SAFE & APPROPRIATE USE OF HYPNOTICS IN OLDER ADULTS

Clinical and Quality Improvement Considerations

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Disclosures

- No financial or conflict of interest disclosures to report
Objectives

- Identify the dangers of using benzodiazepines in older adults
- Describe evidence supporting safe & effective tapering of benzodiazepines in older adults
- Recognize benzodiazepine withdrawal
- Identify key differences between the nonbenzodiazepine hypnotics
- Identify other sedating medications that can be used instead of hypnotics
- Describe efforts underway at Veterans Health Administration through the Psychotropic Drug Safety Initiative program to reduce use of benzodiazepines in older adults
Classes of hypnotics

Benzodiazepines
  • Short-acting (e.g. lorazepam, alprazolam)
  • Long-acting (e.g. clonazepam, diazepam)

Nonbenzodiazepines
  • Eszopiclone
  • Zaleplon
  • Zolpidem and Zolpidem extended-release
  • Ramelteon
BENZODIAZEPINES
Some basic principles

• Not recommended for > 3 weeks of use due to addiction potential

• Not recommended for patients with compromised pulmonary function

• Not ideal for substance abusing patients

• Not first-line treatment for anxiety or insomnia

• Generally speaking, a bad idea in older adults
Benzodiazepines are associated with significant risks in elderly

☑ Falls
☑ Hip fractures
☑ Sedation
☑ Cognitive impairment
☑ Motor vehicle crashes

Both short and long-acting benzos are listed in 2012 Beers Criteria

Bottom line: Prevention is the best strategy. Avoid new starts to avoid long-term, chronic use.

Ray et al. (1987); Ray (1992); Glass et al. (2005); Wang et al. (2001); Chang et al. (2008); Paterniti et al. (2002); Hemmelgarn et al. (1997); JAGS 2012;60(4):616
Increasing use of benzos with age

Figure. Percentage of Population in the United States in 2008 With Any Benzodiazepine Use by Sex and Age

Women > men

Olfson et al., 2015;72(2):136-142
What do older patients think about benzodiazepine use?

• Long-term users have become psychologically dependent
  • “That pill is very important to me”

• Lack of awareness, underestimation, or disregard of side effects

• Factors associated with willingness to taper/discontinue
  • Less frequent daily dosing
  • Less anxiety sensitivity

Cook et al. (2007a), Cook et al. (2007b)
What do physicians think about prescribing benzos to older patients?

- Benzo use in elderly not seen as problematic
  - Not seen as addiction problem
  - Minimized risks
  - Stable dose = safe

- Attempts to discontinue will fail
  - Anticipate resistance of patients

- Low-priority relative to medical problems

- Limited physician time

Cook et al. (2007c)
Evidence shows success with combining taper and Cognitive Behavior Therapy (CBT)

- 76 adults mean age 62, mean benzo use 19+ years

- 10-week intervention at research-based sleep clinic

- Randomized Control Trial with 3 arms:
  1. Supervised benzo taper
  2. Cognitive Behavior Therapy-I alone (weekly small group)
  3. Combination taper + CBT-I

- Key result: all 3 were successful, combo was best (85% benzo-free)

Morin et al. (2004)
FIGURE 1. Weekly Quantity of Benzodiazepine Medication Used by Older Adults With Insomnia in a Randomized Clinical Trial of Three Interventions to Facilitate Benzodiazepine Discontinuation

- Patients receiving cognitive behavior therapy (N=24)
- Patients receiving medication taper (N=25)
- Patients receiving cognitive behavior therapy combined with medication taper (N=27)

Morin et al. (2004)
More evidence supporting combination taper and CBT

- 65 adults, mean age 67, mean benzo use 12+ years

- 8-week intervention

- RCT with 2 arms:
  1. Taper alone (25% q1-2 weeks)
  2. Combination taper + CBT (weekly small groups)

- Key result: combined was better (77% vs 38% completely stopped benzo use), persisted at 12-month follow up

Baillargeon et al. (2003)
Direct patient education works too

- **EMPOWER (Eliminating Medications Through Patient Ownership of End Results) cluster randomized trial**
  - Community pharmacies randomized to intervention
  - Participants: 65+ yo, receiving long-term benzo therapy (3 mo of Rx fills prior to study)

- Intervention: distributed patient education booklet about dangers of benzos with taper recommendations & instructions to talk to a pharmacist or physicians

- Key result: 62% of intervention group initiated conversation about taper; more had discontinued benzos at 6 mo f/up (27% vs 5% of the control group)

*Tannenbaum et al. (2014)*
Benzodiazepine withdrawal

- Who is at risk for withdrawal?
  - Anyone taking benzodiazepines for > 2 weeks

- Symptoms of withdrawal
  - Agitation
  - Anxiety
  - Dysphoria
  - Increased awareness of sensory stimuli
  - Perceptual disturbances (aka hallucinations)
  - Depersonalization
  - Confusion
  - Delirium
  - Seizures

Often misattributed to other medical & psych conditions, especially dementia
NONBENZODIAZEPINES
Nonbenzodiazepines

- Less potential for abuse, tolerance, withdrawal
- Increased risk of rebound insomnia
- Amnestic reactions at higher doses
- All on Beers Criteria list of potentially inappropriate medications for use in the elderly except Ramelteon
Ramelteon

- Only non-scheduled drug in class
  - Melatonin MT1 and MT2 agonist
- Recommended 1\textsuperscript{st} line treatment by the American Academy of Sleep Medicine
- No rebound insomnia or withdrawal with prolonged use
- Helps decrease sleep latency but does not appear to have effect on sleep maintenance
The “Z” drugs

- Zaleplon is useful for indications requiring short-half life (e.g. sleep on airplanes, jet lag, middle of night dosing)
- Zolpidem has the most side effects, including dizziness, dyspepsia, diarrhea, anterograde amnesia, hangover, and hallucinations
- Zolpidem & Zaleplon should be for short-term use only
- Eszopiclone has best documented safety in long-term use
- Tolerance and rebound insomnia a problem with all
Other sedating medications

**Maybe consider using**
- Antidepressants
  - Trazodone
  - Mirtazapine
  - Doxepine
- Over the counter (OTC) supplements
  - Melatonin

**Do not consider using**
- Antipsychotics
- Barbiturates
- OTC supplements
  - Valerian → hepatotoxic and no evidence of efficacy
- Diphenhydramine

Risks > benefits
Risks associated with other sedating medications

• Trazodone: Priapism (risk is 1/6000), falls, hyponatremia/SIADH, gastrointestinal upset, bleeding/altered anticoagulation

• Mirtazapine: Increased appetite and weight gain associated (typically occurs in first 6 weeks of treatment)

• Doxepin: Tricyclic antidepressants generally NOT safe in elderly, but is okay < 6mg

• Melatonin: headache, dizziness and nausea

• Diphenhydramine: dry mouth, dizziness, drowsiness, impaired coordination, hypotension, confusion, urinary retention, worsening of narrow angle glaucoma

Educate everyone about the “PM” OTC meds
QUALITY IMPROVEMENT
CONSIDERATIONS

Veterans Health Administration (VHA)
Psychotropic Drug Safety Initiative (PDSI)
What is PDSI?

- A VHA nation-wide psychopharmacology quality improvement initiative coordinated through the Office of Mental Health Operations (OMHO) in collaboration with Mental Health Services (MHS) and Pharmacy Benefits Management (PBM)

- Aims to improve the safety and effectiveness of psychopharmacological treatment in VHA focusing on:
  - Avoiding overprescribing
  - Addressing problems in clinical management
  - Eliminating misalignment between prescribing and diagnosis
  - Decreasing missed opportunities for providing evidence-based care

- Began in December 2013
Participants

• Office of Mental Health Operations Program Evaluation Centers

• Pharmacy Benefits Management

• Psychopharmacology Fields Advisory Committee

• Veterans Integrated Service Network (VISN) Mental Health Leads

• Champions at each facility
Progress to date

- Developed measures and shared data with VISNs and facilities

- Mobilized VISNs and facilities to identify priorities and create action plans for psychopharmacology quality improvement

- Established a collaborative community of practice

- Provide ongoing support to QI initiatives in the field
Using initial data to inform local priorities

- OMHO developed 20 measures that evaluate psychotropic prescribing
  - Provided facilities with data describing how they perform individually and in comparison to other facilities around the country

- Example measure: **BENZO_ge75** – the proportion of patients 75 years or older that receive one or more fill for a benzodiazepine in outpatient setting
  - 21 facilities prioritized this measure for this year’s QI cycle
Provide ongoing support

- Regular review and feedback on QI action plans
- Quarterly updates of data on all 20 measures
- PDSI Dashboard
  - A tool that helps identifying those Veterans who may benefit from a more thorough clinical review of current treatment
  - Provides lists of patients that meet indicators for clinical review (actionable patients) along with relevant information to guide decision-making
  - Updated nightly – hence “real time,” actionable information
Example of local PDSI initiative: Empower Veterans pilot in VISN 22

- Goal: reduce benzodiazepine use in older veterans
- Based on the EMPOWER trial
- Conducted through VISN 22 Academic Detailing group, lead by Maggie Mendes, PharmD
- Combines patient education and provider education
- Using dashboards to track relevant clinical information and identify patients with upcoming appointments as targets for educational mailings
- Ongoing – first mailing sent to Veterans at the end of 2014
Patient Decision Aid

You May Be at Risk
You are currently taking a sedative-hypnotic drug

- Alprazolam
- Chlordiazepoxide
- Clonazepam
- Diazepam
- Estazolam
- Flurazepam
- Lorazepam
- Oxazepam
- Temazepam
- Triazolam
- Eszopiclone
- Zaleplon
- Zolpidem

Please Bring This Information With You To Your Next Medical Appointment

TEST YOUR KNOWLEDGE ABOUT A SEDATIVE-HYPNOTIC DRUG

1. The medication you are taking is a mild tranquilizer that is safe when taken for long periods of time.
   - [ ] TRUE
   - [ ] FALSE

2. The dose that I am taking causes no side effects.
   - [ ] TRUE
   - [ ] FALSE

3. Without this medication I will be unable to sleep or will experience unwanted anxiety.
   - [ ] TRUE
   - [ ] FALSE

4. This medication is the best available option to treat my symptoms.
   - [ ] TRUE
   - [ ] FALSE
Provider component

Provider Meetings
- Academic Detailers will visit providers and alert providers to the initiative to provide context and information for tapering and alternative treatments that are available
- More time will be spent in a one to one encounter with Priority Providers

Provider Education
- Shared Decisions Journal Club created to outline the findings from the EMPOWER Trial
Elderly patients empowered to discontinue chronic benzodiazepine use.

**Question**
What impact does a direct-to-consumer education tool have on discontinuation rate of chronic benzodiazepine (BZD) use versus usual care in a community dwelling elderly population?

**Context**
Sedative-hypnotics are a known risk for falls, motor vehicle accidents and cognitive impairment in the elderly. The Reitzenstein criteria and the American Geriatric Society have indicated that they should be avoided in the elderly. Despite this knowledge, difficulties exist in reducing the use of this category of medications in the elderly.

**Setting**
30 community pharmacies in the Greater Montreal area. Eligibility criteria for clusters included local community pharmacies with 50 or more of their clients consisting of older adults and a minimum of 30 eligible participants.

**Patients**
500 adults 65 years and older receiving long-term BZD therapy were randomized. Exclusion criteria included diagnosis of severe mental illness of dementia, an active prescription for any antipsychotic medication and of a benzodiazepine inhibitor or monoamine in the preceding 3 months, and residence in a long-term facility.

**Intervention**
An 8-page booklet was mailed to study participants. The intervention was deliberately intended to create cognitive dissonance in the participant through the use of social constructivist learning and self-efficacy theory. A 31-week taper guide (applicable to any BZD) was included in the intervention for patient autonomy.

**Outcomes Measured**
The primary outcome was complete cessation of BZD use in the 6 months following randomization. Dose reduction was reported in addition, though not prospectively in the statistical analysis.

**Main Result**
27% of patients given the intervention discontinued BZD use (Table 1). An additional 11% of individuals who received the intervention achieved dose reductions.

**Author's Conclusion**
Direct-to-consumer education successfully leads to discussions to stop unnecessary or harmful medications. Discontinuation or dose reductions of benzodiazepines occurred in more than one-third of the participants who received the empowerment intervention.

**Table 1. Primary and secondary outcomes reported.**

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<th>Variable</th>
<th>N</th>
<th>Outcome (%N)</th>
<th>NNT</th>
<th>Adj OR (95% CI)</th>
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<tr>
<td>Discontinuation of BZD</td>
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<td></td>
<td></td>
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<tr>
<td>Intervention</td>
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<td>40 (27.0)</td>
<td>4.30</td>
<td>2.33 (2.23-2.40)</td>
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<td>7 (4.5)</td>
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<td>Discontinuation of BZD plus dose reduction</td>
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<tr>
<td>Intervention</td>
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<td>3.70</td>
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<td>Usual Care</td>
<td>155</td>
<td>17 (11.0)</td>
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Moreover, recent data supports a stepped-care approach to BZD reduction. In a paper by Vinas et al., a primary-care based, structured, taper intervention is described that supports the role of primary care. Access to care was not impaired by this intervention, implying real-world translation. A meta-analysis by Gould et al. demonstrated a robust effect with benzodiazepine withdrawal plus concomitant cognitive behavioral therapy.

The recent surge in evidence is promising for the implementation of strategies aimed at reducing the use of BZDs in the elderly. Shared decision making is a disruptive tool that can be leveraged by the health care system to promote the practice of patient centered care.

**References**
Conclusions

• Hypnotic medications are commonly used in older adults despite significant risks

• There are safe and effective ways to help older adults taper off benzodiazepines, even with chronic use

• Other sedating medications may offer a safer alternative to hypnotics, but also come with risks

• The VA has made improving the safety and effectiveness of psychopharmacological treatment a priority, with one goal being reduction of benzodiazepine use in older adults
References