Sleep Problems in the Elderly

“To Sleep, Perchance to Dream… Ay There’s The Rub”

MACBETH
Faculty

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Disclosures

- Thomas Weiss, MD serves on the speakers bureau for Merck.
Learning Objectives

• Understand the changes in sleep physiology as people age.
• Describe sleep assessment in an elderly population.
• Choose appropriate non-pharmacological and pharmacological treatments for sleep problems in the elderly.
Effects of Sleep deprivation

- Irritability
- Cognitive impairment
- Memory lapses or loss
- Impaired moral judgement
- Severe yawning
- Hallucinations
- Symptoms similar to ADHD
- Impaired immune system
- Increased heart rate variability
- Risk of heart disease
- Increased reaction time
- Decreased accuracy
- Tremors
- Aches

Other:
- Growth suppression
- Risk of obesity
- Decreased temperature

- Risk of diabetes Type 2
Functions of Sleep

ENERGY CONSERVATION

IMMUNE FUNCTION

HORMONAL RESTORATION

MEMORY CONSOLIDATION

GLYMPHATIC SYSTEM  (Xie,L Science 2013:342;373-7)

SLEEP AS THE FIFTH VITAL SIGN?
WAKE-SLEEP CIRCUIT
AROUSAL PROMOTING SYSTEM
SLEEP PROMOTING SYSTEM
POLYSOMNOGRAPHIC SLEEP STAGES
“Normal” (aging) sleep: decreased sleep efficiency, increased fragmentation, decreased total sleep, increased daytime sleep.
Sleep stage distributions change: decreased slow wave sleep, decreased REM, and increased stage 1 and 2 sleep.
• Disruptions in the circadian sleep-wake pathways:

• Insomnia as a disorder of excessive wakefulness.

• Increased levels of the neuropeptide orexin in the CSF of AD patients are associated with decreased cognition and sleep deterioration.
1. **DEFINITION**
2. **PREVALENCE**
3. **RISK FACTORS**
4. **ETIOLOGIES**
5. **ASSESSMENT**
6. **TREATMENT**
   a) **NONPHARMACOLOGIC**
   b) **PHARMACOLOGIC**
7. **TAKE-AWAYS**
INSOMNIA

DSM V: A sleep-wake disorder of dissatisfaction with sleep quantity or quality associated with sleep initiation, maintenance, and/or early awakening, at least 3 nights/week for at least 3 months despite adequate opportunity to sleep, and not attributable to another sleep-wake disorder, substance use/abuse, mental disorder or medical disorder.
INSOMNIA

PREVALENCE: (National Health and Wellness Survey 2015)

• 1/3 all adults have difficulties with sleep.

• ½ of adults >65 have sleep onset or maintenance problems. Of the 45 million adults 65 and older, 6 million reported sleeplessness with insomnia/sleep difficulties. 1.5 million reported the use of an OTC sleep aid.

• 2/3 of geriatric patient caregivers have sleep complaints.
RISK FACTORS FOR INSOMNIA

Female gender

>45

Divorced, separated, or widowed.

Lower level of education.

Alcohol or tobacco use.

Reduced physical activity.

Caffeine/stimulant use.

Poor sleep hygiene.

Genetic – CLOX gene

Neurotransmitter deficiency – galanin.
CAUSES

Environment (soundproof, lightproof, temperature, electronics)
Poor sleep hygiene
Excessive napping
Use of stimulants/alcohol
Variable sleep times
Pain
Obstructive Sleep Apnea (OSA)
Restless Legs Syndrome (RLS)
Medications
Mr. X, a significantly overweight (BMI=35) 72 y/o white male, presents at the outpatient clinic with a 1-year history of insidious cognitive decline. He has been living independently for the last 3 years following the death of his wife. His family checks on him regularly and helps monitor his medications for hypertension and high cholesterol as he is occasionally non-adherent. He has become more withdrawn and sad following the loss of his wife and has relinquished many activities and hobbies.
He reports chronic snoring and daytime fatigue, although he naps frequently during the day. A recent fall led to a severely bruised hip for which he is taking pain medication. He drinks 2 or 3 beers most evenings but will have more on occasion. His family reports some subtle personality changes, including increased irritability, and they have received a number of phone calls in the middle of the night from the patient who seemed confused and disoriented.
ASSESSMENT

- Shift worker?
- Medical history: psychiatric, neurologic, medical, and primary sleep disorders.
- Pain?
- Sleep history/habits: patient and bed partner.
- Epworth Sleepiness Scale (ESS)
- Mayo Clinic Sleep Partner Questionnaire (MCSPQ)
- Medications: prescription, OTC, and herbal/supplements.
- Stimulants: caffeine, nicotine.
- Alcohol use.
- Bedroom environment: soundproof, lightproof, temperature, and pets.
- Psychosocial: bereavement, lack of exercise, retirement, social isolation.
SLEEP HYGIENE TEN COMMANDMENTS

1. Sleep only as much as you need to feel rested, then get out of bed.
2. Keep a regular sleep schedule.
3. Avoid forcing sleep.
4. Exercise regularly 5 hours before bedtime.
5. Avoid caffeinated beverages after lunch.
6. Avoid alcohol near bedtime.
7. Avoid smoking, especially in the evening.
8. Do not go to bed hungry.
10. Deal with your worries before bedtime.

STIMULUS CONTROL THERAPY RULES:

1. Go to bed only when sleepy.

2. Do not watch television, read, eat, or worry while in bed. Use bed only for sleep and sex.

3. If unable to fall asleep within twenty minutes get out and go to another room. Return to bed only when sleepy.

4. Set an alarm to awaken at a fixed time each morning including weekends.

5. Do not take naps during the day.
TREATMENT - NONPHARMACOLOGIC

Relaxation therapy
Phototherapy
Massage therapy
Cognitive-behavioral therapy (CBT)
“THE WORST WOUNDS ARE SELF-INFLICTED.”

--President Bill Clinton
TREATMENT - PHARMACOLOGIC

- FDA-approved and non-FDA-approved medications.
- Geriatric pharmacokinetics/dynamics.
- Geriatric doses, half-lives, and adverse events.
TREATMENT - PHARMACOLOGIC

• Diphenhydramine
• Melatonin Receptor Agonists
• Antidepressants:
  • Tricyclics
  • Trazodone
  • Mirtazapine
• Antipsychotics
• Benzodiazepine Receptor Agonists
• Orexin Antagonists
DIPHENHYDRAMINE:

• First-generation antihistamine.

• FDA-approved for “occasional sleep disturbance.” Marketed before 1972 OTC Drug Monograph process therefore grandfathered in and not subject to RCTs.

• Increased ½ life and peak concentration on elderly.

• Rare published data. Patients prefer over placebo but significant side effects: next day sedation, compromised cognitive function, falls.

• Beers Criteria listed medication.

TREATMENT - PHARMACOLOGIC

MELATONIN RECEPTOR AGONISTS:

• Unclear if melatonin levels decrease with age.

• Ramelteon is currently the only melatonin receptor agonist approved by the FDA.

• Potent activity at MT1 and MT2 receptors.

• Approved to treat only sleep-onset insomnia.

• Effective for prevention of delirium in the elderly.

• $\frac{1}{2}$ life = 1-2.6 hrs.

• Not associated with cognitive impairment or gait instability.

Hatta, K et al. JAMA 2014;71(4):397-403
TREATMENT - PHARMACOLOGIC

ANTIDEPRESSANTS:

• TRICYCLICS:
  ➢ Doxepin (low dose) FDA-approved 2010 for insomnia secondary to difficulty with sleep maintenance. Long ½ life (15.3 hrs).

• TRAZODONE:
  ➢ Widely used off-label.
  ➢ Few studies. Side effects include daytime sedation, orthostasis, impaired cognition and motor and priapism (rare).

• MIRTAZAPINE:
  ➢ Widely used off-label.
  ➢ Tetracyclic antidepressant, multiple MOAs
  ➢ Side effects include weight gain, next day impairment in motor reaction and orthostasis.

Fagiolini A CNS Drugs 2012;26(12):1033-1049
ANTIPSYCHOTICS:

• Off-label.

• BLACK BOX warning for cardiovascular events (class-related).

• QUETIAPINE low dose (25 mg) studied in elderly patients with primary insomnia and dementia increased total sleep time (TST).

• Adverse events include weight gain and glucose/lipid shifts.

TREATMENT - PHARMACOLOGIC

• BENZODIAZEPINE RECEPTOR AGONISTS (BzRAs): which bind at alpha1-3,5 GABA receptor subunits and mediate sedative and anxiolytic effects.

• Distinct ½ lifes: Long (Temazepam 18.4 hrs) or Short (Triazolam 5 hrs).

• FDA-approved for short-term (7-10 days) treatment of insomnia in improving sleep latency.

• Adverse effects: Tolerance, rebound, confusion, falls, amnesia, and next day sedation.

• Recent evidence linking higher mortality rates and increased incidence of Alzheimer’s dementia in elderly patient using higher doses over 7 years

Weich, S et al. BMJ. 2014;348;g1996
TREATMENT - PHARMACOLOGIC

• NONBENZODIAZEPINE RECEPTOR AGONISTS (NBRAs): the so-called “Z” drugs: Zolpidem, Eszopiclone, Zaleplon. More selective/specific for the alpha1 subunit of the GABA receptor.

• Again ½ life is a distinguishing feature: short (Zaleplon 1hr) or intermediate (Eszopiclone 9hr).

• FDA-approved for short-term (up to 30 days) of insomnia, primarily sleep onset.

• Adverse effects include tolerance, rebound, parasomnias, negative effects on gait, balance and equilibrium.

TREATMENT - PHARMACOLOGIC

- OREXIN ANTAGONISTS: Suvorexant, the first orexin-receptor antagonist approved by the FDA in 2014 for insomnia.
  - Novel mechanism of action: binds to orexin receptors that mediate wakefulness/arousal and partially inhibits wakefulness.
  - Well studied in the elderly. Demonstrated efficacy in sleep onset and sleep maintenance.
  - Adverse effects include next-day somnolence (1/2 life 9-12 hrs), muscle weakness, vivid dreams, and sleep paralysis.
  - No tolerance, withdrawal or rebound noted after 12 months use.
  - NOT on Beers criteria.

THE PERFECT HYPNOTIC

- Rapid onset of action.
- Adequate duration for sleep maintenance but short enough to avoid daytime sedation.
- No abuse/dependency potential.
- Minimal/none drug-drug interactions.
- No rebound.
- Trialed in the elderly.
- No changes in sleep architecture.
- No respiratory depression.
- No parasomnias.
TAKEAWAYS

• SLEEP IS A MEDICINE.

• SLEEP DISTURBANCES ARE COMMON. SCREEN CAREFULLY.

• ASSESS ALL MEDICATIONS, INCLUDING OTCs AND SUPPLEMENTS.

• REVIEW/REINFORCE SLEEP HYGIENE.

• BEGIN WITH LIGHT THERAPY AND REGULAR EXERCISE.

• TREAT WHO WE CAN OPTIMALLY.

• REFER PATIENTS WHEN NECESSARY FOR SPECIALIZED TREATMENT.