Benzos and Opioids

CCNC Opioid SPARC ECHO
What is a Benzo?

Benzodiazepines act via CNS GABA receptors, enhancing the effects of endogenous GABA, the main inhibitory neurotransmitter.

In other words, benzos help the brain chemical called GABA to cause the brain to feel calm and relaxed.
Epidemiology and Problems of Benzo Use
Epidemiology of Benzo Use - US

- 7-18% of US population uses a benzo for medical purposes each year
- Average duration < 1 month
- About 1% are prescribed benzos for > 1 year
- Who is more likely to be prescribed benzos long term?
  - Older, women, chronic health and emotional problems
  - i.e., older women seen in primary care
- 8% of US population acknowledge having ever used a benzo for a non-medical purpose
Concurrent Benzo and Opioid Use

• Over 30% of overdoses involving opioids also involve benzos\(^1\)
• More than 115 Americans die daily as a result of opioid overdose\(^1\)
• In 2017, 22.34% of NC Medicaid beneficiaries 18-64 who picked up 2+ opioid prescriptions also picked up 2+ concurrent benzo prescriptions\(^2\)
• In 2017, 5.64% of NC Medicaid beneficiaries 0-64 picking up the first opioid prescription covered by Medicaid in at least a year had also picked up a benzo prescription in the prior 30 days\(^2\)

\(^1\) https://www.drugabuse.gov/drugs-abuse/opioids/benzodiazepines-opioids
\(^2\) NC Medicaid Database
Problems with Benzo Use

• Effective for anxiety and panic disorders, but dependence can develop within weeks, and the meds are often very difficult to discontinue

• Patients on high-dose benzos (>50 mg valium/day) have reduced social functioning and quality of life and high levels of psychological distress

• Benzo use in elderly is more common than among younger patients and is associated with greater risk of hip fracture, MVA, cognitive impairment, and mortality
Problems with Benzo Use

- Problematic use of benzodiazepines has been increasing in the US:
  - In 1992, 2% of inpatient admissions for addiction were for benzodiazepines
  - In 2007, this had increased 10-fold to 20% [TEDS data]
- The proportion of US drivers in fatal crashes using benzos has more than doubled over the past decade (from 24/1000 to 60/1000)
- In 2010, 29% of overdose deaths in the United States involved BZDs, and 77% of those deaths also involved opioid analgesics
- Proportion meeting criteria for drug dependence among people prescribed benzos in primary care (40%), psychiatric outpatient (62%), and self-help groups (80%) [1994 study from Netherlands]
Examples of Problematic Use

1. Difficulty tapering prescribed benzos
   • We have data on how to address this
   • Can be very challenging for patient and clinician

2. “Addictive” patterns of use, often to “boost” the euphoric effect of methadone or other opiates
   • Few data on how to address this problem

3. Obtaining prescriptions for diversion
   • Street value: $5 per 2 mg alprazolam; 60 tabs = $300
   • Consider random urine drug testing for anyone who is prescribed a benzo
   • Note that some common benzos may show false negative on dip testing, including clonazepam
Treatment Options
for patients taking both opioids and benzos
Treatment Options

• Is patient ready to contemplate change?
• Use Motivational interviewing
• Few data to guide treatment in this situation
• Education on dangerous combination of benzo and opioid use
• Limit-setting is important in order to decrease risk of diversion, serious harm
Does a Brochure Work?

- RCT of 260 seniors prescribed long-term benzos [Tannenbaum, 2014]
- Brochure explaining benzo risks given to seniors at pharmacy
- Follow-up showed 62% initiated conversation about benzodiazepine therapy cessation with a physician and/or pharmacist
- At 6 months, 27% of the intervention group had discontinued benzodiazepine use compared with 5% of the control group
- Dose reduction occurred in an additional 11%
- Studies have shown similar very strong impact of a letter from the provider
Other Treatments for Anxiety

• Counseling (CBT) is as effective as medications in managing anxiety [Mitte, 2005]
• Adding counseling while trying to taper benzos has shown some benefit; odds ratio 1.82 [Parre, 2008]
• Also consider adding another anti-anxiety medication to help control anxiety during and after the taper (e.g. SSRI, buspirone)
Tapering off Benzos

Substitution, Slow Taper, Adjunctive Meds
### Benzo Substitution

#### Benzodiazepine Equivalency Table

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approximately Equivalent Oral Doses, mg</th>
<th>Time to Peak Level, hours</th>
<th>Half-life, hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam (Xanax)</td>
<td>0.5</td>
<td>1-2</td>
<td>12</td>
</tr>
<tr>
<td>Chlordiazepoxide (Librium)</td>
<td>25</td>
<td>1-4</td>
<td>100</td>
</tr>
<tr>
<td>Clonazepam (Klonopin)</td>
<td>0.25</td>
<td>1-4</td>
<td>34</td>
</tr>
<tr>
<td>Diazepam (Valium)</td>
<td>5</td>
<td>1-2</td>
<td>100</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>1</td>
<td>1-4</td>
<td>15</td>
</tr>
<tr>
<td>Oxazepam (Serax)</td>
<td>15</td>
<td>1-4</td>
<td>8</td>
</tr>
<tr>
<td>Temazepam (Restoril)</td>
<td>10</td>
<td>2-3</td>
<td>11</td>
</tr>
<tr>
<td>Triazolam (Halcion)</td>
<td>0.25</td>
<td>1-2</td>
<td>2</td>
</tr>
</tbody>
</table>

• Choose a long-acting, rarely-abused substitute (typically clonazepam)
• Translate current dose into equivalent dose of long-acting med
• Begin slow taper

Medscape, May 2014
Slow Taper

- Gradual taper over 3-6 months is better tolerated than rapid taper
- For example, gradual dose reduction was more effective than routine care in achieving cessation of use (51% vs. 15%)
- At 15-month follow-up, 36% of those who received gradual dose reduction were abstinent based on benzodiazepine prescription data, compared with 15% of those who received routine care [Oude Voshaar et al., 2006]
## SAMPLE TAPER SCHEDULE

<table>
<thead>
<tr>
<th>week</th>
<th>Dosage mg/day from 6 mg/day clonazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
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<td>8</td>
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<td>10</td>
<td>1.75</td>
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<tr>
<td>12</td>
<td>1.5</td>
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<tr>
<td>14</td>
<td>1.25</td>
</tr>
<tr>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>.75</td>
</tr>
<tr>
<td>20</td>
<td>.5</td>
</tr>
<tr>
<td>22</td>
<td>.25</td>
</tr>
<tr>
<td>26</td>
<td>stop</td>
</tr>
</tbody>
</table>
Adjunctive Medications

- Carbamazepine has some modest evidence that it helps the benzodiazepine-free duration after taper [Cochrane 2006]
- Pregabalin has several studies suggesting that it increases success in tapering off of benzos
- However, there is also increasing concern that pregabalin is a drug of abuse, so using it to help stop benzos may be counterproductive
Other Considerations
Prevention, UTOX
Prevention

• Only prescribe benzos for short-term use (< 3 weeks)
• Warn the patient at the outset that this is the plan and stick to it
• Don’t use at all in patients > 65 yo
• If you inherit a patient on long-term use, use a benzo contract
• Never prescribe benzos + opiates
Urine Toxicology

• “Quick-read” vs. quantitative testing
• Protocols and procedures
• Partnership with lab
• Embedded lab techs
• Probation contracts
• Termination policies
• Community referral partners for substance use disorder
References


• Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA 2013;309:657–659

• Lugoboni F, et al., Quality of life in a cohort of high-dose benzodiazepine dependent patients

• Drug and Alcohol Dep June 2014


• Billioti de Gage S, Pariente A, Bégaud B. Is there really a link between benzodiazepine use and the risk of dementia? Expert Opin Drug Saf. 2015 May;14(5):733-47


• Gray S, Dublin S, Yu O, Benzodiazepine use and risk of incident dementia or cognitive decline: prospective population based study. BMJ. 2016 Feb 2;352:i90