Insomnia treatment in primary care

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Update in Internal Medicine
Pittsburgh, PA
October 19, 2017
The authors wish to disclose the following potential conflicts of interest:

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Details of Potential Conflict</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td></td>
</tr>
<tr>
<td>Consultant</td>
<td>Bayer, BeHealth Solutions, Emmi Solutions</td>
</tr>
<tr>
<td>Speakers’ Bureaus</td>
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<tr>
<td>Financial support</td>
<td></td>
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<tr>
<td>Other</td>
<td>CME Institute</td>
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The material presented in this lecture has no relationship with any of these potential conflicts.

This talk presents material that is related to one or more of these potential conflicts, and references are provided throughout this lecture as support.
Insomnia in primary care

- Diagnosis and assessment
- Practical behavioral treatment
- Practical pharmacologic treatment
<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>Difficulty falling or staying asleep</td>
</tr>
<tr>
<td>Sleep-related breathing disorders</td>
<td>Obstructive and central sleep apnea; sleep-related hypoventilation, hypoxemia</td>
</tr>
<tr>
<td>Central disorders of hypersomnolence</td>
<td>Conditions causing severe daytime sleepiness (e.g., narcolepsy, idiopathic hypersomnia)</td>
</tr>
<tr>
<td>Circadian rhythm sleep-wake disorders</td>
<td>Sleep disturbances resulting from problems with the biological clock (e.g., shift work problems)</td>
</tr>
<tr>
<td>Parasomnias (NREM, REM related)</td>
<td>Unusual behaviors or experiences during sleep (e.g., sleep terrors, sleepwalking, nightmares)</td>
</tr>
<tr>
<td>Sleep-related movement disorders</td>
<td>Restless Legs Syndrome, periodic leg movements, body rocking</td>
</tr>
</tbody>
</table>
Insomnia disorder, DSM-5

A. Complaint of dissatisfaction with sleep quantity or quality, with one (or more) of the following symptoms:
   1. Difficulty initiating sleep
   2. Difficulty maintaining sleep, characterized by frequent awakenings or problems returning to sleep after awakenings.
   3. Early morning awakening with inability to return to sleep

B. Significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning.

C. Occurs at least 3 nights per week

D. Present for at least 3 months

E. The sleep difficulty occurs despite adequate opportunity for sleep

F. Not better explained by and does not occur exclusively during the course of another sleep-wake disorder, effect of drug/medication, or mental/medical disorder

G. Can occur with or without comorbid mental, medical, sleep-wake disorder
Insomnia assessment: 24-hour history

- Sleep quality, satisfaction
- Temporal aspects of sleep
  - Bed time (vs. sleep time)
  - Out of bed time (vs. wake time)
- “Quantitative” aspects of sleep
  - Sleep latency
  - Awakenings
  - Sleep duration
- Sleep-related behaviors (“sleep hygiene”): Caffeine, alcohol, activities
- Day-to-day variability (weekends, vacations)

- Daytime activities and impairments: Napping, fatigue, cognitive function, mood
- Life situation and circumstances
- Other sleep disorder symptoms
  - Apnea (Snoring, sleepiness)
  - Restless legs (Urge to move)
  - Parasomnias (Unusual behavior)
  - Circadian rhythm disorders (Unusual timing)
- Medical and psychiatric disorders
- Sleep diary, wearable fitness/sleep trackers
Daytime rest periods

Irregular wake times

Irregular bedtimes

Graphic sleep diary in insomnia patient
<table>
<thead>
<tr>
<th>Sleep Opportunity</th>
<th>Insomnia</th>
<th>Sleep Deprivation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate</td>
<td></td>
<td>Reduced</td>
</tr>
<tr>
<td>Reduced</td>
<td></td>
<td>Adequate</td>
</tr>
</tbody>
</table>

**Insomnia ≠ Sleep Deprivation**
How to treat insomnia: Practice guideline from the American College of Physicians

**Recommendation 1**
- ACP recommends that all adult patients receive cognitive behavioral therapy for insomnia (CBT-I) as the initial treatment for chronic insomnia disorder.
- Grade: strong recommendation, moderate-quality evidence

**Recommendation 2**
- ACP recommends that clinicians use a shared decision-making approach, including a discussion of the benefits, harms, and costs of short-term use of medications, to decide whether to add pharmacological therapy in adults with chronic insomnia disorder in whom cognitive behavioral therapy for insomnia (CBT-I) alone was unsuccessful.
- Grade: weak recommendation, low-quality evidence

Medications commonly used for insomnia: National Health and Nutrition Epidemiological Survey, 1999-2010

- NHANES 1999-2010 (n=32,328), ≥ 20 y.o.
- Review of medication bottles for all Rx meds
- Zolpidem = 87% of Non-Bz BzRA
- 55% of hypnotic users take at least one other sedating medication (opioids, Bz)
- 10% take ≥3 other sedating medications
- *When specifically asked, 19.2% said they took at least one medication to sleep*

Bertisch, *SLEEP* 2014; 37:343-349.
<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Examples</th>
<th>Potential Advantages</th>
<th>Potential Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine receptor agonists (BzRA)</td>
<td>Zolpidem, zaleplon, eszopiclone, temazepam</td>
<td>• Efficacious</td>
<td>• Cognitive effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Variety of half-lives</td>
<td>• Falls</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Dependence</td>
</tr>
<tr>
<td>Sedating antidepressants</td>
<td>Doxepin, amitriptyline, nortriptyline</td>
<td>• No abuse</td>
<td>• Anticholinergic at high doses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Effective for WASO</td>
<td>• Cardiac effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Falls</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Diphenhydramine, doxylamine</td>
<td>• Widely available</td>
<td>• Cognitive effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Limited efficacy data</td>
</tr>
<tr>
<td>Melatonin, receptor agonist</td>
<td>Melatonin, ramelteon</td>
<td>• “Natural” mechanism</td>
<td>• Limited efficacy on WASO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Some efficacy data</td>
<td></td>
</tr>
<tr>
<td>Orexin antgonist</td>
<td>Suvorexant</td>
<td>• Novel mechanism, blocks wake signal</td>
<td>• Limited efficacy, effectiveness data</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedating antipsychotics</td>
<td>Quetiapine, olanzapine</td>
<td>• Not BzRA</td>
<td>• Metabolic, neurological, cardiovascular</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Efficacy for psychosis, depression</td>
<td>effects</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Gabapentin, pregabalin</td>
<td>• Not BzRA</td>
<td>• Limited sleep efficacy data</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Efficacy for pain</td>
<td></td>
</tr>
</tbody>
</table>

WASO = Wakefulness After Sleep Onset. *Italics = Not FDA-approved for insomnia*
Clinical practice guideline for pharmacologic treatment of chronic insomnia in adults

<table>
<thead>
<tr>
<th>Weak evidence FOR</th>
<th>Weak evidence AGAINST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suvorexant (Belsomra)²</td>
<td>Trazodone (Desyrel)</td>
</tr>
<tr>
<td>Eszopiclone (Lunesta)¹²</td>
<td>Tiagabine (Gabitril)</td>
</tr>
<tr>
<td>Zaleplon (Sonata)¹</td>
<td>Diphenhydramine (Benadryl)</td>
</tr>
<tr>
<td>Zolpidem (Ambien)¹²</td>
<td>Melatonin</td>
</tr>
<tr>
<td>Triazolam (Halcion)¹</td>
<td>Tryptophan</td>
</tr>
<tr>
<td>Temazepam (Restoril)¹²</td>
<td>Valerian</td>
</tr>
<tr>
<td>Ramelteon (Rozerem)¹</td>
<td></td>
</tr>
<tr>
<td>Doxepin (Silenor)²</td>
<td></td>
</tr>
</tbody>
</table>

- Based on systematic review using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology.
- 2,821 studies reviewed, 129 studies included
- ¹ = For sleep onset insomnia. ² = For sleep maintenance insomnia

Sateia, Buysse, Krystal, Neubauer, Heald, 2017; JCSM 13; 307-349.
Benzodiazepine receptor agonists: Guidelines for clinical use

- Ensure proper diagnosis
- Evaluate and treat comorbid conditions
- Assess risk of dependence, abuse
- Start with short-acting agent in “therapeutic trial”
- Break the cycle of insomnia with consistent use for 1-4 weeks
- Aim for intermittent use if needed chronically
- Periodically evaluate for side effects
- Taper very slowly and by lowest doses possible when discontinuing
Practical aspects of pharmacotherapy for insomnia

- Realistic expectations
  - Sleeping pills vs. general anesthesia
  - Modest effects
  - The Olympic Sleep Team
- Characteristics of medications
  - Pharmacokinetics
  - Effects
  - Side effects
What do you do when BzRA don’t work?

- Suvorexant
- Sedating antidepressants
  - Trazodone
  - Mirtazapine
  - Tricyclic
- Combination: BzRA + sedating cyclic drug
- Sedating antipsychotic drugs: Only when consistent with psychiatric diagnosis
- Other sedating drugs
  - Gabapentin, pregabalin
  - Tiagabine?
- Sedating antihistamines
- Other?
# Behavioral treatments for insomnia

<table>
<thead>
<tr>
<th>Technique</th>
<th>Aim</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Sleep hygiene” education</td>
<td>Promote habits that help sleep; eliminate habits that hurt sleep</td>
</tr>
<tr>
<td>Stimulus control</td>
<td>Strengthen bed/bedroom as sleep stimulus</td>
</tr>
<tr>
<td>Sleep restriction therapy</td>
<td>Restrict time in bed to improve sleep depth/consolidation</td>
</tr>
<tr>
<td>Cognitive therapy</td>
<td>Address maladaptive thoughts and beliefs; behavioral experiments</td>
</tr>
<tr>
<td>Relaxation training</td>
<td>Reduce physical/psychological arousal</td>
</tr>
<tr>
<td>Cognitive Behavioral Therapy for Insomnia (CBTI)</td>
<td>Combines elements of each of the above techniques</td>
</tr>
</tbody>
</table>

A diverse set of behavioral prescriptions designed to improve the quality of nocturnal sleep.
Cognitive-behavioral treatments for insomnia: New approaches

- **Brief(er) Treatments**
  - Brief Behavioral Treatment for Insomnia
  - ≤4 sessions, single session treatments, classroom/lecture

- **Single-component treatments (stimulus control, sleep restriction)**

- **Other types of therapists**
  - Master’s-level therapist, nurse, social worker, peer specialist

- **Groups**

- **Telephone, Video tele-health/Skype**

- **Self-help approaches**

- **Online treatments: Sleepio™, SHUTi™, others**

- **Mobile app-based: VA CBTI coach, iREST™, others**

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Brief Behavioral Treatment of Insomnia

- Healthy Sleep Practices
- What Controls Sleep
- Brief Behavioral Treatment
- Action Plan
What controls sleep? The hourglass, the clock, and the alarm

How long you’ve been awake

Time of day

Level of arousal

Homeostatic sleep drive

Circadian sleep propensity

Psychophysiological arousal
# Getting started

<table>
<thead>
<tr>
<th>What are your sleep times? (self-report, diary)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed time</td>
</tr>
<tr>
<td>Time out of bed (morning)</td>
</tr>
<tr>
<td>Total time in bed</td>
</tr>
<tr>
<td>Time to fall asleep</td>
</tr>
<tr>
<td>Awake during the night</td>
</tr>
<tr>
<td>Total awake during the night</td>
</tr>
<tr>
<td>Total sleep time</td>
</tr>
<tr>
<td>(Time in bed – Awake time)</td>
</tr>
</tbody>
</table>
4 behavioral recommendations

1. Reduce your time in bed
2. Get up at the same time every day of the week, no matter how much you slept the night before
3. Don’t go to bed unless you’re sleepy
4. Don’t stay in bed unless you’re asleep

Buysse, Arch Int Med, 2011; 171:887-895
Behavioral aspects of pharmacotherapy: Timing is key
### Your Sleep “Prescription”

<table>
<thead>
<tr>
<th>Rules for better sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wake-up time: No LATER than...</td>
</tr>
<tr>
<td>...every day!</td>
</tr>
<tr>
<td>Bed time: No EARLIER than...</td>
</tr>
<tr>
<td>Total time in bed at night</td>
</tr>
<tr>
<td>Sleep medication</td>
</tr>
<tr>
<td>Sleep diary</td>
</tr>
<tr>
<td>Return visit</td>
</tr>
</tbody>
</table>
Acute response to BBTI vs. information control (IC) in older adults with chronic insomnia

Brief Behavioral Treatment of Insomnia (BBTI)

- Reduce your time in bed
- Get up at the same time every day of the week, no matter how much you slept the night before
- Don’t go to bed unless you’re sleepy
- Don’t stay in bed unless you’re asleep

Buysse, Arch Int Med, 2011; 171:887-895
Pragmatic trial of behavioral interventions for insomnia in hypertensive patients (HUSH) HL-125103

MD Referral via Research Recruitment Alert in Electronic Health Record

Telephone Screen

Baseline Evaluation

Randomize n = 625

Brief Behavioral Treatment of Insomnia n=250
Sleep Healthy Using The Internet n=250
Enhanced Usual Care n=125

Outcome Evaluations:
- Patient-reported outcomes
- Sleep-wake diary
- Home Blood Pressure Monitoring

For UPMC physicians:
- Research Recruitment Alerts (e-mail buyssedj@upmc.edu)
- Consult HUSH in Epic
Treatment of insomnia disorder

Evaluate
- Sleep and daytime symptoms
- Sleep, psychiatric, and medical disorders

Evaluate treatment options (cost, preference, availability)

Optimize treatment of comorbid disorders

Cognitive-Behavioral Treatment
1. CBT-I, BBTI
2. Other behavioral-psychological treatment
3. Other behavioral-psychological treatment (2)

Combined Behavioral-Pharmacological Treatment
- Evaluate response
- Re-evaluate diagnosis
- Consider switching treatment modality

Pharmacological Treatment
1. Bz, BzRA, ramelteon, doxepin, or suvorexant
2. Switch to different drug class
3. Combine 2 drugs of different classes
4. Consider other drugs