



Antipsychotics for Dementia

Under Control or Over-Prescribed?

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Learning Objectives

- Summarize the disease progression and most common symptoms of dementia.
- Describe the risks and benefits of antipsychotic medication in patients with dementia.
- Recommend potential pharmacologic and non-pharmacologic treatment options for symptoms associated with dementia patients in hospice.



Types of Dementia

Irreversible	Reversible
Alzheimer's Disease	Normal pressure Hydrocephalus
Vascular Dementia	Wernicke-Korsakoff Syndrome
Lewy-Body Dementia	Infections
Parkinson's Disease Dementia	Electrolyte abnormalities
Frontotemporal Dementia	

NH. The Dementias: Hope through research. Published Sept 2013, Last updated: January 22, 2015

Symptoms of Dementia

Cognitive

- Memory loss, mental decline, disorientation, forgetfulness, inability to speak or understand, making things up, mental confusion, or inability to recognize common things

Behavioral

- Aggression, irritability, personality changes, lack of restraint, or wandering and getting lost

Mood

- Anger, apathy, general discontent, loneliness, mood swings, or nervousness

NIH. The Dementias: Hope through research. Published Sept 2013, Last updated: January 22, 2015

Symptoms of Dementia

Muscular

- Inability to combine muscle movements or unsteady walking

Sleep

- Difficulty falling asleep or sleep disturbances

Psychological

- Anxiety, depression, hallucinations, and paranoia

NIH. The Dementias: Hope through research. Published Sept 2013, Last updated: January 22, 2015

Treatment

- No cure for dementia
- The main goal is slowing symptom progression
 - Cholinesterase inhibitors
 - NMDA receptor antagonists
 - Non-pharmacological techniques
 - Symptom management

NIH. The Dementias: Hope through research. Published Sept 2013, Last updated: January 22, 2015

Treatment for cognitive and functional losses

- Cholinesterase Inhibitors:
 - Rivastigmine (Exelon®), donepezil (Aricept®), galantamine (Razadyne®)
- NMDA receptor antagonists:
 - Memantine (Namenda®)
- Both mechanisms serve only to delay symptom progression and become less effective as the disease worsens.

Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias. APA 2010

Neuropsychiatric symptoms (NPS)

- Include: Delusions, aggression, agitation, withdrawal, anxiety, psychosis, refusal, insomnia, depression
- NPS affect up to 97% of people with dementia over the course of their illness.
- These symptoms can be distressing to patients, family, and caregivers
- Multiple pharmacological and non-pharmacological approaches to managing these symptoms

Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias. APA 2010

Depression

- Over the last 15 years, 8 placebo-controlled trials have examined the efficacy of antidepressants in patients with dementia.
 - Results were mixed
- Selective serotonin reuptake inhibitors (SSRIs) appear to be the most effective.
- Sertraline and citalopram in particular showed the most consistent improvement for depression.
- Cognitive Behavioral Therapy (CBT)

Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias. APA 2010

Anxiety

- Identify potential causes of anxiety
- Benzodiazepines can be useful when anxiety is present with or without agitation
 - Short-term use and as needed for acute symptoms
 - Lorazepam is often the drug of choice
- Adverse effects and worsening of target behaviors
 - Sedation, confusion, falls, paradoxical behavior, delirium
 - Long-term use can lead to dependence

Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias, APA 2010

Insomnia

- Current studies have not found any specific medications to be more advantageous over another.
- Practice good sleep hygiene
- Adjust timing of other medications
- Current best practices recommend one or more of the following:
 - ▶ Melatonin
 - ▶ Mirtazapine
 - ▶ Temazepam
 - ▶ Zolpidem
 - ▶ Trazodone
 - ▶ Clonazepam
- **Avoid: diphenhydramine (Benadryl!)**

Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias, APA 2010

Behavioral or Psychiatric Symptoms of Dementia (BPSD)

- Psychosis, hallucinations, and agitation
 - The term BPSD is used to describe behavior or other symptoms in individuals with dementia that cannot be attributed to a specific medical or psychiatric cause.
- These symptoms impair quality of life, are distressing to patients and to caregivers, and are commonly a major contributor to the decision to move a family member with dementia into a nursing home
- Many patients are treated with antipsychotics

Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias, APA 2010

Antipsychotics – Risks and concerns

- Large scale meta-analyses of clinical trials have consistently demonstrated a 1.5–1.7 times increased risk of **mortality** with their use in dementia.
- All antipsychotics carry a black box warning from the FDA about this risk
- Also linked to a 2–3 fold higher risk of cerebrovascular events
- **No antipsychotic is approved for the treatment of any NPS in dementia.**

Antipsychotics – Adverse effects

- **General:** Anticholinergic effects, falls, excessive sedation
- **Cardiovascular:** Cardiac arrhythmias, hypotension, stroke, transient ischemic attack (TIA)
- **Metabolic:** Increase in total cholesterol and triglycerides, unstable or poorly controlled blood sugar, weight gain
- **Neurologic:** Akathisia, tardive dyskinesia, delirium, neuroleptic malignant syndrome (NMS), parkinsonism, cognitive worsening

Antipsychotics – The Problem

- According to the Center for Medicare and Medicaid Services (CMS), in 2010, 39.4% of nursing home residents nationwide who had cognitive impairment and behavioral issues but no diagnosis of psychosis or related conditions received antipsychotic medications
- Another 2008 study found that 44.8% of the residents studied with dementia were taking an antipsychotic
- Because of this, in 2012, CMS launched an initiative to reduce the amount of antipsychotics used in nursing homes and long term care facilities
 - Partnership to Improve Dementia Care in Nursing Homes

1. Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias, APA 2010
2. J Geriatr Psychiatry Neurol 2010;23(4):237-247

Antipsychotics – Inadequate indications for use

- Wandering
- Poor self-care
- Restlessness
- Impaired memory
- Mild anxiety
- Insomnia
- Inattention or indifference to surroundings
- Sadness or crying alone that is not related to depression or other psychiatric disorders
- Fidgeting
- Nervousness
- Uncooperativeness (e.g. refusal of or difficulty receiving care).

Centers for Medicare and Medicaid Services, Dementia Care in Nursing Homes P399

Final Rule 2017

Psychotropic Agents should be given ONLY:

- To treat a **specific condition as diagnosed and documented in the clinical record**
- With **gradual dose reductions, and behavioral interventions**, unless clinically contraindicated, in an effort to discontinue these drugs

Psychotropic Agents

PRN Orders

- **PRN orders for psychotropic drugs are limited to 14 days.**
- The **attending physician or prescribing practitioner** may extend the PRN order beyond 14 days with documentation of their rationale and expected duration for the PRN order.
- PRN orders for **antipsychotic drugs** are limited to 14 days and cannot be renewed without a direct examination of the resident by the attending physician or prescribing practitioner.

Antipsychotics

As part of the evaluation, the attending physician or prescribing practitioner should, at a minimum, determine and document the following in the resident's medical record:

- Is the antipsychotic medication still needed on a PRN basis?
- What is the benefit of the medication to the resident?
- Have the resident's expressions or indications of distress improved as a result of the PRN medication?

Digging Deeper

- No Hospice Exceptions!
- All indications (agitation, nausea, hallucinations) are included.
- A report of the resident's condition from facility staff does not constitute an evaluation
- Telemedicine may be used in place of an in person evaluation

Antipsychotics

- Despite the risks, several studies have looked at the safety and efficacy of antipsychotics in dementia
- The majority of these studies found improvement when an antipsychotic was compared to placebo, especially for the following symptoms:
 - Aggression
 - Agitation
 - Psychosis
 - Behavioral disturbances

Case 1

AR is a 78 year old male nursing home resident admitted to hospice with a primary diagnosis of Alzheimer's dementia. Over the last few days he has had worsening confusion and agitation. Today, he tried to hit one of his caregivers but was able to be redirected afterward. His physician would like to start Haloperidol 2mg tablets q6h around the clock to control his symptoms.

What assessments should be done before this medication is started?

Starting Antipsychotics

- Before any medication is started, exclude any potential remedial causes of behavior
 - Delirium
 - Infection
 - Pain
 - Environmental factors
 - Other medications
- Consider the individual patient's needs and abilities
 - Ability to swallow
 - Current medications and symptoms
 - Intermittent or continual behaviors?

Starting Antipsychotics

- Use the lowest effective dose necessary to control symptoms, start low and titrate up as needed
- Keep in mind that these medications can take time to work and increasing doses too quickly often leads to increased side effects, not rapid efficacy
- Continue to assess the effects of any intervention and identify benefits or complications, adjust accordingly

Case 1 continued

AR has no obvious underlying causes for his recent agitation and his symptoms continue to escalate. AR's roommate has become fearful of him. Upon further investigation, it seems most of his symptoms are occurring in the evening.

Should haloperidol 2mg ATC be started?

If haloperidol is started, what continued monitoring should be done?

What alternative options could be utilized?

If antipsychotic is started PRN, what documentation is needed?

Choosing an antipsychotic

- Typical (1st Generation)
 - Haloperidol (Haldol®)
 - Prochlorperazine (Thorazine®)
- Atypical (2nd Generation)
 - Quetiapine (Seroquel®)
 - Risperidone (Risperdal®)
 - Olanzapine (Zyprexa®)
 - Aripiprazole (Abilify®)
 - Ziprasidone (Geodon®)

Haloperidol (Haldol®)

- Starting Dose 0.25mg – 1 mg per day
 - Generally effective at 0.5mg-1mg every 2-12 hours
- Can be given PO, PR, SubQ, IV, IM
- High potency agent – less sedation than other typicals but increased parkinsonian symptoms and akathisia
- A trial comparing quetiapine to haloperidol showed quetiapine to be statistically more tolerable than haloperidol
- Can prolong the QTc interval – can lead to arrhythmia
- Very cost effective – especially tablets

Risperidone (Risperdal®)

- Starting dose 0.5mg – 1mg per day
- Generally effective at 0.5mg-1mg every 12-24 hours
- Can be given PO (tablet, liquid, ODT), IM
- Low to moderate risk of parkinsonism (dose dependent)
- Greater sedation risk and falls compared to haloperidol
- Highest risk of cerebrovascular events in studies
- Lower risk of QTc prolongation compared to haloperidol

Olanzapine (Zyprexa®)

- Starting dose 1.25mg – 5mg per day
- Generally effective at 2.5mg to 5mg every 12-24 hours
- Can be given PO (liquid, tablet, ODT) and IM
- Similar side effect profile and efficacy to risperidone
- Increased metabolic effects (caution in diabetics)
- Increased clearance in smokers

Quetiapine (Seroquel®)

- Starting dose 12.5mg – 50mg per day
- Generally effective at 25mg-100mg every 8-12 hours
- Can only be given PO as a tablet
- **Preferred antipsychotic for Parkinson's dementia**
- Generally more sedating when compared to risperidone
- Data from two randomized trials have shown that quetiapine is better tolerated when compared to other antipsychotics in patients with parkinson's dementia or lewy-body dementia
 - Less movement related side effects, EPS, akathisia
- Carries small risk of QTc prolongation - less than haloperidol

Non-Pharmacological Approaches

- Many clinicians recommend implementing non-pharmacologic psychosocial treatments.
- Studies have shown that these techniques can improve quality of life and help to maximize a patient's function.
- Have not been shown to provide lasting benefit if not continued regularly

Non-Pharmacological Approaches

- Behavior oriented
 - Reinforced habits of daily living
 - Scheduled toileting
 - Positive reinforcement techniques
 - Patient tailored interventions
- Emotion oriented
 - Reminiscence therapy
 - Simulated presence therapy
 - Validation therapy
 - Animal-assisted therapy

Non-Pharmacological Approaches

- Cognition oriented
 - Skillstraining
 - Classroom activities
 - Memory training
- Stimulation oriented
 - Acupuncture
 - Aromatherapy
 - Light therapy
 - Massage or touch therapy
 - Music therapy
 - Exercise

Case II

GM is an 81 year old female with Parkinson's disease and underlying dementia. She was started 1 week ago on haloperidol 1mg q8h ATC to help with agitation and restlessness throughout the day. Her agitation has improved significantly but she has developed worsening tremors and impaired muscle rigidity.

What changes could be made to her medications to improve these symptoms?

Case II Continued

GM has found improvement in her agitation after switching to quetiapine. She has been titrating up on the dose steadily over the last week and is now taking quetiapine 50mg PO TID. However, her last dose increase caused significant sedation and she wants to be awake to visit with her family.

What changes could be made to maintain her improvement while limiting over-sedation?
What other interventions should be completed and documented if therapy is to continue?

Conclusions

- In general, antipsychotics should only be used in patients with dementia after careful evaluation and when the patient is a danger to themselves or others
- Using the lowest effective dose of a given antipsychotic for the shortest period of time can help to mitigate side effects
- Medication choices and doses should be re-evaluated frequently to maximize benefit
- Non-pharmacological approaches should be utilized to decrease the amount of medication required

Questions

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