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Guest Editors: Whitney Hanks, Stephen Jamison, and Brett Parrish, Pharm.D. Candidates 2012



Key Inforbits

- Insomnia Introduction and Diagnosis
- Treatment Goals
- Treatments of Insomnia
- Good Sleep Habits
- New Drug Therapies
- References



March 5-11 2012 is.... Sleep Awareness Week!!

Insomnia: Introduction and Diagnosis

Insomnia is the most common complaint fielded by physicians in general practice. During their lifetime, over half of the population reports insomnia. Approximately 9% to 12% of adults are estimated to have chronic insomnia, which is defined by *The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)* as lasting over one month.² However, only 5% of individuals suffering from insomnia seek medical attention for it, while 10% to 20% of patients self-treat with alcohol or over-the-counter (OTC) drugs.

Normal sleep physiology is complicated and not fully understood. A variety of neurotransmitters and brain structures are involved in the mechanisms of sleep. The sleep-wake cycle is driven by a circadian rhythm and lasts approximately 24 hours, even in environments without light cues to stimulate changes in wakefulness. Healthy sleep is divided into two phases: non-rapid eye movement (NREM), which consists of four stages, and rapid eye movement (REM). Typical sleep progresses through NREM sleep, characterized by a slowing of metabolic activity and brain waves, to REM sleep characterized by a dramatic increase in metabolic and electrical activity in the brain along with rapid eye movement and dreaming. The entire sleep cycle lasts between 70 and 120 minutes.

Insomnia is described by subjective patient reports of difficulty falling asleep, difficulty maintaining sleep, or experiencing non-restorative sleep. These symptoms cannot be attributed to another disorder such as depression. Patients who are young adults typically complain of difficulty falling asleep, while older adults and the elderly report difficulty maintaining sleep. Diagnosis of insomnia consists of patient interview and sleep studies to identify potential causes or contributing factors to the disorder.

Primary insomnia is a disorder caused by a neurochemical imbalance or structural damage to areas involved in regulating sleep. Comorbid insomnia appears as a symptom of another condition and chronic insomnia is often due to concurrent psychiatric or medical disorders. The cause of a patient's insomnia can sometimes be addressed, such as withdrawing a pharmacologic agent.

Insomnia Risk Factors

- Female gender
- Elderly
- Unemployment
- Separation or widowed from spouse
- Lower socio-economic status
- Concurrent psychiatric disorder

Goals of Treatment

Primary Goals of treatment:

- Improve sleep quality and time asleep
- Improve lack of sleep daytime impairments (ex: energy, attention or memory difficulties, cognitive dysfunction, fatigue, or bodily symptoms)

Secondary Goals

- Improve insomnia symptoms
 - SOL(sleep onset latency) <30 minutes
 - WASO (wake after sleep onset) <30 minutes
 - Decreased awakening frequency or other complaints with sleeping
 - TST (Total sleep time) >6 hours and improve sleep efficiency >80-85%
- Provide the patient with a positive connotation between the bed and sleeping
- Decrease a patients anxiety about sleeping

Insomnia Treatment

Over-the-counter Treatments

Antihistamines and antihistamine-analgesic combinations (ie:Tylenol PM, Benadryl) are widely used self-remedies for insomnia even though their efficacy and safety is limited. Antihistamines have the potential for serious side effects (ie, tachycardia, dizziness, hypertension) arising from their parallel anticholinergic properties. Very few herbal or alternative treatments have been studied for the treatment of insomnia. Of these, the greatest amount of evidence is available for valerian extracts and melatonin. Evidence suggests that valerian has small but consistent effects on shortening time until falling asleep but with inconsistent effects on staying asleep and sleep duration. On the other hand, melatonin has been tested in many clinical trials which have demonstrated that melatonin has small effects on the time it takes to fall asleep. Melatonin may shift a patients phase time of sleeping rather than act as a hypnotic. Long-term use of non-prescription (over-the-counter) treatments is not recommended due to lack of efficacy and potential side effects.^{1,3}

Prescription Medications for Insomnia³

The choice of which pharmacological agent should be utilized is based on:

- symptom pattern
- treatment goals
- past treatment response
- patient preference and cost
- availability of other treatments
- side effects



Three main drug classes for treating insomnia are:^{3,4,5}

- **Non-Benzodiazepines**
 - Mechanism of action: selectively binds to the BZ1 (GABA benzodiazepine receptor subtype a1) receptor subtype, explaining their more targeted action as sleeping agents. Compared with conventional benzodiazepines, these agents have similar hypnotic action, but an improved profile for rebound insomnia, withdrawal, tolerance, and abuse or dependence potential.
 - Potential ADRs: Behaviors during sleep (such as sleepwalking), drug interactions, residual sedation, memory and daytime performance alterations, and concern for increased risk of motor vehicle accidents and falls.
- **Benzodiazepines**
 - Mechanism of action: modulate GABAA receptors, which are gated ion channels that mediate effects of GABA. These agents decrease the time to sleep onset and enhance stage 2 sleep. These drugs bind to the GABA-benzodiazepine receptor complex, rather than directly on GABA. Benzodiazepines bind to the benzodiazepine receptor so that the inhibitory action of GABA is allosterically enhanced.
 - Potential ADRs: Benzodiazepines may be associated with tolerance, abuse potential, morning-after sedation, and cognitive impairment. Also associated with rebound insomnia
- **Melatonin Receptor antagonists**
 - Mechanism of Action: binds to the MT1 and MT2 receptors, which are normally acted upon by endogenous melatonin, contributes to sleep-promotion and maintenance of the circadian rhythm underlying the normal sleep-wake cycle.
 - Potential ADRs: nausea, dizziness, fatigue, exacerbated insomnia, somnolence

Drug	Trade Name ⁴	Recommended Dose	Indications/Comments
Benzodiazepine Receptor Agonistic Modulators			
Non-benzodiazepines			
eszopiclone	Lunesta [®]	<ul style="list-style-type: none"> • 2-3 mg hs • 1 mg hs in elderly; max 2 mg • 1 mg hs in severe hepatic impairment; max 2 mg 	<ul style="list-style-type: none"> • Primarily used for sleep-onset and maintenance insomnia • Intermediate-acting • No short-term usage restriction
zolpidem	Ambien [®] , Edluar [™] , Zolpimist [®]	<ul style="list-style-type: none"> • 10 mg hs; max 10 mg • 5 mg hs in elderly, or hepatic impairment 	<ul style="list-style-type: none"> • Primarily used for sleep-onset insomnia • Short-to intermediate-acting
zolpidem (controlled release)	Ambien CR [®]	<ul style="list-style-type: none"> • 12.5 mg hs • 6.25 mg hs in elderly, or hepatic impairment 	<ul style="list-style-type: none"> • Primarily used for sleep-onset and maintenance insomnia • Controlled release-swallow whole, not divided, crushed or chewed
zaleplon	Sonata [®]	<ul style="list-style-type: none"> • 10 mg hs; max 20 mg • 5 mg hs in elderly, mild to moderate hepatic impairment 	<ul style="list-style-type: none"> • Primarily used for sleep onset insomnia • Maintenance insomnia as long as 4 hours is available for further sleep • Short acting
Benzodiazepines			
estazolam	Prosom [®]	<ul style="list-style-type: none"> • 1-2 mg hs • 0.5 mg hs in elderly 	<ul style="list-style-type: none"> • Short to intermediate-acting
temazepam	Restoril [™]	<ul style="list-style-type: none"> • 15-30 mg hs • 7.5 mg hs in elderly 	<ul style="list-style-type: none"> • Short to intermediate-acting
triazolam	Halcion [®]	<ul style="list-style-type: none"> • 0.25 mg hs; max 0.5 mg • 0.125 mg hs in elderly; max 0.25 mg 	<ul style="list-style-type: none"> • Short-acting
flurazepam	Dalmane [®]	<ul style="list-style-type: none"> • 15-30 mg hs • 15 mg hs in elderly 	<ul style="list-style-type: none"> • Long-acting • Risk of residual daytime drowsiness
Melatonin Receptor Agonists			
ramelteon	Rozerem [®]	<ul style="list-style-type: none"> • 8 mg hs 	<ul style="list-style-type: none"> • Primarily used for sleep-onset insomnia • Short-acting • No short-term usage restriction

Adapted from: Schutte-Rodin S; Broch L; Buysse D; Dorsey C; Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med. 2008;4(5):487-504.

Good Sleep Habits

Sleep hygiene consists of the practices that contribute to a regular sleep. Good sleep hygiene can help prevent sleep disturbances and disorders like insomnia. Here are some tips to help with good sleep hygiene^{6,7}:

- Establish a regular sleep-wake pattern by going to bed and waking up at the same time each day
- Avoid these right before bedtime: large meals, caffeine, nicotine, and alcohol
- Establish the association between bed and sleep by avoiding activities such as: watching TV, reading, or playing with your phone
- Exercise can help provide good sleep, however heavy activity should be done during the daytime
- Light plays a natural role in sleep patterns, so sleep should occur in a quiet and dark room
- Ensure the bedroom is comfortable and relaxing regarding linens as well as temperature
- Bedtime should be a time for mental relaxation.

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The last “dose” ...

"I love sleep. My life has a tendency to fall apart when I'm awake, you know?"
-Ernest Hemingway, American author and journalist [1899 - 1961]



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