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TREATMENT RESISTANT INSOMNIA

From the Johns Hopkins Sleep Disorder Center comes a recent review of approaches to persistent insomnia by David Neubauer, MD. He cautions that prior to upping a medication dosage when a patient continues to complain of insufficient sleep, or leaping to switch sleep medications, re-evaluate all the patient's current medications, behaviors surrounding sleep hygiene, sleep-wake cycles and co-morbidities. While 30% of adults have occasional insomnia, as many as 10% experience persistent insomnia. Advanced age, chronic medical conditions and females in general, tend to present with higher rates of insomnia.

Dr. Neubauer recommends five points in the evaluation process:

- Review the 24-hour sleep cycle by means of a sleep log, noting periods of daytime sleepiness and sleeplessness.
- Review all ingested medications including over-the-counter, and revisit use of caffeine, nicotine, and alcohol.
- Look into things that may interfere with the homeostatic sleep drive such as napping.
- Look into things that may interfere with circadian rhythm¹, such as irregular schedules.
- Evaluation of progress and improvement relies on following insomnia-related daytime symptoms as key outcome indicators (fatigue, irritability, worry about sleep, memory problems, poor concentration, etc.)

Let's drill down to identify the eight key questions to pursue in evaluating on-going chronic insomnia.

1. What does the patient actually mean with his complaint of insomnia?
 - Difficulty falling asleep
 - Difficulty maintaining sleep
 - Awakening too early
 - Nonrestorative sleep.

The key clinical point is that it is the daytime consequences that define progress or failure of treatment: fatigue, worry, irritability, lowered concentration, procrastination, difficulty completing tasks. If daytime functioning is improving, treatment is working despite patient complaints to the contrary.

¹ Zee PC, et al. The brain's master circadian clock: implications and opportunities for therapy of sleep disorders. "Sleep Med Rev" 2007; 11 (1): 59-70.

2. What co-morbidities have been undiagnosed or under treated? Pain syndromes and mental diagnoses are top sleep disrupters². Also, substance abuse and cardiovascular, pulmonary, endocrine, neurological and orthopedic conditions are prominent as sleep disturbers.
3. Is the patient taking medications with stimulating side effects? Many antidepressants such as the SSRI's have a stimulating profile. Caffeine can last in the body for extended periods of time; so, for the insomnia patient, avoiding coffee and other caffeinated drinks may be the best policy.
4. Homeostatic Sleep Drive: The biological urge for rest and sleep occurs for 1/3rd of the time in a 24-hour period, namely any 8 hours/24 hours. Many things can disrupt this drive, including purposefully "staying up late" or shift work.
5. Circadian Rhythm process³ is primarily an alerting system that works with the CNS (brain) master timekeeper and feedback loops that include daylight, melatonin and other brain neurotransmitters. The short explanation is that alertness is inhibited maximally in the middle of the night mostly by maximal production of melatonin.
6. Does the patient know the basics of good sleep hygiene?
 - Regular bedtime and wake-up times.
 - Peaceful bedroom environment.
 - Darkened bedroom with attention to blocking outside lights, minimizing led lights from clocks, cable box, telephones, night-lights, etc.
 - Remove televisions, computers and other stress-inducing distractions from bedroom.
 - Avoid daytime napping
7. Does the patient experience hyperarousal at bedtime? Several things contribute to this phenomenon:
 - Worry about not falling asleep.
 - Extended time (beyond 10-20 minutes) in bed while "trying" to fall asleep reinforces insomnia.
 - Daytime naps.
8. Is the patient taking appropriate medication for his specific condition? Are other psychotropic medications contributing to chronic insomnia?

Type of Medication

Elimination half-life (hrs)

Immediate-release benzodiazepines:

Estazolam (Pro-Som)	8-24
Flurozepam (Dalmane)	48-120
Quozepam (Doral)	48-120
Temazepam (Restoril)	8-20
Triazolam (Halcion)	2-4

Immediate-release nonbenzodiazepines:

² Morin CM, et al. Psychological and behavioral treatment of insomnia: update of the recent evidence. "Sleep" 2006; 29:1398-414.

³ Manthana P, et al. Neurobiology of circadian rhythm sleep disorders. "Curr Neurol Neurosci Rep" 2006; 6: 163-8.

Eszopiclone (Lunesta)	5-7
Zaleplon (Sonata)	1
Zolpidem (Ambien)	1.5-2.4
<i>Extended-release nonbenzodiazepine:</i>	
Zolpidem ER (Ambien CR)	2.8-2.9
<i>Selective melatonin receptor agonist:</i>	
Ramelteon (Rozerem)	1-2.6

In conclusion:

It is best to prescribe these medications on the lower dose side rather than the higher side. Most of these are sedating medications and as the dose goes up, the risk of adverse side effects goes up. Some of these effects are: daytime sleepiness, headache, dizziness, nausea, diarrhea and memory problems. There have been reports of sleep walking and confused behavior.