Benzodiazepines: Minimizing Harm in Older Adults

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Disclosure

*Dr. Eisenhower has no actual or potential conflicts of interest associated with this presentation.*

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**How common is benzodiazepine use in the elderly?**

**What is the harm?**
Benzodiazepine Types

- **Short- and intermediate-acting:**
  - Alprazolam
  - Lorazepam
  - Oxazepam
  - Temazepam
  - Triazolam

- **Long-acting:**
  - Chlordiazepoxide
  - Clonazepam
  - Diazepam
  - Quazepam

*Benzodiazepines available in the U.S.

Use of Benzodiazepines by Older Adults

- Population-based retrospective observational study in the U.S. using 2008 prescription database
- Assessed any benzodiazepine (BZD) use, long-term use (>= 120 days), and long-acting type use for ages 18-35, 36-50, 51-64, and 65-80
- Of adults ages 65-80, 8.7% used any BZD
  - 31.4% used BZDs long-term
  - 23.8% used long-acting BZDs


Use of Benzodiazepines by Older Adults (continued)

- Compared to younger age groups, adults ages 65-80 were more likely to:
  - Use BZDs long-term
  - Use BZDs not prescribed by a psychiatrist
- Use was twice as likely in women than men
- Highest rate of use observed in 80 y/o women

2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Table 1. Designations of Quality and Strength of Evidence.

<table>
<thead>
<tr>
<th>Quality of Evidence</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Evidence is sufficient to determine effects on health outcomes, but the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes.</td>
</tr>
<tr>
<td>Low</td>
<td>Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large &amp; unexplained inconsistencies, important flaws.</td>
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<table>
<thead>
<tr>
<th>Strength of Recommendation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>Benefits clearly outweigh risks and burden or risks and burden clearly outweigh benefits.</td>
</tr>
<tr>
<td>Weak</td>
<td>Benefits finely balanced with risks and burden.</td>
</tr>
<tr>
<td>Insufficient</td>
<td>Insufficient evidence to determine net benefits or risks.</td>
</tr>
</tbody>
</table>

Adapted from: The American Geriatrics Society 2012 Beers Criteria Update Expert Panel.

Benzodiazepines

- **Action:** avoid BZDs (any type) for treatment of insomnia, agitation, or delirium.

- **Reasons:**
  - Older adults have increased sensitivity to BZDs and decreased metabolism of long-acting agents.
  - In general, all BZDs increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults.
  - May be appropriate for seizure disorders, rapid eye movement sleep disorders, BZD or ethanol withdrawal, severe generalized anxiety disorder, periprocedural anesthesia, end-of-life care.

- **QE = High; SR = Strong**

Delirium

- **Action:** avoid use
- **Reason:** ability to induce or worsen delirium in older adults
- **QE = Moderate; SR = Strong**

Cognitive impairment

- **Action:** avoid use
- **Reason:** adverse central nervous system (CNS) effects
- **QE = High; SR = Strong**

Falls and Fractures

- **Action:** avoid unless safer alternatives are not available
- **Reason:** ability to produce ataxia, impaired psychomotor function, syncope, and additional falls; shorter-acting BZDs are not safer than long-acting ones.
- **QE = High; SR = Strong**
Based on the 2012 AGS Beers Criteria, which one of the following older adults is receiving an appropriately prescribed benzodiazepine?

A. 73 year old woman prescribed lorazepam three times daily for agitation.
B. 85 year old man prescribed alprazolam as needed for generalized anxiety disorder.
C. 68 year old man prescribed clonazepam daily at bedtime for insomnia.
D. 77 year old woman prescribed lorazepam as needed for delirium.

Outcomes of new benzodiazepine prescriptions to older adults in primary care

Study Details

• **Objective:** identify indications for new BZD use, as well as baseline demographics of patients, duration of use, and clinical outcomes

• **Population:** adults >= 60 years at primary care group practice

• **Methods:**
  – Computerized records
  – Baseline telephone survey
  – Two-month follow-up survey
Study Results

- Most common indications: insomnia (42%), anxiety (36%)
- BZDs prescribed by PCPs (77%), psychiatrists (6%), and other specialists (17%)
- Approximately 17% (22) reported not taking their BZD at baseline; 13/22 did not think it was necessary
- Two-month follow-up:
  - Thirty percent of patients continued treatment
  - No difference between continued users and users who discontinued in terms of sleep quality and depression

Simon GE, et al. 2006

Inappropriate prescribing to the oldest old patients admitted to hospital: prevalence, most frequently used medicines, and associated factors

San José A et al, 2015

Study Details

- Objectives: identify potentially inappropriate medicines (PIMs) and potentially prescribing omissions (PPOs) and associated factors
- Population: patients >/= 75 years admitted to seven hospitals in Spain over one year; subgroup was >/= 85 years
- Methods:
  - 2003 Beers Criteria and STOPP criteria for PIMs
  - START criteria and ACOVE-3 criteria for PPOs
Most Common PIMs

- All patients
  - Use of BZDs in those who are prone to falls (18.3%)

- Patients ≥ 85 years
  - Use of short- to intermediate-acting BZDs in those with previous falls or syncope (10.7%)
  - Use of long-acting BZDs independent of diagnoses or conditions (10.5%)

San José A et al, 2015

My patient’s benzodiazepine is no longer appropriate, and the physician and patient are okay with discontinuation.

WHAT HAPPENS NOW?

Benzodiazepine Discontinuation

- Rebound or withdrawal symptoms can occur if discontinued abruptly

- Consider how long the patient has been taking the medication

- Consider half-life elimination of the BZD
Half-Life Elimination of BZDs

<table>
<thead>
<tr>
<th></th>
<th>Half-Life (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short- and Intermediate-acting</strong></td>
<td></td>
</tr>
<tr>
<td>Alprazolam</td>
<td>11.2</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>14</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>8</td>
</tr>
<tr>
<td>Temazepam</td>
<td>3.5-18.4</td>
</tr>
<tr>
<td>Triazolam</td>
<td>1.5-5.5</td>
</tr>
<tr>
<td><strong>Long-acting</strong></td>
<td></td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>6.6-28</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>17-60</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Parent drug: 25-50 hours and increased in elderly and those with severe hepatic disorder; active metabolite: 30-100 hours</td>
</tr>
<tr>
<td>Quazepam</td>
<td>Active metabolite: 39 hours; inactive metabolite: 73 hours</td>
</tr>
</tbody>
</table>

Discontinuation of BZDs

- Twelve months of structured interventions or usual care to achieve BZD discontinuation
  - Gradual tapering with follow-up visits every 2 weeks
  - Gradual tapering with written instructions

- Both structured interventions led to discontinuation in 45% of patients versus 15% with usual care

- Limitations
  - Can patients get transportation to 2-week follow-up visits?
  - Can they afford co-pays for follow-up visits?
  - Can patients read and comprehend written instructions?

Eliminating Medications Through Patient Ownership of End Results (EMPOWER)

- Community-dwelling adults ages 65-95
- Patients educated regarding risks of BZDs
- Provision of step-wise tapering protocol

- Results
  - 62% of patients initiated conversation about BZD discontinuation with physician and/or pharmacist
  - 27% of patients discontinued BZD at 6 months
  - Additional 11% of patients had dose reduction
Alternatives to BZD therapy

- Insomnia
- Agitation
- Delirium

Vidán MT et al, 2009

PATIENT CASES

Time to practice!

Case #1 – Community Pharmacist

A 79 year old man steps up to the drop-off counter. He comments on how long it took him to drive to the pharmacy, due to traffic. He hands you a new prescription for lorazepam 2 mg three times daily, and also asks you to renew the following:

- Sertraline 200 mg daily at bedtime
- Lisinopril 10 mg daily
- Aspirin 81 mg daily
- Zolpidem 10 mg daily at bedtime as needed for sleep
Case #1 - Discussion

Case #2 – Pharmacy Technician

- LB, who is 76 years old, stops in. You have known him for a long time, and have observed that he has difficulty walking and trouble seeing. He always jokes with you about his nights out at the bar with his friends. He gives you a few prescriptions to enter:
  - Temazepam 15 mg daily at bedtime for sleep
  - Hydrocodone/APAP 5/325 mg 1 tablet every 6 hours as needed for pain
  - Aspirin 81 mg daily
  - Albuterol inhaler 2 puffs every 4-6 hours as needed for shortness of breath or wheezing

Case #2 - Discussion
Case #3 – Consultant/LTC Pharmacist

- You are reviewing the medication list for an 84 year old woman, DH, who ambulates with a walker:

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin EC 81 mg daily</td>
<td>Primary prevention</td>
</tr>
<tr>
<td>Clonazepam 0.5 mg twice daily</td>
<td>Generalized anxiety</td>
</tr>
<tr>
<td>Senna Plus – 2 tablets daily at bedtime</td>
<td>Constipation</td>
</tr>
<tr>
<td>Escitalopram 10 mg daily</td>
<td>Depression</td>
</tr>
<tr>
<td>Lisinopril 5 mg daily</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Lorazepam 0.5 mg daily as needed</td>
<td>Agitation</td>
</tr>
<tr>
<td>Omeprazole 20 mg daily</td>
<td>Reflux</td>
</tr>
<tr>
<td>Tramadol 50 mg twice daily as needed</td>
<td>Pain</td>
</tr>
</tbody>
</table>

Case #3 – Discussion

Case #4 – Inpatient Pharmacist

- You are verifying orders for an 87 year old man, GS, who is admitted for pneumonia and dehydration. GS has dementia and is very anxious about being in the hospital.

- The internal medicine resident has ordered the following new medications:
  - IV fluids
  - DuoNeb as needed
  - Piperacillin/tazobactam 3.375 grams IV every 6 hours
  - Alprazolam 0.5 mg three times daily
Case #4 - Discussion

Case #5

• You are an ambulatory care pharmacist meeting with an 81 year old woman who is prescribed clonazepam 1 mg four times daily for panic disorder.

• PMH includes: hypertension, CKD, falls, osteoporosis, lumbago, depression

• Medications include:
  – Hydrocodone/APAP 5/325 mg twice daily
  – Calcium carbonate 600 mg/vitamin D 400 IU twice daily
  – Lisinopril 5 mg daily
  – Sertraline 50 mg daily
Stay tuned!

Public comment for the AGS Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults ended May 5.

Differences between the 2015 and 2012 versions of the Beers Criteria will be presented at the annual AGS meeting on May 16.

QUESTIONS?

References


References (continued)


