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Key Inforbits

- Overview of insomnia
- Insomnia prescription medications
- Over-the-counter products
- Sleep hygiene
- Belsomra® (suvorexant)
- Medications that induce insomnia

Sleepless in Auburn

https://viewsfromthehorizon.wordpress.com/2013/09/11/insomnia-natures-caffeine/

Overview of Insomnia

Insomnia is one of the most common medical complaints.[1] Patients may describe it as a difficulty falling asleep, difficulty staying asleep, or not feeling "well rested" after sleep. Insomnia can affect many aspects of a person's life including their productivity during the day, workplace stress, and personal relationships.[1,2]

Insomnia usually occurs in adulthood and may continue on throughout life. Insomnia that is present fewer than three months is considered short-term and insomnia greater than three months is considered chronic. Often patients will have other co-morbid psychiatric disorders such as anxiety or depression. Like many other conditions, insomnia can be classified as either primary or secondary; primary being caused by either a neurochemical disorder or a structural abnormality affecting the sleep-wake cycle. Secondary insomnia is that which is caused by another medical disorder. Transient or short-term insomnia can often be attributed to a recent event such as a death in the family, school exams, or recent stressors. Whether short-term or chronic, every patient with insomnia should be counseled on non-pharmacologic treatment options.

Common Causes of Insomnia

- Situational events: financial stress, personal conflicts, shift work
- Medically related events: arrhythmias, heart failure, sleep apnea, asthma, GERD, epilepsy, pregnancy, depression, anxiety, substance withdrawal

Guideline Recommendations

Multiple guidelines for the management of insomnia have been published by organizations such as the American College of Physicians and the American Academy of Sleep Medicine.[3,4] The most recent set of guidelines concerning insomnia was published in February of this year by the American Academy of Sleep Medicine.[4] Below is a summation of key points from these most recent guidelines.

High Points:

- Cognitive behavioral therapy (including behavioral interventions and sleep hygiene education) should be used as initial treatment for all patients with chronic insomnia.[3,4]
- If insomnia is comorbid with another sleep disorder or medical disorder that is contributing to the insomnia, it is recommended to optimize the treatment for that comorbid disorder before adding pharmacologic treatment for insomnia.[4]
- The decision to initiate pharmacologic treatment and which pharmacologic agent to use should involve patient specific factors.[3,4]
- Generally, short acting benzodiazepine receptor agonists (such as eszopiclone or zolpidem) or ramelteon are first-line options. If these are insufficient, second-line treatment options could involve switching to another short acting benzodiazepine or switching to a sedating antidepressant such as trazodone.[4]
- Often an initial pharmacologic treatment period of 2 to 4 weeks is appropriate. This should be followed by a reevaluation to determine need for continued treatment.[4]
- Patients with more severe chronic insomnia may be candidates for long-term pharmacologic treatment. However specific characteristics of these candidates for long-term therapy are still not fully understood. Additionally, data is still lacking on which medications are best to use for long term treatment of insomnia.[4]

1. Dopp JM, Phillips BG. Sleep-Wake Disorders. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. Pharmacotherapy: A pathophysiologic approach. 10th ed. New York: McGraw-Hill Medical; c2017. Chapter 72.
2. Winkleman JW. Insomnia disorder. N Engl J Med. 2015;373:1437-44.
3. Qaseem A, Kansagara D, Forciea MA, et al. Management of chronic insomnia disorder in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2016;165:125-133.
4. Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(2):307-349.

Prescription Medications

There are many options when it comes to treating insomnia in patients, and many factors contribute to choosing the most appropriate therapy.[1] For example, antidepressants are often an effective choice in patients with Major Depressive Disorder (MDD) in which insomnia is a symptom. However, there are certain prescription medications in which treating insomnia is their primary role.

Prescription Medications for Insomnia	
Drug	**Comments**
Antidepressants	
Oleptro® (trazodone) Silenor® (doxepin) Remeron® (mirtazapine) Elavil® (amitriptyline)	- useful in treatment patients with a history of substance abuse because dependence is not a problem - useful in patients with comorbid condition of depression - can improve sleep continuity
Orexin Receptor Antagonist	
Belsomra® (suvorexant)	- recently approved - aids in maintaining sleep - C-IV
Melatonin Receptor Agonist	
Rozerem® (ramelteon)	- helps to improve sleep onset
Benzodiazepines	
Estazolam, flurazepam, Restoril® (temazepam), Halcion® (triazolam) Doral® (quazepam)	- reduce sleep latency and increase total sleep time - should not be used in the elderly or women who are pregnant - side effects are dose dependent - most common side effects are daytime sedation and psychomotor incoordination - flurazepam, quazepam, and temazepam are the most commonly used for insomnia - often shows withdrawal effects - C-IV
Benzodiazepine Receptor Agonists	
Ambien® (zolpidem)	- commonly used for insomnia - duration of 6-8 hours - reduces sleep onset latency, nocturnal awakenings, and increases total sleep time - should be taken on an empty stomach - often shows withdrawal effects - C-IV
Sonata® (zaleplon)	- rapid onset of action and a short half-life - does not have significant effect on psychomotor performance - targeted at decreasing time to sleep onset - C-IV
Lunesta® (eszopiclone)	- reduces time to sleep onset, wake time after sleep onset, number of awakenings, and increasing total sleep time and quality - labeled for long-term use; may be taken for up to six months - C-IV

-Alcohol should be avoided with all prescription insomnia medications

1. Dopp JM, Phillips BG. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, editors. Pharmacotherapy: A pathophysiologic approach. 9th ed. New York: McGraw-Hill Medical; c2014. Chapter 55.
2. Drugs for insomnia. Med Lett Drug Ther. 2015;57(1472):95-101.

https://www.pinterest.com/pin/13792342584901248/

Over-The-Counter Products

It is common for patients to have questions about over-the-counter (OTC's) medications and herbal remedies used for sleep. There are many options for self-treatment of insomnia; however, few products have evidence to support their use. The most common and efficacious of these products is diphenhydramine; it is an antihistamine with significant sedation effects.[1] Diphenhydramine can be found in nearly every OTC sleep aid marketed. This provides a valuable counseling opportunity when talking with patients. Another antihistamine, doxylamine is pharmacologically similar to diphenhydramine. There is less safety and efficacy to support the use of doxylamine, however the FDA allows the drug to remain on the market for use in insomnia.

Many patients may also ask about herbal remedies for their insomnia. Complementary therapies include melatonin, valerian, and kava. Melatonin has conflicting data to support broad use; however it does have data to support its use for delayed sleep phase syndrome and can be used for jet lag. The general recommended dose is 3 to 5 mg by mouth 30 minutes prior to bedtime. Valerian must be taken continuously for several days to weeks for required effect. Taking valerian at large doses for extended periods of time has been known to cause benzodiazepine-like withdrawal and cardiac complications and should therefore be tapered when discontinuing. Lastly, kava has been associated with severe hepatotoxicity and limited data to support use and therefore should be avoided.

1.Melton ST, Kirkwood CK.. Insomnia, Drowsiness, and Fatigue. In: Krinsky DL, Ferreri SP, Hemstreet BA, Hume AL, Newton GD, Rollins CJ, Tietze KJ, editors. Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care. 18th ed. Washington, DC: American Pharmacists Association; c2015. P.855-858.

Sleep Hygiene Tips[1,2]

- Establish and maintain a regular sleeping schedule; try to stick to the schedule even on weekends
- Avoid forcing sleep; if not asleep within 20-30 minutes, get up and perform a relaxing activity until drowsy
- Reserve the bedroom for sleep and intimacy only; avoid TV watching, reading, or activities on cell phone while in bed
- Don't "clock watch"
- Create a relaxing pre-bedtime routine
- Avoid daytime napping
- Exercise routinely throughout the week
- Avoid rigorous exercise right before bedtime
- Discontinue or decrease amount of alcohol, caffeine, and nicotine intake

https://www.cuteness.com/blog/content/puppies-sleeping-habits

1. Dopp JM, Phillips BG. Sleep-Wake Disorders. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. Pharmacotherapy: A pathophysiologic approach. 10th ed. New York: McGraw-Hill Medical; c2017. Chapter 72.
2. "Sleep Hygiene Tips". American Sleep Association [Internet]. Lititz (PA): American Sleep Association; c2017. [cited 2017 Feb 22]. Available from: https://www.sleepassociation.org/patients-general-public/insomnia/sleep-hygiene-tips/

Belsomra® (suvorexant)

The most recent insomnia medication approved by the FDA is Belsomra® (suvorexant). It was approved in 2014. Belsomra® is an orexin receptor antagonist, and works by altering the signals of orexins, the neurotransmitters responsible for the sleep-wake cycle.[1] Suvorexant doses of 10-20 mg at bedtime are indicated for difficulty initiating and maintaining sleep. If the patient has no relief of insomnia after 7-10 days, the patient may have underlying condition. Clinical studies have shown patients treated with Belsomra® fall asleep 5-10 minutes sooner and remain asleep 15-25 minutes longer than placebo. This indicates its use in patients whose primary complaint is difficulty falling and/or staying asleep. The most common side effects reported are next day somnolence and drowsiness. It is also important that patients be counseled on the possibility of sleep paralysis, cataplexy, and other narcolepsy-like symptoms. Of note: food decreases absorption, and several absolute drug contraindications. All CYP3A4 inhibitors and inducers should not be given with suvorexant. It is also a C-IV substance. Belsomra® is fairly expensive averaging about $12 a tablet.

1. Suvorexant [2017] In: Clinical Pharmacology [AUHSOP Intranet]. Tampa, FL: Elsevier/Gold Standard [updated 2017, cited 2017 Feb 20]. [about 10 p.]. Available from http://www.clinicalpharmacology-ip.com/Forms/drugoptions.aspx?cpnum=3895&n=Suvorexant&t=0
2. Drugs for insomnia. Med Lett Drug Ther. 2015;57(1472):95-101.

Medications That Induce Insomnia

Insomnia is a common side effect of prescriptions and over the counter medications.[1] Often proper timing of administration can decrease the risk of developing medication induced chronic insomnia. Some common medications that can cause insomnia include: anticonvulsants, alpha and beta agonists, diuretics, selective serotonin reuptake inhibitors, corticosteroids, amphetamines, levodopa, weight loss medications, and acetylcholinesterase inhibitors. Common OTC medications that can cause insomnia include: appetite suppressants, caffeine, prolonged or excessive use of alcohol, nicotine, and nasal decongestants. Proper counseling and timing of medication counseling from pharmacists can help patients rest easily.

1. Dopp JM, Phillips BG. Sleep-Wake Disorders. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, editors. Pharmacotherapy: A pathophysiologic approach. 10th ed. New York: McGraw-Hill Medical; c2017. Chapter 72.

The last "dose" …

"Early to bed and early to rise makes a man healthy, wealthy, and wise."
- Benjamin Franklin [a founding father of the United States, 1706-1790]

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