“Doc, You Have to Give Me More Sleep Medication or I Won’t Sleep at All”

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Overview

• Discuss the consequences of sleep medication.
• Review the efficacy of CBT-I as a means to promote successful discontinuation.
• Review the efficacy of Sleep Medications
• Understanding dependence vs. addiction.
• Are other problems being missed?
• Introduce key concepts for success
  – Habit/Conditioning
  – Placebo effects
  – Fear/Avoidance
  – Varying medication half-life
• Review a model of integrating CBT-I with gradual taper for successful discontinuation.
• Case Discussion (time permitting)
General Hypnotic Use Statistics

• The most common treatment for insomnia
• 3% to 10% of general population; 20% of older adults
• Majority of users take hypnotics for ≥ 1 year
• 56 million prescriptions for sleeping medications in 2008; up 54% from 2004
• Adults under age 45 are fast replacing the elderly as the prime market for sleeping pills with the most dramatic growth seen among college-age adults

Factors Associated with Hypnotic Use in Insomnia Patients

- Sleep Onset Insomnia and Insomnia Severity
- Female Gender and Age > 50
- Anxiety or Depression Symptoms
- Health Problems
- Shift Work

Risk factors for prolonged use (> 12 months):
- Frequency of Benzodiazepine Use
- State Anxiety

Johnson et al., 1998; Morin et al., 2004b; Ohayon and Caulet, 1996;
MORTALITY with HYPNOTICS

HYPNOTIC DOSES / YEAR

Hazard Ratio

0.4 - 18
18 - 132
> 132

http://bmjopen.bmj.com/content/2/1/e000850.full
CANCER INCIDENCE

HAZARD RATIO

NONE  0.4 - 18  18 - 132  > 132

HYPNOTIC DOSES / YEAR

http://bmjopen.bmj.com/content/2/1/e000850.full
Other Undesired Effects of Hypnotics

- Parasomnia
- Depression
- Cognitive Impairments
- Falls and Motor Impairments
- Changes in Sleep Architecture
- Dependence and Loss of Efficacy

Curran et al., 2003; Glass et al., 2005; Hohagen et al., 1993; Kripke, 2007; Leufkens and Vermeeren, 2009; McAndrews et al., 2003; Perlis et al., 2008; Vermeeren, 2004;
From: Randomized Clinical Trial of Supervised Tapering and Cognitive Behavior Therapy to Facilitate Benzodiazepine Discontinuation in Older Adults With Chronic Insomnia

"Sleep Drugs Found Only Mildly Effective, but Wildly Popular"

The Efficacy and Safety of Drug Treatments for Chronic Insomnia in Adults: A Meta-analysis of RCTs (2007)
Buscemi, Vandermeer, Friesen, Bialy, Tubman, Ospina, Klassen, & Witmans

Summary:
Hypnotics put people to sleep 12 minutes faster than placebo pills according to polysomnography and 17 minutes faster according to sleep diaries.
Conclusions:

- These data suggest that the placebo response is a major contributor to the effectiveness of Z drugs.
- The remaining effect needs to be balanced against the harms associated with these drugs.
- The substantial proportion of the drug response accounted for by the placebo response indicates the importance of non-specific factors in the treatment of insomnia.
- As the placebo effect is a psychological phenomenon, these data suggest that increased attention should be directed at psychological interventions for insomnia.
The Emperor’s New Clothes

• Kirsch et al. 2002
  – Meta-analysis (47 trials) of data submitted to the FDA from 1987 to 1999 on the 6 most popular SSRI’s
  – Mean difference between placebo and drug was ~2 points out of 50 and 62 point scales
  – 80% of the effect due to placebo

• Authors conclude that drug effect was clinically negligible
Sir William Osler (1849-1919) – The “Father of Modern Medicine”

“We should use new remedies quickly, while they are still efficacious”
The Powerful Placebo

• Belanger and colleagues assessed the response to placebo hypnotic drugs and compared it with sleep changes among patients placed on a waiting list.

• Compared with those on a waiting list, there were significantly greater improvements in subjective sleep onset latency (19.55 min vs. 2.43 min), subjective total sleep time (31.13 min vs. 7.30 min), and objective total sleep time (18.27 min vs. 10.34 min) in the placebo group.

Dependence vs. Addiction

- Psychological Dependence on sleep medication involves development of the belief they must have the medication to sleep.
- Physiological Dependence infers experience of withdrawal symptoms upon discontinuation.
- Addiction infers cravings.
- Z-drugs typically involve more psychological dependence than physiologic dependence, although both may be present.
- Benzodiazepines usually involve both.
Half Life and Taper process

• In order to successfully taper a patient from their medication, you first need to know the half life.
• Short acting drugs are best to reduce the dose gradually. I typically recommend a 25% reduction even 2-4 weeks.
• Longer acting drugs need to first be reduced by dose, and then by days used.
• NEVER tell a patient to just stop taking benzos!
Benzodiazepines in equivalent doses of diazepam

Diazepam 10 mg is approximately equivalent to:
- Alprazolam (Xanax) 1 mg
- Chlordiazepoxide (Librium) 20 mg
- Flunitrazepam (Rohypnol) 2 mg
- Lorazepam (Ativan) 1 mg
- Nitrazepam (Mogadon) 10 mg
- Oxazepam (Serepax) 30 mg
- Temazepam (Restoril) 20 mg
# Benzodiazepines

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Trade name</th>
<th>Half-life (hrs)</th>
<th>Dosage (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long-acting benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>Valium</td>
<td>20-80</td>
<td>2-60</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>Librium</td>
<td>24-48</td>
<td>15-100</td>
</tr>
<tr>
<td>Clorazepate</td>
<td>Tranxene</td>
<td>100</td>
<td>7.5-60</td>
</tr>
<tr>
<td>Estazolam</td>
<td>ProSom</td>
<td>10-24</td>
<td>0.5-2.0</td>
</tr>
<tr>
<td>Prazepam</td>
<td>Centrax</td>
<td>100</td>
<td>20-60</td>
</tr>
<tr>
<td>Quazepam</td>
<td>Doral</td>
<td>30-100</td>
<td>7.5-15</td>
</tr>
<tr>
<td>Halazepam</td>
<td>Paxipam</td>
<td>15-100</td>
<td>20-160</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Klonopin</td>
<td>34</td>
<td>1.5-20</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Dalmane</td>
<td>100</td>
<td>15-30</td>
</tr>
<tr>
<td><strong>Short-acting benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxazepam</td>
<td>Serax</td>
<td>8</td>
<td>30-120</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Ativan</td>
<td>15</td>
<td>2-6</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Xanax</td>
<td>12</td>
<td>0.5-6</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Restoril</td>
<td>11</td>
<td>15-30</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Halcion</td>
<td>2</td>
<td>0.125-0.5</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Versed</td>
<td>2</td>
<td>2-4</td>
</tr>
</tbody>
</table>
## Non-Benzodiazepines (GABA-A Receptor Allosteric Modulators)

<table>
<thead>
<tr>
<th>Drug &amp; class</th>
<th>Half Life (hr)</th>
<th>Dose (mg)</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eszopiclone (Lunesta)</td>
<td>5-7</td>
<td>1-3</td>
<td>Unpleasant taste, dry mouth, drowsiness, dizziness</td>
</tr>
<tr>
<td>Zolpidem (Ambien, Ambien CR)</td>
<td>3</td>
<td>5-10; 6.25-12.5 (CR)</td>
<td>Drowsiness, dizziness, occasionally amnesia</td>
</tr>
<tr>
<td>Zaleplon (Sonata)</td>
<td>1</td>
<td>5-20</td>
<td>Drowsiness</td>
</tr>
</tbody>
</table>
Common Benzodiazepine withdrawal symptoms

- Anxiety
- Somatic symptoms of anxiety
- Depressed mood
- Depersonalisation, de-realisation
- Sleep disturbance
- Hypersensitivity to touch, pain
- Tremor, shakiness
- Muscular aches, pains, twitches
- Headache
Guide for Cessation

• Goal
  – Define a realistic goal with the patient

• Withdrawal symptoms
  – Explaining the likely course of withdrawal and likely length and intensity of withdrawal symptoms may result in patients experiencing reduced withdrawal severity.
  – The severity and duration of withdrawal syndrome is influenced by factors such as duration of drug use, doses used, drug half life, individual personality style and the expectations of both patient and doctor.

• Regimen and rate
  – Define the rate of reduction together with the patient giving the patient a sense of control helps to increase commitment and success.
  – Convert short acting to long acting benzodiazepines
    • Short acting drugs result in repeated withdrawal as the drug wears off, and repeated use (which relieves withdrawal symptoms) reinforces drug use. The use of long acting drugs reduces and gives better control of withdrawal symptoms
Guide for Cessation

• Review
  – Maintain close contact with patient during the withdrawal phase
  – Titrate dose reduction according to withdrawal symptoms
  – Monitor for increased alcohol or nicotine consumption during withdrawal
  – Be aware of any mood shifts or relationship difficulties
  – Give patient information about withdrawal

• Support
  – Keep an ‘open door’ policy
  – If unsuccessful, encourage patient and try again when they are ready
How Do Patients get Dependent on Sleep Drugs?

1. Before conditioning
   - Food: Unconditioned stimulus
   - Salivation: Unconditioned response
   - Response: Salivation

2. Before conditioning
   - Tuning fork: Neutral stimulus
   - Salivation: No salivation
   - Response: No salivation

3. During conditioning
   - Tuning fork + Food: Unconditioned stimulus
   - Salivation: Unconditioned response
   - Response: Salivation

4. After conditioning
   - Tuning fork: Conditioned stimulus
   - Salivation: Conditioned response
   - Response: Salivation
How to Think About Insomnia in the Context of Sleep Medication Dependence

• Insomnia is a specific phobia, fear of not sleeping.
• We avoid that which we fear, and increasingly fear that which we avoid.
• Sleep drugs (and anxiety drugs) represent an avoidance strategy, and hence maintain anxiety/fear of not sleeping!
• The only way to conquer a fear is to?
CBT-I and Hypnotic Taper

• Goal is to build confidence/self-efficacy in their ability to sleep without medications.
• Try to stack the deck in their favor.

  – Re-entrain circadian rhythm
  – Implement sleep compression and began taper process.
  – Maintain sleep compression until taper is complete.
  – Introduce to stimulus control therapy to cope with bad nights/rebound insomnia
  – Teach patients relaxation and cognitive strategies to cope with future anxieties to avoid falling back into sleeping pill habit.
Points for Consideration

• All patients will be different.
• Base reductions on assessment of patient confidence and comfort. There is no “one size fits all” reduction strategy.
• Setbacks are common, be ready to normalize and provide motivation enhancement.
• Be sure to assess for depression, many chronic hypnotic users are using sleep drugs to treat depression.
• Recognize that the mere suggestion of discontinuation of use of sleep medication is TERRIFYING for most chronic users. They have often tried numerous times before and failed.
Case Discussion

• Middle aged Specialist Physician
• History of mild sleep apnea with nightly use of PAP.
• Insomnia since childhood
  – “Always had trouble getting to sleep, nervous kid, test anxiety”.
• Current sleep parameters:
  – Sleep Latency: “an hour or more”
  – Wake after sleep onset: “5 minutes to hours”
  – Sleep Time: 5 hours of sleep per night
• Contributors:
  – “stress, can’t shut off thoughts”.

Case Discussion

• **Insomnia Treatment History:** Trials of numerous medications including Remeron, Seroquel, trazodone, Valium, Xanax, Ambien, and clonazepam.

• **Current Treatment:** Klonopin 2-3 mg AND Ambien 10 mg on a nightly basis.

• **Medical history:** seasonal allergies, insulin resistant diabetes, gastroesophageal reflux disorder, and hiatal hernia.

• **Social/behavioral history:**
  – satisfactory marital relations
  – unsatisfied with his occupation indicating "stress and frustration with computer system".
  – 3 children- "still supporting them”.
  – no family conflicts or problems
  – no use of tobacco products
  – 1-2 caffeinated beverage(s) per day.
Psych Testing Results

- **Sleep Disorders Screener** suggests signs and/or symptoms of sleep apnea, insomnia, and circadian rhythm sleep disorder. He reports no signs or symptoms of restless legs syndrome, narcolepsy, parasomnia, or bruxism. He is not maintaining a regular sleep/wake schedule and is spending a disproportionate amount of time in bed relative to time sleeping.
- **Insomnia Severity Index** suggests severe insomnia.
- **Sleep Hygiene Practice Scale** suggests a couple of poor sleep hygiene practices.
- **Epworth Sleepiness Scale** suggests minimal daytime sleepiness.
- **Pre-Sleep Arousal Scale** suggests experience of very severe cognitive arousal (worry/thinking) and mild somatic arousal (anxiety) prior to sleep onset.
- **Daytime Alertness Scale** suggests physiologic hyperarousal.
- **Dysfunctional Beliefs and Attitudes about Sleep Scale** suggests counterproductive beliefs about sleep.
Psych Testing Results

• **Weekly Sleep Log** suggests intermittent prolonged sleep onset latency, intermittent prolonged wake after sleep onset and intermittent short total sleep time despite nightly use of both clonazepam 2-3 mg and Ambien 10 mg.

• **Motivation for Change Index** suggests good motivation for change.

• **Personality Assessment Inventory** testing was valid.

He reports clinical problems in the following areas: None

He reports subclinical problems in the following areas: Anxiety, depression, and psychosocial stressors.

He reports no problems in the following areas: Somatic complaints, anxiety related disorder, mania, paranoia, schizophrenia, borderline personality, antisocial personality, alcohol abuse, drug abuse, aggressiveness, suicidal ideation, or social nonsupport.

The PAI clinical profile reveals no marked elevations should be considered to indicate the presence of clinical psychopathology. He does indicate moderate subclinical anxiety and depression.
Treatment Process/Outcome

- Visit 1: Assessment feedback, Circadian timing, Sleep consolidation, Ambien to 5mg, Clonazepam to 2.0mg.
- Visit 2: Stimulus Control Therapy, Patient already had discontinued Ambien and reduced clonazepam to 1.5mg.
- Visit 3: Relaxation training, clonazepam to 1.25mg.
- Visit 4: Cognitive therapy, clonazepam to 1.0mg.
- Visit 5: Introduction to mindfulness, clonazepam to 0.75mg.
- Several brief follow-up calls, patient reduced clonazepam to 0.25mg nightly, then reduced by one day per week for several weeks.
- He has now been drug free for 2-years with all sleep parameters maintained within normal limits.
Questions?
Discussion Points?