs by decreasing the dose by half for two weeks. If there is no clinical change, stop the medication.
- Patients should be carefully monitored for changes in cognition, function, and behavior following discontinuation of anti-dementia medication. Tapering the dose may minimize the potential of withdrawal syndrome, including agitation, sleep disturbance, and mood changes. If symptoms worsen significantly, consideration may be given to restarting anti-dementia medication.

How should psychological and behavioral symptoms be managed?

- **Treat underlying causes of symptoms first:**
 - Verbal/vocal behaviors - Associated with pain, loneliness or depression
 - Agitation - Associated with pain or boredom and the need for activity and stimulation
 - Aggressive behaviors - Associated with avoiding discomfort, the communication of needs or a demand for personal space
- **Non-pharmacological management should be initiated first line:**
 - Monitor personal comfort
 - Calm and simplify the environment
 - Provide a security object
 - Avoid being confrontational
 - Acknowledge requests and respond
 - Redirect the person's attention
 - Psychosocial Interventions (behavioral therapy, cognitive stimulation, physical activity)
 - Structured socialization (i.e., pet therapy)
 - Other (i.e., music, massage and touch, reminiscence, aromatherapy)
- **Pharmacological Management**
Serotonin-Selective Reuptake Inhibitors (SSRIs) and Trazodone (Desyrel®)
 - Despite having little statistically significant evidence in controlling depression in patients with dementia, antidepressants have been extensively studied and may be effective in treating agitation and psychotic symptoms in these patients.⁴
 - Both SSRIs (i.e., citalopram (Celexa®), sertraline (Zoloft®)) and trazodone appear to be tolerated well when compared to placebo, typical antipsychotics and atypical antipsychotics for agitation and psychosis in dementia according to a Cochrane database review in 2011.⁵
 - A 2014 study reviewed the addition of citalopram compared with placebo in patients with Alzheimer's disease and found significantly reduced patient agitation and caregiver distress.⁶

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Antipsychotics⁷⁻⁹

- Antipsychotics are associated with an increased mortality when used to treat behavioral disturbances in older patients with dementia. Both atypical (i.e., Risperdal®) and conventional (i.e., Haldol®) antipsychotics are labeled with this black box warning.
- Despite years of off-label use of this class, atypical antipsychotic drugs are not reliably more effective than placebo for psychotic symptoms of dementia

When is antipsychotic use appropriate in the elderly dementia population?

- Antipsychotics should be used to treat agitation or psychosis in patients with dementia **ONLY** where environmental manipulation fails and/or when symptoms persist despite non-pharmacological and medication intervention:
 - Behavioral symptoms are due to mania or psychosis
 - Symptoms present a danger to the patient or others
 - Patient is experiencing inconsolable or persistent distress
 - Patient is experiencing a significant decline in function or substantial difficulty receiving needed care

For additional information on this topic, please review these references:

Enclara Pharmacia's On Demand Educational Webinar, "Dementia Care at End-of-Life". Click [here](#) to log in.

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