Modern Management of Sleep Disorders in Women

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No disclosures

Case

• 58 yr. old WF with >4 yr. of “poor sleep”
• Asleep by 9-10 PM, but difficulty with maintenance of sleep; awake at 3 AM
• Few daytime symptoms. No naps.
• Denies depression, anxiety, bad habits
• Previous MD prescribed ambien 5-10 mg 3-5 times per week.
• What else would want to know and what do you want to do?
Topics Covered

- Prevalence and potential consequences
- Sleep physiology
- Insomnia evaluation and treatment
- Sleep disordered breathing and parasomnias

Sleep Disorders

- Average sleep/night: 9 hr in 1910, 6.9 hr now
- 40 million in US suffer from sleep disorders
- 95% are undiagnosed and untreated
- Prevalence of sleep disorders higher in women and increases with age
- Frequent complaint in primary care…
Percent Reporting Symptoms of Insomnia

2002 ‘Sleep in America’ poll, National Sleep Foundation

Definitions

- Insomnia (insufficient or poor quality sleep)
  - Latency (time to fall asleep)
  - Efficiency (proportion of time in bed asleep)
- Hypersomnia (excessive daytime sleepiness)
  - Sleep disordered breathing/sleep apnea
  - Narcolepsy
- Parasomnia (coordinated motor activity)
  - Restless leg syndrome
Sleep Architecture

- REM (Rapid Eye Movement)
  - Characteristic eye movement
  - EEG resembles wakefulness
- Non REM
  - 75% of sleep
  - Four stages: correlate with depth of sleep
  - Progressive cortical inactivity
- Sleep architecture changes over age 65
  - Reduced stage 3 and 4, phase advancement
  - ↓ total time, ↑ latency, ↓ efficiency

Insomnia Special Populations

- Elderly
  - High prevalence (> 50%)
  - Secondary sleep disorder more common
  - Commonly associated with psychiatric disorders or depression
- Women
  - 50% more common than in men
  - Increases dramatically after menopause
Insomnia Special Populations: Perimenopausal Women

- Prospective study of >3000 women 42-52 followed for 7 yr (SWAN)
- Sleep complaints worse in peri and postmenopausal women (40% vs. 22%)
  - Both initiation and maintenance of sleep impaired
  - Partly attributable to hot flushes
  - Improved but not fully reversed with HRT
  - Other neurocognitive effects?

Kravitz et al, Sleep, 2008

Presentation and Screening for Insomnia

- Typical presentation
  - Difficulty initiating or maintaining sleep
  - Wake after sleep onset, early AM awakening
  - Awakening not rested

- Recommended screening question: “Do you have trouble falling asleep or staying asleep?”

- If positive, consider full sleep questionnaire
Sleep Quality Assessment (PSQI)

What is PSQI, and what is it measuring?
The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument used to measure the quality and patterns of sleep in adults. It differentiates "poor" from "good" sleep quality by measuring seven areas (components): subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month.

INSTRUCTIONS:
The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

During the past month,

1. When have you usually gone to bed?
2. How long (in minutes) has it taken you to fall asleep each night?
3. What time have you usually gotten up in the morning?
4. A. How many hours of actual sleep did you get at night?
   B. How many hours were you in bed?
5. During the past month, how often have you had trouble sleeping because you
   A. Cannot get to sleep within 30 minutes
   B. Wake up in the middle of the night or early morning
   C. Have to get up to use the bathroom
   D. Cannot breathe comfortably
   E. Cough or snore loudly
   F. Feel too cold
   G. Feel too hot
   H. Have bad dreams
   I. Have pain
   J. Other reason (s), please describe, including how often you have had trouble sleeping because of this reason (s):
6. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?
8. During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?
9. During the past month, how would you rate your sleep quality overall?
   A. Very good (0)
   B. Fairly good (1)
   C. Fairly bad (2)
   D. Very bad (3)

Medical Conditions That Cause Insomnia

- Hyperthyroidism
- Arthritis
- Chronic renal failure
- Chronic lung disease
- Heart failure
- Neurological disorders
- Dementia/AD
- Parkinson’s disease
## Drugs That Cause Insomnia

- Alcohol
- CNS stimulants
- Beta-blockers
- Bronchodilators
- Calcium channel blockers
- Corticosteroids
- Decongestants
- Stimulating antidepressants
- Thyroid hormone (T3)
- Nicotine

## Evaluation of Insomnia: History, Exam and Labs

- General history and exam
- Sleep pattern (patient and bedroom partner)
  - Insufficient sleep time
  - Delayed onset vs. frequent/early awakening
  - Associated nocturnal symptoms and daytime symptoms
- Lab testing: thyroid function, glucose, UA
- Formal sleep study rarely indicated
Insomnia Therapies

Which of the following is known to be superior to benzodiazepine receptor agonists for primary insomnia?
1) sleep hygiene instruction
2) cognitive behavioral therapy
3) anti-histamines
4) anti-depressants (TCA, SSRI, and trazadone)

Treatment of Insomnia: Non-Pharmacologic

- Treat underlying disorders
- Document sleep patterns with Sleep Diary
- Begin with non-pharmacologic treatment
  - Sleep education (changes with aging)
  - Sleep hygiene: diet, exercise, habits, environment (e.g. computer screens)
  - Establish optimal sleep pattern
Cognitive Behavioral Therapy for Insomnia (CBTi)

- Cognitive therapy
  - Change maladaptive thought processes
- Behavioral therapy
  - Stimulus control, sleep restriction, relaxation, good sleep hygiene
- RCT of 46 adults with chronic insomnia
  - Superior short and long-term (6 mo) outcomes with CBT compared to zopiclone or placebo

Buysse et al, Arch Intern Med, 2011
Trauer et al, Annal Int Med, 2015

CBTi: Face-to-face Vs. Internet-based

- Insufficient CBTi-trained therapists and may not be covered by insurance
- Internet-base CBTi
  - More convenient, less expensive
  - Multiple vendors/programs
  - SHUTi Self Help extensively studied
    - 6 weekly 40 minute sessions, sleep diary feedback, Fitbit integration ($150 for 26 wk access)
    - Not easy, but if motivated…
SHUTi vs. Face-to-face CBT

SHUTi Clinical Trial Outcomes Comparable to Published Data for Face-to-Face CBT-I

- F2F CBT-I (N=80, ES=2.0)
- SHUTi-RM (N=22, ES=2.34)
- SHUTi Cancer (US)/N=14, ES=2.24
- SHUTi-BPI (US)/N=151, ES=1.96
- SHUTi (Norway)/N=96, ES=1.71
- Goodnight (Australia)/N=574, ES=1.91

65 days

Before SHUTi
After SHUTi
Post 6 months
Post 12 months

SLEEP WINDOW BASIC GROUND RULES

RULE 1: STAY AWAKE UNTIL YOUR SLEEP WINDOW BEDTIME

What if you can’t stay awake until your bedtime? This is a good sign if your Sleep Window Bedtime is midnight, you should not go to bed before that time even though you feel as if you could fall asleep by 11:00 p.m. You may have to fight your sleepiness in order to stick to your Sleep Window.

RULE 2: GO TO BED ONLY WHEN YOU ARE SLEEPY

Sometimes you might find yourself struggling to stay awake until your bedtime, but when your Sleep Window finally arrives, you are wide awake. If this is the case, stay up until you start to feel sleepy. Your Sleep Window is a period of time you MAY sleep, but MUST sleep. Feeling wide awake after your Sleep Window will disrupt the sleep/wake rhythm (altered sleep/wake cycle) and your body will not know that it is time to sleep.

RULE 3: IF YOU CAN’T SLEEP, GET OUT OF BED

Never stay in bed awake for more than 15-20 minutes. If you feel sleepy, but then get instead and can’t fall asleep within 15-20 minutes, get out of bed. Or, if you wake in the middle of the night and can’t fall asleep within 15-20 minutes, get out of bed. You are helping to teach your body and mind the right time to sleep.

RULE 4: MAINTAIN A REGULAR ARISE TIME IN THE MORNING

Keep your Arise Time the same. Set your alarm clock for your Arise Time the same time each day and make sure you get up at the same time every day. Your body is sensitive to how much you sleep the previous night. Although it may be tempting to stay in bed longer because you feel sleepy at work, or to stay in bed later on weekends, try to maintain exactly sleep schedule. This is the best way to reset your biological clock and get your sleep back on track.

RULE 5: NO NAPS

Although many people with sleep problems try to nap to make up for lost sleep, this strategy often backfires. For people with insomnia, napping disrupts the sleep/wake rhythm and interferes with nighttime sleep. Remind that staying awake all day will help you feel sleepier at night and increase your chances of falling asleep.

RULE 6: USE YOUR BEDROOM FOR SLEEP AND SEX ONLY

Do not read, watch TV, talk or listen to the phone, or work in bed during the day or at night. In fact, it is important that you use your bed and bedroom only for sleep and sex. Engaging in other activities teaches your mind and body that bed is a place for wakefulness, not sleep.
Treatment of Insomnia: Pharmacologic

- From depression (use PHQ9)
  - TCA, trazadone, SSRI, SNRI, combinations
- From anxiety, panic (use GAD-7)
  - SRRI, SNRI >> benzodiazepines
- From hot flashes
  - HRT
- Primary insomnia: what to use?
Treatment of Insomnia: Pharmacologic

• Anti-histamines
  – No data on efficacy
  – Anti-cholinergic, sedation, cognitive dysfunction

• Benzodiazepines
  – Short-term benzodiazepine use (<2 wk) may be helpful in some patients
  – Habit forming, tachyphylaxis, suppression of REM sleep, cognitive dysfunction, falls

• Alternatives?
Benzodiazepine Receptor Agonists

• Zolpidem (generic), zaleplon (Sonata), eszopiclone (Lunesta)
  - Activate 1 of 3 benzodiazepine receptors
  - No anxiolytic or muscle relaxing effects
  - Preserves REM, less tolerance and withdrawal
  - Rapid onset, half life 2-3 hours

• Zolpidem dosing: limit to 3-4 times per wk, use 5 mg in women or >65
  – CR zolpidem if awakens too early with generic
  – Sublingual zolpidem (Intermezzo) for middle of the night awakening. Note: women 1.75 mg, men 3.5 mg

An unexpected side effect…
Other Drugs for Insomnia

• Trazadone (50-100mg qhs)
  - Antidepressant, sedation from H1 effects
  - Short term trials: improved sleep latency, self reported sleep quality
  - Off-label use but few serious side effects

• Melatonin (OTC)
  - From pineal gland, receptors in hypothalamus
  - Poor evidence for insomnia; jet lag or phase delay?
  - Not regulated

Buysse Jama 2017

Other Drugs for Insomnia

• Ramelteon (Rozerem)
  – Melatonin receptor agonist for sleep onset
  – FDA approved but no long-term safety data

• Suvorexant (Belsomra)
  – Orexin receptor antagonist for sleep maintenance
  – FDA approved but no long-term safety data

Buysse Jama 2017
Suggested Approach to Insomnia In Primary Care

Insomnia

Acute <4 wks

Assess trigger
Consider brief tx

Hypersomnia or parasomnia?
Evaluate and treat

Chronic >4 wks

Primary?
Sleep hygiene CBTi
Refer if persists

Secondary cause?
Treat and reassess

Hypersomnias: Sleep Apnea

- Obstructive more common than central
- Apneic episodes, loud snoring, choking, gasping during sleep
- Key feature: insomnia not common but usually associated with daytime sleepiness
- Risk factors include:
  - Older age
  - Male sex
  - Obesity
  - Craniofacial structure
Sleep Study Definition of Sleep Apnea

- Apnea = complete cessation of respiration
- Hypopnea = partial decrease (>50%) of respiration
- Duration ≥10 seconds
  \[\Rightarrow\ \text{Respiratory Disturbance Index (RDI):}\]
  - # apneas + hypopneas / hour while asleep
  - Normal RDI < 5, severe apnea ≥ 15

Prevalence of Sleep Apnea

- Heavily dependent on definition
- Population-based surveys:
  - 2-4% under 60, >10% in elderly
- At least moderate OSA (all ages):
  - 4% women, 9% men

Young, Wiscon Med J, 2009
Consequences of Sleep Disordered Breathing

- Impaired QOL
- Increased risk of accidents & injuries
- Mild cognitive impairment/dementia
  - 85% increased risk if RDI>15 in older women
- Increased risk of hypertension
  (particularly women) and maybe CHD

Yaffe et al Jama, 2011

Sleep Heart Study:
HTN by Quartiles of RDI

Detection of Sleep Apnea: Symptom Questionnaires

- Several screening questionnaires available (Berlin, OSA50, STOP-Bang):
  - High sensitivity but low specificity
- In symptomatic outpatients:
  - STOP-Bang ≥ 3 most predictive
- USPSTF recommendation: inadequate evidence to screen asymptomatic patients

Kee, J Clin Sleep Med, 2018
USPSTF, Jama, 2016

Evaluation of Sleep Disorders: Sleep Studies

- Polysomnography (oximetry, EEG, EKG, EMG, observation)
- Home monitoring (oximetry + 1-2 others) if not medically complicated
- Indications:
  - Unexplained hypersomnia (esp. with snoring)
  - Unexplained sleep-related CV abn (pulm HTN)
  - Abnormal complex sleep behavior
  - Chronic unremitting insomnia that does not respond to therapy

ACP Guidelines, 2016
Other Causes of Hypersomnia: Narcolepsy

- Extreme daytime sleepiness, frequent brief naps, cataplexy
- Rare, familial, presents in 20s and 30s
- Requires sleep study and daytime Multiple Sleep Latency Test (MSLT)
- Treatment: stimulants, anticholinergics

Parasomnias: Restless Leg Syndrome

- Intense dysesthesias, repetitive jerking
  - Worse at bedtime, frequently awakens patient
  - Often familial, progresses with age
- Etiology unknown but associated with Fe deficiency
- Treatment
  - Iron 325 mg/d if ferritin <75 mcg/L
  - Sinemet 25/100 qhs, clonazepam 0.5-2 mg qhs
  - Dopamine agonists (rotingotine, pergolide, etc) effective but intolerance common

Scholz et al, Cochrane Database, 2011
Conclusions

• Sleep disorders common, particularly in women
• Associated with significant morbidity
• Primary care providers can diagnose and treat most patients with insomnia
• Drugs treatment over-utilized, non-pharmacologic treatment often successful
• CBTi is treatment of choice for insomnia
• Specialty referral (sleep study) for selected patients with symptoms of OSA, unexplained hypersomnia or severe insomnia

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• Previous MD prescribed ambien 5-10 mg 3-5 times per week.
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Scuba Driving Near Kawaihae