Management of neuropsychiatric symptoms of dementia

Andrea Smith, MD
Providence Broadway Internal Medicine
Providence Long Term Mobility Care
Disclosures

• I have no financial disclosures
Objectives

- Assess underlying causes for behavioral disturbance
- Diagnosing urinary tract infections in advanced dementia
- Non-pharmacologic management
- Pharmacologic management
- Sleep disturbance
Neuropsychiatric Symptoms


<table>
<thead>
<tr>
<th>Types of behavioral and psychological symptoms of dementia*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delusions (distressing beliefs)</td>
</tr>
<tr>
<td>Hallucinations</td>
</tr>
<tr>
<td>Agitation:</td>
</tr>
<tr>
<td>– Easily upset</td>
</tr>
<tr>
<td>– Repeating questions</td>
</tr>
<tr>
<td>– Arguing or complaining</td>
</tr>
<tr>
<td>– Hoarding</td>
</tr>
<tr>
<td>– Pacing</td>
</tr>
<tr>
<td>– Inappropriate screaming, crying out, disruptive sounds</td>
</tr>
<tr>
<td>– Rejection of care (for example, bathing, dressing, grooming)</td>
</tr>
<tr>
<td>– Leaving home</td>
</tr>
<tr>
<td>Aggression (physical or verbal)</td>
</tr>
<tr>
<td>Depression or dysphoria</td>
</tr>
<tr>
<td>Anxiety:</td>
</tr>
<tr>
<td>– Worrying</td>
</tr>
<tr>
<td>– Shadowing (following care giver)</td>
</tr>
<tr>
<td>Apathy or indifference</td>
</tr>
<tr>
<td>Disinhibition:</td>
</tr>
<tr>
<td>– Socially inappropriate behavior</td>
</tr>
<tr>
<td>– Sexually inappropriate behavior</td>
</tr>
<tr>
<td>Irritability or lability</td>
</tr>
<tr>
<td>Motor disturbance (repetitive activities without purpose):</td>
</tr>
<tr>
<td>– Wandering</td>
</tr>
<tr>
<td>– Rummaging</td>
</tr>
<tr>
<td>Night-time behaviors (waking and getting up at night)</td>
</tr>
</tbody>
</table>
The husband of an 82-year-old woman calls the clinic to report changes in behavior over the last few days. She is confused, becomes agitated with ADLs, and she will not eat because she thinks she is being poisoned.

PMH: htn, depression, osteoarthritis, Alzheimer disease, urinary incontinence. MMSE was 22/30 two months ago

Meds: APAP 325mg, donepezil 5mg/d, memantine 14mg/d, HCTZ 25mg/d, lisinopril 10mg/d, tolterodine 2mg BID, citalopram 20mg/d. Donepezil and memantine started 2 years ago. Tolterodine increased 1 week ago, citalopram increased 2 months ago.

Labs: BUN 18, creatinine 1.1, sodium 138, glucose 81, UA 0-5 WBC, negative for bacteria and leukocyte esterase

Which one of the following is most appropriate at this time?

A. Discontinue tolterodine
B. Increase extended release memantine to 28mg/d
C. Start lorazepam 0.5mg BID
D. Start risperidone 0.25mg/d
Underlying Causes

- Review medications
  - Anticholinergic
  - Opioids
  - Muscle relaxants
  - Hypnotics
  - Sedatives
  - Corticosteroids

<table>
<thead>
<tr>
<th>Drugs with high anticholinergic activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antihistamines</strong></td>
</tr>
<tr>
<td>Diphenhydramine, meclizine, hydroxyzine, doxylamine</td>
</tr>
<tr>
<td><strong>Antimuscarinic (urinary)</strong></td>
</tr>
<tr>
<td>Oxybutynin, tolterodine, trospium, solifenacin</td>
</tr>
<tr>
<td><strong>Antispasmodics</strong></td>
</tr>
<tr>
<td>Atropine, dicyclomine, hyoscyamine, scopolamine</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
</tr>
<tr>
<td>Amitriptyline, clomipramine, doxepin (&gt;6mg), paroxetine</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
</tr>
<tr>
<td>Clozapine, chlorpromazine</td>
</tr>
</tbody>
</table>

Underlying Causes

- Review medications
- Pain
- Depression
- Misperception or Misunderstanding
- Constipation
- Delirium
  - Infections
  - Metabolic
  - Hypoxia

1. Acute onset and fluctuating course
2. Inattention
3. Disorganized thinking
4. Altered level of consciousness
A 72-year-old woman is brought to the emergency department because of declining mental status. She has a history of mild vascular dementia. She lives in a nursing home, and staff reports that she has been more somnolent and agitated over the past week. She has had no fevers, chills, or change in frequency of urination, and she reports no dysuria or suprapubic tenderness. Nursing home staff notes that the patient’s urine has a foul odor. She does not have an indwelling catheter.

Exam: vital signs are normal. She is oriented to person but somewhat difficult to arouse. There is no evidence of suprapubic or costovertebral angle tenderness. Microscopy shows 20 WBC/hpf, 2-4 epithelial cells/hpf, and numerous bacteria. A urine culture is obtained.

Pending results of other diagnostic studies, which one of the following should be administered?

A. Oral nitrofurantoin
B. Oral ciprofloxacin
C. IV ceftriaxone
D. IV piperacillin-tazobactam
E. No antibiotic therapy
Suspected Urinary Tract Infections

• Mental status change alone is NOT a sensitive or specific symptom of UTI\(^1\)

• Asymptomatic bacteriuria is common and should NOT be treated with antimicrobials\(^1,2\)


5 Don’t use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present.

Cohort studies have found no adverse outcomes for older men or women associated with asymptomatic bacteriuria. Antimicrobial treatment studies for asymptomatic bacteriuria in older adults demonstrate no benefits and show increased adverse antimicrobial effects. Consensus criteria has been developed to characterize the specific clinical symptoms that, when associated with bacteriuria, define urinary tract infection. Screening for and treatment of asymptomatic bacteriuria is recommended before urologic procedures for which mucosal bleeding is anticipated.
Risk Factors and Outcomes Associated With Treatment of Asymptomatic Bacteriuria in Hospitalized Patients

Lindsay A. Petty, MD; Valerie M. Vaughn, MD, MSc; Scott A. Flanders, MD; Anurag N. Malani, MD; Anna Conlon, PhD; Keith S. Kaye, MD, MPH; Rama Thyagarajan, MD; Danielle Osterholzer, MD; Daniel Nielsen, MS; Gregory A. Eschenauer, PharmD; Sarah Bloemers, MPH; Elizabeth McLaughlin, BSN, MS; Tejal N. Gandhi, MD

• 2733 hospitalized patients
• Retrospective chart review of patients with positive urine culture without signs of symptoms of UTI

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. (%)</th>
<th>Unadjusted Odds Ratio (95% CI)</th>
<th>Unadjusted P Value</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>Adjusted P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-d Postdischarge mortality</td>
<td>63 (2.8)</td>
<td>1.22 (0.66-2.26)</td>
<td>.53</td>
<td>1.34 (0.72-2.49)</td>
<td>.35</td>
</tr>
<tr>
<td>30-d Postdischarge readmission</td>
<td>362 (16.0)</td>
<td>1.16 (0.87-1.56)</td>
<td>.31</td>
<td>1.29 (0.92-1.81)</td>
<td>.14</td>
</tr>
<tr>
<td>30-d Postdischarge ED visit</td>
<td>272 (12.0)</td>
<td>0.91 (0.70-1.18)</td>
<td>.48</td>
<td>0.90 (0.66-1.24)</td>
<td>.52</td>
</tr>
<tr>
<td>Discharge to post-acute care facility</td>
<td>811 (35.9)</td>
<td>1.98 (1.58-2.48)</td>
<td>&lt;.001</td>
<td>1.19 (0.90-1.57)</td>
<td>.22</td>
</tr>
<tr>
<td><em>Clostridioides difficile</em> infection</td>
<td>14 (0.6)</td>
<td>1.39 (0.41-4.68)</td>
<td>.59</td>
<td>0.88 (0.20-3.86)</td>
<td>.86</td>
</tr>
<tr>
<td>Duration of hospitalization, median (IQR)</td>
<td>4 (3-6)</td>
<td>1.37 (1.28-1.47)</td>
<td>&lt;.001</td>
<td>1.37 (1.28-1.47)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: ED, emergency department; IQR, interquartile range.

- Outcomes were adjusted for patient variables found to be significant (P < .05) and associated with treatment in the bivariate and multivariate analysis.
- Mortality, readmissions, ED visits, and discharge to post-acute care facility were adjusted for age, Charlson Comorbidity Index score, hospitalization in 90 days preceding current admission, admission from nursing home, and insurance type.
- Long-term acute care hospital, skilled nursing facility, inpatient rehabilitation, and subacute rehabilitation.
- Infection occurring within 30 days of discharge was adjusted for age, history of antibiotic use and number of antibiotics in previous 90 days, admission from skilled nursing facility, prior hospitalization, proton-pump inhibitor use, immunosuppression, and Charlson Comorbidity Index score.
- From date of urine testing (either urine culture or urinalysis, whichever was performed first). Adjusted for age, sex, Charlson Comorbidity Index score, prior hospitalization, admission from nursing home, and insurance type.
- Relative risk given because because duration of hospitalization is a continuous variable.
Criteria from both 1 AND 2

1. At least 1 of the following subcriteria of signs or symptoms
   • Acute dysuria or acute pain, swelling, or tenderness of the testes, epididymis, or prostate
   OR
   • Fever or leukocytosis and at least 1 of the following localizing urinary tract subcriteria
     • Acute costovertebral angle pain or tenderness
     • Suprapubic pain
     • Gross hematuria
     • New or marked increase in incontinence
     • New or marked increase in urgency
     • New or marked increase in frequency
   • In the absence of fever or leukocytosis, then 2 or more of the following localizing urinary tract subcriteria
     • Suprapubic pain
     • Gross hematuria
     • New or marked increase in incontinence
     • New or marked increase in urgency
     • New or marked increase in frequency

2. One of the following microbiological subcriteria
   • At least 10^5 cfu/mL of no more than 2 species of microorganisms in a voided urine sample
   • At least 10^2 of any number of organisms in a specimen collected by in and-out catheter

B. Fever, define as: (1) A single oral temperature >100°F (>37.8°C); or (2) repeated oral temperatures >99°F (>37.2°C) or rectal temperatures >99.5°F (>37.5°C); or (3) an increase in temperature of >2°F (>1.1°C) over the baseline temperature (B-III).
Objectives

- Assess underlying causes for behavioral disturbance
- Diagnosing urinary tract infections in advanced dementia
- Non-pharmacologic management
- Pharmacologic management
- Sleep disturbance
Non-pharmacologic Management

- Routine activity
- Separate from an upsetting circumstance
- Travel with them to where they are in time
- Don't disagree
- Maintain eye contact, get to their height level, and allow space
- Speak slowly and calmly in a normal tone of voice
- Avoid finger-pointing, scolding, or threatening
- Redirect
- If you appear to be the cause of the problem, leave the room
- Avoid asking the person to do what appears to trigger an agitated or aggressive response
- Validate
- Reassure

Non-pharmacologic Management

- Music therapy
- Bright light therapy
- Aromatherapy
- Intervention with family caregivers
- Therapeutic touch
- Reminiscence therapy
- Simulated presence therapy
- Acupuncture

Caregiving Support

Caregiving

Caregivers for Alzheimer's and dementia face special challenges.

Caregiver Support

Powerful Tools for Caregivers gives you the skills to take care of yourself while caring for someone else. By taking care of your own health and well-being, you become a better caregiver.

Six class sessions held once a week are led by experienced class leaders. Class participants are given The Caregiver Helpbook to accompany the class and provide additional caregiver resources.

Caregiving takes many forms. You may help a relative or friend with:

- Transportation
- Housekeeping
- Grocery Shopping
- Personal Care
- Medications
- Emotional Support
- Doctor Appointments
- Social Activities
- Living Arrangements
- Financial Concerns
- Legal or Insurance Issues

The 36-Hour Day: A Family Guide to Caring for People Who Have Alzheimer's Disease, Related Dementias, and Memory Loss

NANCY L. MACE, MA, and PETER V. RABINS, MD, MPH

THE DEFINITIVE GUIDE WITH OVER ONE MILLION COPIES IN PRINT

"The best guide of its kind." —Chicago Sun-Times

Caregiver Support
Objectives

- Assess underlying causes for behavioral disturbance
- Diagnosing urinary tract infections in advanced dementia
- Non-pharmacologic management
- Pharmacologic management
- Sleep disturbance
Pharmacotherapy

- Cholinesterase inhibitors and memantine
- Antidepressants
- Benzodiazepines
- Antipsychotics
- Mood stabilizers
An 85-year-old man is brought to the office by his son because of symptoms of Alzheimer disease have significantly worsened over the last 6 months. Medications include maximum dosages of donepezil and memantine. The patient frequently wanders outside the house at night. He is convinced that people are breaking into his home at night, and his son recently found him in the kitchen holding a knife, yelling “intruder” at the window curtains. Reorientation tactics to address this behavior have not been successful. A thorough evaluation for reversible causes of acute psychosis is negative. The patient’s son is requesting pharmacologic management of psychosis, understanding the risks it entails.

Which one of the following regimens should be prescribed to help manage the patient’s symptoms?

A. Begin haloperidol at a low dosage, increase the dosage until symptoms are controlled, then taper as soon as possible.

B. Begin quetiapine at a low dosage, increase the dosage until symptoms are controlled, then taper as soon as possible.

C. Begin duloxetine at a low dosage, increase the dosage until symptoms are controlled, then taper as soon as possible.

D. Prescribe lorazepam at a low dosage as needed.
Figure 2. Forest plot of efficacy of various drugs on the Neuropsychiatric Inventory scale in Alzheimer’s disease patients. Data type: continuous; effect measure: standardised mean difference; analysis model: random effects; statistical method: inverse variance.
Antidementia Drugs

• **Cholinesterase inhibitors**\(^1,2\)
  - Small but **significant** improvement compared to placebo
  - Adverse events
    - Diarrhea, nausea, vomiting
    - Bradycardia and syncope

• **Memantine**\(^1,3\)
  - No significant improvement compared to placebo
  - Adverse events
    - Dizziness, headache, confusion
    - Constipation

# Antidepressants-SSRIs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dosages</th>
<th>Potential Advantages</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>10-20mg daily</td>
<td>Reduction in agitation, non-sedating</td>
<td>Risk of QT prolongation</td>
</tr>
<tr>
<td>Sertraline</td>
<td>25-200mg daily</td>
<td>Reduction in agitation, non-sedating</td>
<td>GI side effects</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>5-20mg daily</td>
<td></td>
<td>Risk of QT prolongation</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>5-60mg daily</td>
<td>Activating, prolonged half life</td>
<td></td>
</tr>
<tr>
<td>Paroxetine</td>
<td>10-40mg nightly</td>
<td>Useful if insomnia</td>
<td>ANTICHOLINERGIC-constipation, dry mouth, drowsiness</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>25-200mg nightly</td>
<td></td>
<td>Short half-life, discontinuation symptoms</td>
</tr>
</tbody>
</table>

• 128 Norwegian nursing home patients with Alzheimer’s disease or vascular dementia
• Prescribed escitalopram, citalopram, sertraline, or paroxetine for 3+ months, treatment continued vs discontinued
• Discontinuation led to increase in depressive symptoms
# Antidepressants-SNRIs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dosages</th>
<th>Potential Advantages</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine</td>
<td>40-60mg daily</td>
<td>May be useful for pain</td>
<td>Nausea, dry mouth, GI, urinary hesitancy, avoid if CrCl&lt;30</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>75-225mg daily</td>
<td>May be useful for pain, Low anticholinergic activity, minimal sedation</td>
<td>May increase BP and QTc, withdrawal symptoms, hyponatremia</td>
</tr>
<tr>
<td>Desvenlafaxine</td>
<td>50-400mg daily</td>
<td></td>
<td>Nausea, dizziness, may increase HR, BP</td>
</tr>
<tr>
<td>Levomilnacipran (Fetzima)</td>
<td>40mg daily</td>
<td>Weight neutral</td>
<td>Increased HR, BP</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>50-100mg twice daily</td>
<td></td>
<td>GI, headache, insomnia, dry mouth</td>
</tr>
</tbody>
</table>

## Antidepressants-Atypical

<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dosages</th>
<th>Potential Advantages</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>75-150mg daily</td>
<td>Consider for SSRI non-responder</td>
<td>May be stimulating, can lower seizure threshold, insomnia, weight loss</td>
</tr>
<tr>
<td>Vilazodone (Viibrd)</td>
<td>40mg daily</td>
<td>Metabolized by CYP3A4, limited geriatric data, diarrhea</td>
<td></td>
</tr>
<tr>
<td>Vortioxetine (Trintellix)</td>
<td>5-10mg daily</td>
<td>Nausea, constipation</td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>50-100mg daily</td>
<td>Useful with insomnia</td>
<td>Orthostasis, bradycardia, hypotension</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>15-45mg daily</td>
<td>Increased appetite, for those with insomnia</td>
<td>Increased appetite, sedating</td>
</tr>
</tbody>
</table>

## Analysis 5.1. Comparison 5 Trazodone versus Typical Antipsychotic, Outcome 1 CMAI Change in Total Score.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Trazodone</th>
<th>Typical Antipsychotic</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean(SD)</td>
<td>N</td>
<td>Mean(SD)</td>
<td>Random, 95% CI</td>
</tr>
<tr>
<td>Sultzer 1997</td>
<td>14</td>
<td>-16 (12.6)</td>
<td>14</td>
<td>-16 (12.6)</td>
<td>49.49%</td>
</tr>
<tr>
<td>Teri 2000</td>
<td>37</td>
<td>-0.8 (16.5)</td>
<td>34</td>
<td>-7.3 (22.5)</td>
<td>50.51%</td>
</tr>
<tr>
<td>**Total ***</td>
<td><strong>51</strong></td>
<td><strong>-0.8 (16.5)</strong></td>
<td><strong>48</strong></td>
<td><strong>-7.3 (22.5)</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau²=0; Chi²=0.94, df=1(P=0.33); I²=0%

Test for overall effect: Z=0.98(P=0.33)

---

# Antidepressants - TCAs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dosages</th>
<th>Potential Advantages</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desipramine</td>
<td>50-150mg daily</td>
<td></td>
<td>Sedating, orthostatic hypotension, weight gain, anticholinergic effects, cardiac effects</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>75-150mg daily</td>
<td>Helpful for insomnia</td>
<td>Sedating, orthostatic hypotension, weight gain, anticholinergic effects, cardiac effects</td>
</tr>
</tbody>
</table>

Antidepressants

• Limited data for dementia with neuropsychiatric symptoms other than depression
• SSRI first line
  • Most data for citalopram and sertraline
• If insomnia consider trazodone
• If insomnia and weight loss use mirtazapine
• Start low and go slow
• Monitor for adverse effects
• At least 6-8 weeks of therapy to monitor for effect
<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dosage</th>
<th>Onset (hours)</th>
<th>Half-life (hours)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>0.5-6mg daily</td>
<td>1</td>
<td>6-27</td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td>0.5-4mg daily</td>
<td>0.5-1</td>
<td>18-50</td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>4-40mg daily</td>
<td>0.25-0.5</td>
<td>20-50</td>
<td>Active metabolites</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.5-6mg daily</td>
<td>0.5-1</td>
<td>10-20</td>
<td></td>
</tr>
</tbody>
</table>

Don’t use benzodiazepines or other sedative-hypnotics in older adults as first choice for insomnia, agitation or delirium.

Large scale studies consistently show that the risk of motor vehicle accidents, falls and hip fractures leading to hospitalization and death can more than double in older adults taking benzodiazepines and other sedative-hypnotics. Older patients, their caregivers and their providers should recognize these potential harms when considering treatment strategies for insomnia, agitation or delirium. Use of benzodiazepines should be reserved for alcohol withdrawal symptoms/delirium tremens or severe generalized anxiety disorder unresponsive to other therapies.
Which one of the following is true regarding the risk of prescribing psychotropic medications to patients with dementia?

A. First- and second-generation antipsychotics increase both morbidity and all-cause mortality

B. Second-generation antipsychotics do not increase morbidity and all-cause mortality

C. First-generation antipsychotics do not increase morbidity and all-cause mortality

D. First- and second-generation antipsychotics increase morbidity but not all-cause mortality
Antipsychotics

• Mortality Risk
  • When used to treat behavioral symptoms of dementia associated with excess risk of
    • Myocardial infarction
    • Stroke
    • Death
  • Risk higher for first generation than second generation
    • Haloperidol increased mortality risk of 3.8%, NNH 26
    • Risperidone increased mortality risk of 3.7%, NNH 27
    • Olanzapine increased mortality risk of 2.5%, NNH 40
    • Quetiapine increased mortality risk of 2.0%, NNH 50

Don’t use antipsychotics as the first choice to treat behavioral and psychological symptoms of dementia.

People with dementia often exhibit aggression, resistance to care and other challenging or disruptive behaviors. In such instances, antipsychotic medicines are often prescribed, but they provide limited and inconsistent benefits, while posing risks, including over sedation, cognitive worsening and increased likelihood of falls, strokes and mortality. Use of these drugs in patients with dementia should be limited to cases where non-pharmacologic measures have failed and patients pose an imminent threat to themselves or others. Identifying and addressing causes of behavior change can make drug treatment unnecessary.
Antipsychotics- efficacy

• Typical antipsychotics\textsuperscript{1,2}
  • Haloperidol, thioridazine, thiothixene, chlorpromazine, trifluoperazine, and acetophenazine
  • Low certainty evidence, may improve agitation and psychosis
  • Increased risk of somnolence and extrapyramidal symptoms

• Atypical antipsychotics\textsuperscript{1,2}
  • Clozapine, olanzapine, risperidone, quetiapine, ziprasidone and aripiprazole
  • “Probably” reduce agitation, negligible effect on psychosis
  • Increased risk of somnolence and extrapyramidal symptoms

• Pimavanserin

Pimavanserin

Evaluation of the safety, tolerability, and efficacy of pimavanserin versus placebo in patients with Alzheimer’s disease psychosis: a phase 2, randomised, placebo-controlled, double-blind study

- Efficacy with Alzheimer’s psychosis at 6 weeks but not 12 weeks
- Common adverse events
  - Falls, UTI, agitation

Trial of Pimavanserin in Dementia-Related Psychosis

Pierre N. Tariot, M.D., Jeffrey L. Cummings, M.D., Sc.D., Maria E. Soto-Martin, M.D., Ph.D., Clive Ballard, M.D., Deniz Erten-Lyons, M.D., David L. Sultzer, M.D., Davangere P. Devanand, M.D., Daniel Weintraub, M.D., Bradley McEvoy, Dr.P.H., James M. Youakim, M.D., Srdjan Stankovic, M.D., M.S.P.H., and Erin P. Foff, M.D., Ph.D.

- Phase 3, double-blind, randomized, placebo-controlled discontinuation trial involving patients with psychosis related to Alzheimer’s disease, Parkinson’s disease dementia, dementia with Lewy bodies, frontotemporal dementia, or vascular dementia

- Common adverse events
  - Headache, constipation, UTI, asymptomatic QT prolongation

The American Psychiatric Association Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia

- Nonemergency antipsychotic used only for symptoms that are severe, dangerous, and/or cause significant distress to the patient
- Discuss risks vs benefits with surrogate
- Start low and titrate up to minimum effective dose tolerated
- If no response after a 4 week trial of an adequate dose then taper and withdraw
- Attempt to taper and withdrawal within 4 months
- Only maintain treatment if benefits are apparent
- Haloperidol should not be used as first line for nonemergency use
- Long acting injectable antipsychotics should not be used unless indicated for co-occurring chronic psychotic disorder

Dextromethorphan-quinidine

• Approved for symptomatic treatment of pseudobulbar affect
• Limited evidence for Alzheimer’s dementia
• Consider when other treatments have failed
• Most common adverse events
  • Falls
  • Diarrhea
  • UTI
• Cost $$

# Mood Stabilizers

<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical Dosages</th>
<th>Potential Advantages</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>200-1000 mg/day (therapeutic level 4-12 mcg/ml)</td>
<td>Uncertain benefit</td>
<td>Drug interactions, SIADH, thrombocytopenia, leukopenia</td>
</tr>
<tr>
<td>Valproate</td>
<td>250-2000 mg/day (therapeutic level 50-100 mcg/ml)</td>
<td>Better tolerated in older adults, uncertain benefit</td>
<td>Weight gain, tremor, hair loss, monitor LFTs and platelets</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100-2400 mg/day</td>
<td>Uncertain benefit</td>
<td>Sedation, ataxia, falls</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>25-200 mg/day</td>
<td>Uncertain benefit</td>
<td>Skin rash, rare SJS, dizziness, sedation, neutropenia, thrombocytopenia</td>
</tr>
</tbody>
</table>

Objectives

- ♦ Assess underlying causes for behavioral disturbance
- ✔ Diagnosing urinary tract infections in advanced dementia
- ✔ Non-pharmacologic management
- ✔ Pharmacologic management
- ❑ Sleep disturbance
Sleep Disturbance

• Age related changes
  • Decreased total sleep time
  • Less quality sleep
  • Increase in sleep related disorders
  • Poor health and chronic diseases contribute

• Dementia related changes
  • May be part of pathologic process
  • Association between poor sleep and dementia
  • Circadian rhythm disorders more common

Sleep Disturbance

- Sleep hygiene
- Address polypharmacy
- Pharmacotherapy
  - Melatonin
  - Trazodone
  - Ramelteon
  - Orexin receptor antagonists
- Risks outweigh benefits
  - Benzodiazepines
  - Non-benzodiazepine receptor agonists
  - Antihistamines
  - Antidepressants
  - Anticonvulsants
  - Antipsychotics

Key Points

• Before initiation of treatment for agitation or aggression thorough medication review and evaluation for alternate causes
• Change in behavior alone is NOT a symptom of UTI
• Non-pharmacologic strategies first
• Avoid benzodiazepines
• Trial SSRI first (sertraline, citalopram)
• Only use antipsychotics for symptoms that are severe or cause significant distress
  • Attempt to taper after ~4 months