Improving Antipsychotic Appropriateness in Dementia Patients

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Disclosures

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• 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
  – ~22% of NH residents get antipsychotics\(^1\)
  – Varies widely by state (~16.3-29.1%) and facility
  – 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

\(^1\)Briesacher et al, JAMA 2013;309(5):440-2, Sept 09-Aug 2010 data
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>
</thead>
<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>
</tr>
</tbody>
</table>


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
  - Accumulating evidence suggests conventionals have a higher risk
- 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

Severity and Type of Dementia
Depression/Anxiety/Insomnia
Medical Conditions
Unmet Needs

Communication
Environment
Other Stressors
Drugs

Problem Behaviors or Psychosis

Caregiving for People with Dementia and Psychosis: An 8-Step Evidence-based Approach

1. Medication
2. Environment
3. Communication
4. Other Stressors
5. Drugs
6. Unmet Needs
7. Medical Conditions
8. Depression/Anxiety/Insomnia

Evaluation of Problem Behaviors or Psychosis

Communication
Environment
Other Stressors
Drugs
Unmet Needs
Medical Conditions
Depression/Anxiety/Insomnia
Severity and Type of Dementia

Problem Behaviors or Psychosis

Communication
Environment
Other Stressors
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Problem Behaviors or Psychosis

Communicat...
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.

Non-Pharmacological Approaches

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

• Assessment, Identify and Treat Contributing Factors:
  – Focus on one behavior at a time
  – Identify what leads to or triggers problems
  – Reduce, eliminate things that lead to or trigger the problem
  – Document outcomes

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 if there is a new medical or psychiatric problem

• Changes in living environment or staffing can also change residents behavior.

Non-Pharmacological Approaches

• Focus on one behavior at a time considering:
  – 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

• 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

• 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

• 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

• 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 requesting a medication:
  – What did you do to try and figure out why the resident was doing this?
  – What is the resident trying to communicate to us?
  – Why do you think the resident doing this?
  • Unacceptable answer (Dementia or sun-downing)
  – What did you try before requesting medications?

From Lisa Uhlenkamp, RN, BA, LHNA, summarized from a talk by Dr. David Gifford
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 vs. usual care, 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

Lonergan and Luxenberg, Cochrane Reviews 2009;3:CD003945
Fleisher et al, Arch Neurol Psychiatry 2011;175(1):103-11
Fleisher et al, Neurology 2011;77(13):1263-71
Sedatives/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 due to adverse effects and likelihood of worsening cognition

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, e.g.
  - 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

Jeste et al, Neuropsychopharmacology 2008;33:505-70.
www.effectivehealthcare.ahrq.gov/report/efhrt.cfm

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>
</tr>
</tbody>
</table>

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

http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=786&pageaction=displayproduct
Potentially appropriate antipsychotic treatment targets

- Hallucinations
- Delusions (note: memory problems are often mistaken for delusions, e.g. thinks people are stealing lost items)
- Aggressive behavior (especially physical)

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
- Unsoicability
- 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 can cause syncope)
  - Memantine may produce global improvements
- Frontotemporal Dementia
  - Preliminary data for trazodone and stimulants
  - Mixed data on paroxetine
    - May worsen cognition

Selecting an Antipsychotic

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

Antipsychotic Affinity for Neuroreceptors

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Haloperidol*</th>
<th>Antipsychotic</th>
<th>Buteclozine</th>
<th>Clozapine</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2 - Dopamine</td>
<td>+++</td>
<td>+++ (partial agonist)</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Anti-ETP</td>
<td>+</td>
<td>++</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>5HT2A - Serotonin</td>
<td>0</td>
<td>++</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>5HT2C - Serotonin</td>
<td>0</td>
<td>+</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>α1 - Adrenergic</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>H1</td>
<td>0</td>
<td>0</td>
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PDSP Ki Database: http://pdsp.med.unc.edu/pdsp.php

Selecting an Antipsychotic

<table>
<thead>
<tr>
<th>Drug (daily dose range)</th>
<th>Antipsychotic (2-10 mg)</th>
<th>Haloperidol (0.25-2 mg)</th>
<th>Clozapine (2.5-7.5 mg)</th>
<th>Quetiapine (12.5-150 mg)</th>
<th>Risperidone (0.25-2 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Movement Side Effects</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Sedation</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Confusion, delirium,</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>other cognitive</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Worsening psychotic</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>symptoms</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Cardiovascular/Metabolic</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
</tr>
<tr>
<td>Edema</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
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<tr>
<td>Weight gain/glucose</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
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<tr>
<td>Triglyceride</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
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<tr>
<td>Urinary incontinence/UTI</td>
<td>■</td>
<td>■</td>
<td>■</td>
<td>■</td>
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</tbody>
</table>
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\(^1\)
  - Some evidence shows reduction in depressive symptoms with antipsychotic DC

\(^1\)Gentile, Psychopharmacology 2010;212:119-129.

Relapse Risk

- RCT of DC in 110 risperidone responders after 16 or 32 weeks of treatment
  - 112/180 responded in first 16 weeks
  - Mostly outpatient or assisted living
  - Longer term treatment may benefit some

Discontinuing Antipsychotics

- Use periodic gradual dose reductions to assess continued need
  - At least twice yearly
    - Probably much sooner on initial prescription, e.g. 3 months max, but monitor closely for relapse
- 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

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
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

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• All the participants who so kindly provided their input to improve the products
Summary (Thanks!)

- Quality person-centered caregiving approaches may reduce antipsychotic use
- 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 often don’t need to be…. try to DC