Wisconsin Public Psychiatry Network Teleconference (WPPNT)

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WPPNT Reminders

• Call 877-820-7831 before 11:00 a.m.
• Enter passcode 107633#, when prompted.
• Questions may be asked, if time allows.
• To ask a question, press *6 on your phone to unmute yourself. *6 to remote.
• The link to the evaluation for today’s presentation is on the WPPNT webpage, under today’s date: https://www.dhs.wisconsin.gov/wppnt/2018.htm
Mid-Stage to Late-Stage Dementia

December 20, 2018

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Disclosures

Wisconsin Association of Medical Directors
American Psychiatric Association Press
Advocate Lutheran General
United Way
Eisai Network Companies
Objectives

1. Develop a plan to assess the behavioral and psychological symptoms of dementia (BPSD) during the mid-to-late stages of dementia.

2. Describe the treatment options that may be useful for patients with BPSD.

3. Develop an approach to the management of each of their patients with BPSD that includes behavioral & environmental interventions as primary and psychotropic medications as secondary.
Definition of dementia

Dementia is a syndrome of acquired, persistent decline in several realms of intellectual ability, plus associated functional decline

- impaired memory
- disturbed language
- visuospatial abnormalities
- decreased problem-solving, abstraction and other executive functions
- reduced attention
- apraxia
- agnosia
Types of dementia

- Alzheimer’s disease: 53% (AD alone)
- Vascular dementia: 10%
- Lewy body disease: 8%
- FTD: 6%
- Other: 8%

Diagram showing the distribution of different types of dementia.
# Staging dementia – and safety

<table>
<thead>
<tr>
<th>CDR</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>diagnosis</strong></td>
<td>MCI</td>
<td>mild dementia</td>
<td>moderate dementia</td>
<td>severe dementia</td>
</tr>
<tr>
<td><strong>clinical presentation</strong></td>
<td>mild problems with memory and/or other domains; no significant functional decline</td>
<td>moderate cognitive problems; problems with driving, finances</td>
<td>severe memory problems; problems with meals, other tasks</td>
<td>severe memory loss, problems with judgment; cannot function outside home or institution</td>
</tr>
<tr>
<td><strong>impact on safety</strong></td>
<td>should be encouraged to get formal drivers evaluation</td>
<td>should not be allowed to drive; find alternate method of transportation</td>
<td>financial incapacity nearly universal</td>
<td>should not have access to firearm</td>
</tr>
</tbody>
</table>

- 47-87% have financial problems
Natural history of BPSD

Prevalence of BPSD, by cognitive status

- **Normal cognition**: 82.3%
  - No symptoms: 56.0%
  - 1-2 symptoms: 32.6%
  - 3+ symptoms: 13.3%

- **Mild cognitive impairment**: 4.3%
  - No symptoms: 11.2%
  - 1-2 symptoms: 15.2%
  - 3+ symptoms: 11.2%

- **Mild dementia**: 15.2%
  - No symptoms: 54.5%
  - 1-2 symptoms: 30.3%
  - 3+ symptoms: 15.2%

- **Moderate dementia**: 30.0%
  - No symptoms: 30.0%
  - 1-2 symptoms: 44.3%
  - 3+ symptoms: 31.4%

- **Severe dementia**: 30.4%
  - No symptoms: 30.4%
  - 1-2 symptoms: 38.2%
  - 3+ symptoms: 31.4%

Prevalence of BPSD, by stage of dementia

- Delusions: 28% moderate, 40% severe
- Depression: 29% moderate, 36% severe
- Disinhibition: 9% moderate, 32% severe
- Hallucinations: 21% moderate, 31% severe
- Anxiety: 11% moderate, 30% severe
- Apathy: 25% moderate, 42% severe
- Agitation: 24% moderate, 41% severe
- Irritation: 17% moderate, 16% severe
- Aberrant motor behaviors: 13% moderate, 31% severe
- Elation: 0% moderate, 6% severe

Why do BPSD arise?

Progressively lowered stress threshold model

Smith et al JAGS 2004; 52: 1755-1760.
Assessment of BPSD (1)

• for each BPSD:
  • timing: how often? how long does symptom last? how long has it been present?
  • severity: dangerous? distressing? at risk of escalating?
  • antecedents: precipitants? patterns?
  • consequences: how do caregivers respond? what works and doesn’t work?
  • history: new behavior? if not new, is it different?
• screen for all BPSD
Assessment of BPSD (2)

- screen for caregiver burden
  - consider PHQ-2 to screen for depression
- review medication list & other substances
- consider medical contributions
  - pain, constipation, urinary retention, dehydration, vision loss, hearing loss
  - infection, electrolyte disturbance, head injury
- screen for elder abuse
The DICE approach

**Describe:** caregiver describes problematic behavior: context, environment, patient perspective, degree of distress

**Investigate:** provider investigates possible causes: meds, pain, medical conditions, psychiatric comorbidity, sleep, sensory changes, loss of control, boredom

**Create:** caregiver and team collaborate to create and implement treatment plan: respond to physical problems, strategize behavioral interventions

**Evaluate:** provider evaluates whether interventions have been implemented, and have been safe and effective

Kales et al JAGS 2014; DOI:10.1111/jgs.12730
Overview of management

- address medical, environmental & psychosocial problems that may underlie behaviors
- caregiver education & training
- behavioral & environmental interventions
- psychopharmacological interventions
  - use when behavioral & environmental measures have failed, or when behavior poses a threat to patient or others
- set realistic expectations

Try non-pharmacological interventions first

Review the clinical response to nonpharmacological interventions prior to nonemergency use of an antipsychotic medication
Behavioral & environmental interventions

- most studies done in nursing homes – little data about effective interventions at home
- strongest evidence for:
  - caregiver training (effect size 0.3-1.8)
  - sensory interventions (0.6-1.3)
  - increased activities (0.6-0.8)
  - music therapy (0.5-0.8)
- ineffective: aromatherapy, light therapy, therapeutic touch
- insufficient evidence to draw conclusions:
  - training families in behavioral or CBT approaches
  - pet therapy
  - exercise

Practical tips

- increase activity levels, tapping into preserved capabilities and previous interests
- educate and support caregivers
- improve communication, e.g.,
  - use a calm, reassuring voice
  - provide 1- to 2-step simple verbal commands
  - allow sufficient time to respond
- reduce clutter, noise & distractions in the environment (or, if it’s too bland, enhance it)
- simplify tasks and provide structured daily routines

Referral options

• education:
  • NIA website
  • *The 36 Hour Day* by Mace and Rabins

• organizations:
  • Alzheimer’s Association
  • Alzheimer’s & Dementia Alliance of Wisconsin

• county agencies:
  • Aging & Disability Resource Centers (ADRCs)
  • Senior centers
  • Dementia Care Specialists or Dementia Leads
→ When to turn to medications for BPSD

Nonemergency antipsychotic medication should only be used for the treatment of agitation or psychosis in patients with dementia when symptoms are severe, are dangerous, and/or cause significant distress to the patient (*emphasis added*)

Before treatment, the potential risks and benefits from antipsychotic medication should be assessed by the clinician and discussed with the patient, surrogate decision maker, or other family member.
Pharmacological options for agitation & psychosis

- in general, limited benefits with significant potential for side effects
- best evidence base for atypical antipsychotics, specifically risperidone, olanzapine, and aripiprazole
- modest evidence for antidepressants, pain control, and pimavanserin
- weakest evidence for anticonvulsants, benzodiazepines, cognitive enhancers, dextromethorphan & prazosin
- all choices are off-label usages and some choices have significant safety concerns
Antipsychotics

atypical antipsychotics
risperidone
olanzapine
aripiprazole
quetiapine
clozapine
typical antipsychotics
haloperidol
Antipsychotics: the data that led to the FDA Black Box warning

<table>
<thead>
<tr>
<th></th>
<th>trials N</th>
<th>deaths Rx</th>
<th>deaths placebo</th>
<th>OR (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>risperidone</td>
<td>5 1954</td>
<td>3.8%</td>
<td>2.8%</td>
<td>1.30 (0.76-2.23)</td>
</tr>
<tr>
<td>olanzapine</td>
<td>5 1662</td>
<td>2.6%</td>
<td>1.3%</td>
<td>1.91 (0.79-4.59)</td>
</tr>
<tr>
<td>quetiapine</td>
<td>3 637</td>
<td>5.4%</td>
<td>2.8%</td>
<td>1.67 (0.70-4.03)</td>
</tr>
<tr>
<td>aripiprazole</td>
<td>3 951</td>
<td>3.5%</td>
<td>1.7%</td>
<td>1.73 (0.70-4.30)</td>
</tr>
<tr>
<td>overall</td>
<td>16 5204</td>
<td>3.5%</td>
<td>2.2%</td>
<td>1.54 (1.06-2.23)</td>
</tr>
</tbody>
</table>

NNH=100 (95% CI = 53-1000)

Schneider et al JAMA 2005; 294: 1934-43
Atypical antipsychotics: other side effects

- weight gain
- diabetes
- stroke
- extrapyramidal symptoms
- sedation
- falls
- cognitive impairment

Atypical antipsychotics: efficacy

- best evidence for risperidone, olanzapine and aripiprazole (agitation) and risperidone (psychosis)
- overall, small effect on behavioral symptoms:
  - pooled effect size = 0.16
  - NNT = 6 (range 5-14)
  - significant placebo effects (30-50% response rates)
- response usually in first 2-4 weeks
- three head-to-head trials compared atypicals – none was found superior
- no studies of: ziprasidone, lurasidone, asenapine, brexpiprazole, cariprazine

AHRQ Comparative Effective Review 43, 2011;
### Comparative effectiveness review

<table>
<thead>
<tr>
<th>Effect in dementia</th>
<th>aripiprazole</th>
<th>olanzapine</th>
<th>quetiapine</th>
<th>risperidone</th>
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</thead>
<tbody>
<tr>
<td>overall</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>psychosis</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>agitation</td>
<td>+</td>
<td>++</td>
<td>+/-</td>
<td>++</td>
</tr>
</tbody>
</table>

++ moderate or high evidence of efficacy  
+ low or very low evidence of efficacy  
+/- mixed results
Starting antipsychotics

- Treatment should be initiated at a low dose and titrated up to the minimum effective dose as tolerated.
- If the patient experiences a clinically significant side effect, the potential risks and benefits of the antipsychotic should be reviewed by the clinician to determine if tapering and discontinuing is indicated.
- If there is no clinically significant response after a 4-week trial of an adequate dose of an antipsychotic drug, the medication should be tapered and withdrawn.
→ Stopping antipsychotics

• An attempt to taper and withdraw the drug should be made within 4 months of initiation, unless the patient experienced a recurrence of symptoms with prior attempts at tapering of antipsychotic medication.

• In a patient who has shown a positive response to treatment, decision-making about possible tapering of antipsychotic medication should be accompanied by a discussion with the patient, surrogate decision maker, or other family member.

• In patients with dementia whose antipsychotic medication is being tapered, assessment of symptoms should occur at least monthly during the taper and for at least 4 months after medication discontinuation to identify signs of recurrence and trigger a reassessment of the benefits and risks of antipsychotic treatment.

The American Psychiatric Association Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients with Dementia (2016)
Other medication options

- antidepressants: citalopram, escitalopram, sertraline, trazodone
- anticonvulsants: valproate, carbamazepine
- cognitive enhancers: cholinesterase inhibitors, memantine
- pain medications: acetaminophen
- dextromethorphan
- prazosin
- stimulants (for apathy)
Other causes of dementia (besides Alzheimer’s disease)

- **Lewy body disease:**
  - clozapine, quetiapine, olanzapine
  - pimavanserin
- **frontotemporal dementia:**
  - trazodone
  - mixed data on SSRIs
  - one small trial of quetiapine (ineffective)
  - one small trial of D-amphetamine (helpful for apathy and disinhibition)
Summary

• identify & address contributing factors, such as pain, nutrition, hearing & vision loss, constipation, falls, medications, UTI, electrolyte disturbance

• address caregiver burden & safety issues

• start with behavioral & environmental interventions

• judiciously use medications, if safety issues are present or if other interventions ineffective

• monitor, regularly reassess & consider discontinuation
Thank you

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