Pharmacologic Interventions for Challenging Behaviors in Dementia

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Disclosures

• IA-ADAPT is funded by AHRQ R18 HS19355-01, and I am supported by HRSA (Iowa Geriatric Education Center).
• I have had no financial relationships in the past 12 months with any companies that produce proprietary products discussed in this presentation.
• No drug is FDA approved to treat neuropsychiatric/behavioral disturbances in dementia.

The Challenge

• Very few drugs help for problem behaviors or psychosis in dementia
• Antipsychotics are the main drug treatment
  – Effectiveness is modest
  – Serious side effects, including death
• Non-drug methods are preferred
  – Providers may feel or be poorly trained to use non-drug behavior management techniques

The Problem

• ~22% of antipsychotic prescriptions in nursing homes are problematic per Centers for Medicare and Medicaid Services (CMS) standards

<table>
<thead>
<tr>
<th>Problem per CMS standards</th>
<th>% of claims</th>
</tr>
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<tbody>
<tr>
<td>Excessive dose</td>
<td>10.4%</td>
</tr>
<tr>
<td>Excessive duration</td>
<td>9.4%</td>
</tr>
<tr>
<td>Without adequate indication</td>
<td>8.0%</td>
</tr>
<tr>
<td>Without adequate monitoring</td>
<td>7.7%</td>
</tr>
<tr>
<td>In the presence of adverse effects that indicate the dose should be reduced or discontinued</td>
<td>4.7%</td>
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Antipsychotics and Mortality in Dementia

• Black Box Warning Issued in 2004
  – Elderly with dementia-related psychosis treated with these drugs at increased risk for death compared to placebo
• Consistent across all antipsychotics
• Relative risk = 1.6-1.7
  – Absolute risk = 3.5% vs. 2.3% with placebo
• Number Needed to Harm = 83
  – Number need to treat = 5-14
  – For every 9-25 persons helped, 1 death associated with use


Antipsychotic Adverse Effects

• Sedation
• Postural hypotension
• Falls
• Extrapyramidal
  – Parkinsonism
• Cerebrovascular
  – OR 2.1, ARI ~1%
• Mortality
  – Infection and cardiac
• Metabolic side effects (weight gain, etc.)

Problem Behaviors and Psychosis in Dementia

Communication

Other Stressors

Environment

Drugs

Severity and Type of Dementia

Depression/Anxiety/Insomnia

Medical Conditions

Unmet Needs

Need-Driven Model

Background/Individual factors
- Cognitive function
- Physical function
- Longstanding personality
- Habits, traits

Proximal/Environmental factors
- Physical needs
- Psychological needs
- Social environment
- Physical environment

Behavioral & Psychological Symptoms

Discuss the Person & Situation

Approach to Problem Behaviors or Psychosis in Dementia

Establish
- dangerousness of situation
- clear diagnosis/etiology
- severity and frequency of symptoms

Explore
past treatments and outcomes

Discuss
risks and benefits of potential treatments

Mrs. Annabel Klein

- 71 yo female
- Moderate dementia
- PMH: Constipation, urinary incontinence
- Medications:
  - Prescribed at home and continued in nursing home
  - Docusate Sodium 100 mg BID
  - Oxybutynin ER 10 mg QHS
  - Multivitamin QD

Mrs. Annabel Klein

- 10 days after admission to the nursing home
  - Became quiet and withdrawn, irritable at meal times, intermittent refusal of meals and poor fluid intake
- What assessments do you recommend?

Approach to Problem Behaviors or Psychosis in Dementia

Discuss the Person & Situation

Assess the Person & Situation

- Proximal Factors ➔ Identify, assess, treat, eliminate Antecedents and/or Triggers to problem behaviors
  - Unmet physical needs
  - Unmet psychological needs
  - Environmental causes
  - Psychiatric causes

Algase et al, J Alz Dis 1996;11(6):10-19

Meeks and Jeste, Current Psychiatry 2008;7(6):50-65
### Non-Pharmacological Approaches

- **Overall person-centered approach**
  - Consider behavior as a form of communication of an unmet need
    - Psychosocial
    - Physical
    - Etc.
  - Try to meet that need
    - Individualized activities
    - Treatment of medical problem
    - Etc.

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**Social Histories**
- What did they do for a living?
- Did they work evening/night shifts?
- Did the family experience any behavioral problems?
- What were their habits?
- What were their interests?
- What was their average day like?
Non-Pharmacological Approaches

• Behavioral disturbances can be produced by problems with other residents, staff, or the environment
• Behavioral abnormalities require a thorough assessment of the physical and mental health
  – Determine in there is a new medical or psychiatric problem
• Changes in living environment or staffing can also change resident behavior

Non-Pharmacological Approaches

• Interventions
  – Select interventions based on the type of problem and assessment of retained abilities, preferences and resources:
    • Cognitive level
    • Physical function level
    • Long-standing personality, life history, interest/abilities
    • Preferred personal routines and daily schedule
    • Personal/family/facility resources

Non-Pharmacological Approaches

• Intervention
  – Adjust caregiver approaches
    • Personal approach, daily routines, communication style, unconditional positive regard, involvement/engagement
  – Change the environment
    • Eliminate misleading stimuli, reduce environmental stress, adjust stimulation, enhance function, involve in meaningful activities, adapt the physical setting
  – Use evidence-based interventions
    • Agitated/irritable, resistant to care, wandering/restless/bored, disruptive vocalization, apathetic/withdrawn, repetitive questions/mannerisms, depression/anxiety

Non-Pharmacological Approaches

• Staffing
  – Train staff to use selected interventions appropriately.
  – Tailor interventions to individualized needs.
  – Develop a person-centered plan:
    • Adjust caregiver approaches
    • Adapt/change the environment

Non-Pharmacological Approaches

• Focus on one behavior at a time:
  – Unmet physical needs:
    • Pain, illness, hungry, thirsty, sleep disturbance, constipation, incontinence, elimination needs, medications
  – Unmet psychological needs:
    • Loneliness, boredom, apprehension, worry, fear, lack of socialization, loss of intimacy, lack of enjoyable activities
  – Environmental causes:
    • Level/type of stimulation, noise, confusion, lighting, caregiver approach, institutional routines/expectations, lack of cues
  – Psychiatric causes:
    • Depression, anxiety, delirium, psychosis, other mental illness

Non-Pharmacological Approaches

• Monitor outcomes & adjust as needed:
  – Track behavior problems
  – Assure adequate “dose” (intensity, duration, frequency) of interventions
  – Adapt/add interventions as needed to get the best possible outcomes
  – Make sure all people working with the person understand and cooperate with the treatment plan and are trained as needed.
Non-Pharmacological Approaches

- Questions to ask before using an antipsychotic:
  - What did you do to try and figure out why the resident was doing ________?
  - What is the resident trying to communicate to us?
  - What is the reason for resident doing ________?
  - Unacceptable answer (Dementia or sun-downing)
  - What did you try before requesting medications?

From Lisa Uhlenkamp, RN, BA, LIHNA: IHCA/ICAL

Overview of RCT Evidence for Drugs

- Pain medications
- Anticonvulsants
- Antidepressants
- Benzodiazepines
- Cholinesterase inhibitors
- Memantine
- Antipsychotics

Pain Medications

- Empiric pain management protocol in nursing home residents with agitation
  - 8 week cluster RCT, n=352
    - Step 1: acetaminophen (68%)
    - Step 2: oral morphine (2%)
    - Step 3: buprenorphine patch (23%)
    - Step 4: pregabalin (7%)
  - Agitated symptoms improved at 8 weeks with treatment vs. usual care, and worsened in 4 week washout

Husebo et al, BMJ. 2011;343:d4065
### Antidepressants

- **SSRIs**
  - 5 studies vs. placebo
  - 3 studies vs. typical antipsychotics
  - Possible small benefits on agitated symptoms
- **Other Antidepressants**
  - Trazodone
    - 2 studies = haloperidol, small N
    - 1 study = placebo

Seitz et al, Cochrane Reviews 2011;2:CD008191

### Anticonvulsants

- **Divalproex**
  - 4 studies = placebo, poorly tolerated
  - Cognitive decline and hippocampal damage?
  - Not recommended
- **Carbamazepine**
  - Mixed evidence
  - Concerns of poor tolerability, drug interactions

Lenzergs and Lassenberg, Cochrane Reviews 2005;1:CD005045
Tarut et al, Arch Gen Psychiatry 2011;68:1083-61
Fleisher et al, Neurology 2011;77:1261-71
Sink et al, J Am Med Assoc 2005;293:996-688

### Benzodiazepines/anxiolytics

- **Oxazepam, alprazolam, diphenhydramine, buspirone**
  - 3 studies = haloperidol
  - No placebos, trial design problems, cognitive impairment issues with most of these drugs
- **Not recommended for scheduled use**

Meeks and Jeste, Current Psychiatry 2008;7(6):50-65

### Pharmacologic Options for Behavioral Disturbances

- **Cognitive enhancers**
  - Very small benefits seen in studies for cognition
  - No benefit when studied for behavioral symptoms
- **Miscellaneous**
  - Transdermal estrogen in men: failed trial
  - Propranolol (average 106 mg/day)
    - 1 small positive trial

Meeks and Jeste, Current Psychiatry 2008;7(6):50-65

### Antipsychotic Choice

- Evidence supports modest symptom improvements with
  - Haloperidol (*Haldol®)*
  - Olanzapine (*Zyprexa®)*
  - Quetiapine (*Seroquel®*)
    - less supportive evidence
  - Risperidone (*Risperdal®)*
  - Aripiprazole (*Abilify®*)
- Research does not support use of other antipsychotics in dementia

*available as less expensive generic


### Evidence for the Use of Antipsychotics for Behavioral Disturbances

- **Modest efficacy in RCTs with some drugs**
  - Risperidone for psychosis
  - Aripiprazole and Risperidone for neuropsychiatric symptoms
    - Benefits ↑ in those without psychosis, in nursing homes, and with severe cognitive impairment
  - Haloperidol similar efficacy to atypicals
  - 4 negative placebo controlled trials with quetiapine


Evidence for the Use of Antipsychotics for Behavioral Disturbances

- CATIE-AD
  - Time to discontinuation was primary outcome
    - Olanzapine, Quetiapine, Risperidone no better than placebo
  - Time to discontinuation due to lack of efficacy favored Olanzapine and Risperidone
  - Time to discontinuation due to adverse effects favored placebo

AHRQ Summary of Efficacy: Atypical Antipsychotics

<table>
<thead>
<tr>
<th></th>
<th>Aripiprazole</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia-Overall</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Dementia-Psychosis</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Dementia-Agitation</td>
<td>+</td>
<td>++</td>
<td>+/-</td>
<td>++</td>
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</tbody>
</table>

Legend:
++ = Moderate or high evidence of efficacy
+ = Low or very low evidence of efficacy
+/- = Mixed results

Appropriate antipsychotic treatment targets

- If the symptom presents a danger to the patient or others
- Or, causes the patient to experience
  - Inconsolable or persistent distress
  - Significant decline in function
  - Substantial difficulty receiving needed care

Inappropriate antipsychotic treatment targets

- Wandering
- Unsociability
- Poor self-care
- Restlessness
- Impaired memory
- Inattention or indifference to surroundings
- Verbal expressions or behaviors that do not represent a danger to the resident or others
- Nervousness
- Uncooperativeness
- Fidgeting
- Mild anxiety

Antipsychotics for Behavioral Problems in Dementia

- Clearly document treatment targets before starting drug therapy
  - Frequency
  - Severity
  - Time of day
  - Environmental or other triggers
- Use quantitative and qualitative descriptions
- Be specific (biting rather than agitation)
- Continue to document during use
Antipsychotic Choice

- If an antipsychotic is thought to be necessary, follow these steps
  - Does the patient have Parkinson’s disease, Lewy body dementia, or frontotemporal dementia?
  - If yes, special considerations.....

Dementia Type-Specific Issues

- Parkinson’s Disease / Lewy Body Dementia
  - Tolerate antipsychotics poorly
  - Reduce antiparkinson med doses for psychosis
  - Cholinesterase inhibitors may reduce hallucinations (but beware of syncope)
  - Memantine may produce global improvements

- Frontotemporal Dementia
  - Preliminary data for trazodone and stimulants
  - Mixed data on paroxetine
    - May worsen cognition

Antipsychotic Choice

- Receptor Binding – and effects
  - Consider adverse effect impact on patient co-morbidities when choosing an antipsychotic
    - Metabolic Disease (Diabetes, Hyperlipidemia)
      - Avoid olanzapine
    - Parkinson’s Disease
      - Avoid haloperidol (quetiapine may be preferred, though evidence for efficacy is poor1,2)
  - Start with a low dose

Antipsychotic Affinity for Neuroreceptors

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Haloperidol</th>
<th>Aripiprazole</th>
<th>Risperidone</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2</td>
<td>+++</td>
<td>++++</td>
<td>+++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>5HT1A</td>
<td>+</td>
<td>++</td>
<td>++++</td>
<td>+++</td>
<td>+</td>
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<td>5HT2A</td>
<td>0</td>
<td>++</td>
<td>+++</td>
<td>0</td>
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<td>α1</td>
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<td>+++</td>
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Antipsychotic Choice

<table>
<thead>
<tr>
<th>Drug (daily dose range)</th>
<th>Brand Name</th>
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<tbody>
<tr>
<td>Aripiprazole (2-10 mg)</td>
<td>Abilify</td>
</tr>
<tr>
<td>Haloperidol (0.25-2 mg)</td>
<td>Haldol</td>
</tr>
<tr>
<td>Olanzapine (2.5-15 mg)</td>
<td>Zyprexa</td>
</tr>
<tr>
<td>Quetiapine (12.5-150 mg)</td>
<td>Seroquel</td>
</tr>
<tr>
<td>Risperidone (0.25-2 mg)</td>
<td>Risperdal</td>
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Movement Side Effects

- Sedation
  - Central Nervous System
  - Confusion, delirium, other cognitive worsening
  - Worsening psycotic symptoms

Cardiovascular /Metabolic

- Orthostatic hypotension
- Edema
- Weight gain/glucose ↑
- Triglyceride ↑
- Urinary incontinence/UTI
Monitoring Antipsychotic Use

- Start with a time limited trial
- Monitor for effectiveness
  - Specific target behaviors
- Monitor for adverse effects

Discontinuing Antipsychotics

- Continue medication only if there is clear evidence of efficacy
- Many do not experience exacerbation of agitation when medication withdrawn
  - Some evidence shows reduction in depressive symptoms with antipsychotic DC

Relapse Risk

- RCT of DC in 110 risperidone responders after 16 or 32 weeks of treatment
  - 112/180 responded
  - Mostly outpatient or assisted living

Discontinuing Antipsychotics

- Use periodic gradual dose reductions to assess continued need
  - At least twice yearly
- If used in delirium, DC or taper after resolution
- Consider 25% decrease every 4-6 weeks as a general GDR guideline
  - More precise schedules are half-life dependent
**Initial Steps to Reduce Unnecessary Antipsychotics**

- No role for PRN antipsychotic medications
- Look at discontinuation or gradual dose reduction for residents on medications for greater than 12 weeks (3 months)
- Evaluate need for antipsychotics being started on residents during the evening/night shift or over the weekend

*(information reviewed from a presentation by Dr. David Gifford, AHCA/NCAL)*

**IA-ADAPT Training**

- Case-based mini-lectures
- Pocket guides and algorithms
- Supporting written materials online
  - Explain rationale and evidence
- Dementia care online training course
  - Focused on caregivers, but good for anyone
  - Teaches the principles of non-drug management
  - Fulfills training requirement for dementia unit care providers

**Pocket Guides and Algorithms**

1. Overview of stepwise approach to management
   - Pocket guide, includes common causes of problem behaviors
2. Delirium screening and management
   - Pocket guide
3. Drugs that can cause delirium or problem behaviors
   - Pocket guide

**Pocket Guides and Algorithms**

4. Managing a Crisis
   - Tip sheet
5. Non-pharmacologic management algorithm
   - Poster and pocket guide
6. Antipsychotic Guides
   - Clinician version to guide prescribing and monitoring
   - Caregiver version focused on monitoring

**Shared Decision Making on Antipsychotic Use**

- Handout to help discuss the risks and benefits of antipsychotics with families
  - And patients if appropriate
- Written with a focus on health literacy
- Lawsuits are less likely if the family is involved with these decisions

**Family Guide**

Page 1
IA-ADAPT Training and Resource Website

- Iowa Geriatric Education Center
- http://www.healthcare.uiowa.edu/igec/IAADAPT

- Hard copy laminated pocket guides and algorithms are $10 per set plus shipping (our cost)
- PDF copies free
- Free CE/CME for physicians, pharmacists, nurses

Special Thanks

- Content / Lecture Developers:
  - Marianne Smith, PhD, RN
  - Michael Kelly, BS, PharmD, MS
  - Jeff Reist, PharmD, BCPS, FASCP
  - Michelle Weckmann, MD, MS
  - Susan Schultz, MD
  - Susan Lenoch, MA
- Brian Gryzlak, MA, MSW: project manager
- The rest of the IA-ADAPT team
- All the participants who so kindly provided their input to improve the products

Summary (Thanks!)

- Quality person-centered caregiving approaches may reduce antipsychotic use
- Pain management may reduce behaviors
- When antipsychotics are needed, clearly document justification and monitor effects
- Antipsychotics differ in their effectiveness and side effects
  - Select based on patient characteristics
- Antipsychotics are not forever
  - or sometimes don’t need to be…. try to DC