



Treatment of Insomnia

By Whitney Breunsbach, PharmD Candidate, UNMC

Insomnia is defined as difficulty initiating or maintaining sleep, waking up too early, or restless sleep despite adequate opportunity for sleep. Patients diagnosed with insomnia are more likely to suffer from mental health problems, drug and/or alcohol abuse, cardiac morbidity, and musculoskeletal conditions, as well as increased healthcare utilization. Insomnia may lead to an increase in indirect costs of healthcare by loss of productivity, absenteeism, and occupational or motor vehicle accidents.

Insomnia may result from poor sleep habits or lifestyle. Examples of poor sleep hygiene include an irregular sleep schedule, engaging in behaviors other than sleep in the sleep environment, and the use of alcohol, caffeine, or nicotine.

Treatment

The treatment of insomnia is guided by the International Classification of Sleep Disorders 2nd Edition (ICSD-2) as well as the duration of symptoms. Insomnia symptoms are segregated into three categories: transient, short-term, and long-term. Transient symptoms are those lasting less than 3 days and are related to situational stress. Short-term symptoms last 3 days to 3 weeks and are often related to stress associated with illness, grief, or work. Long-term insomnia is characterized by symptoms lasting more than 3 weeks without identification of a specific stressor. Treatment of transient insomnia should last for only 2-3 nights, while treatment for short-term symptoms should include attempts to improve sleep hygiene and with no more than 7-10 nights of intermittent drug therapy. Intermittent therapy is defined as omitting use after 1 or 2 nights of quality sleep. Patients with transient or short term insomnia need to be reevaluated if pharmacologic treatment continues beyond 2-3 weeks. Long-term insomnia, also known as chronic insomnia, should first be assessed for an underlying cause. Sedative therapy may be required despite treatment of the underlying condition. Long-term therapy should last no more than several months. Intermittent use, for example administering every third night, is best practice.

Nonpharmacologic Therapy

Insomnia may often be treated without utilization of sedative hypnotics by voluntary sleep hygiene interventions. For the treatment of insomnia, with or without the aid of medication, proper sleep hygiene, also referred to as stimulus control, is key. To promote quality sleep, patients should adhere to the following practices:

1. Establish regular bed and wake times.
2. Relax prior to bedtime.
3. Avoid clock watching.
4. Do not lie awake in bed. After 20 minutes without falling asleep, get up.
5. The bedroom is only used for sleep and sex.
6. Avoid daytime napping.
7. Avoid caffeine, alcohol, and nicotine within 6 hours of sleep.
8. Exercise regularly, but avoid within 3 hours of bedtime.

Pharmacologic Therapy

Hypnotic drugs should be used in combination with behavioral therapies such as Cognitive Behavioral Therapy or good sleep hygiene. Treatment should begin at the lowest dose and slowly titrate upward as needed. In addition, caution should be used in patients with a history of substance abuse. Patients utilizing hypnotics should be advised of "hangover" sedative effects. To discontinue a hypnotic, a gradual taper is advised to prevent withdrawal symptoms or rebound insomnia.

The American Academy of Sleep Medicine (AASM) recommends the following sequence as a guideline to the treatment of primary insomnia. A short or intermediate-acting benzodiazepine, GABA receptor agonist (zolpidem), or ramelteon should be the first step in a patient's treatment. Agents with relatively longer half-lives, such as temazepam, are best suited for patients experiencing awakenings after sleep onset. Shorter acting medications, such as zaleplon and ramelteon, are superior in patients suffering from sleep latency (not falling asleep within 30 minutes of going to bed).

If a patient's first medication is unsuccessful, an alternative benzodiazepine, GABA receptor agonist or ramelteon should be tried. Selection of a second agent should be based upon the patient's response to the first medication. For example, a patient experiencing residual sedation from a longer acting agent would benefit from a medication with a shorter half-life.

If a patient experiences a third treatment failure or suffers from comorbid depression, treatment with low-dose sedating antidepressants is warranted. Doses appropriate for use in insomnia are lower than doses effective for the treatment of depression. Examples include trazodone, mirtazapine, doxepin, amitriptyline, and trimipramine. Only doxepin, however, has been FDA-approved for insomnia. Medication selection should be individualized and based upon side effects and cost. For example, trazodone may produce less anticholinergic effects than doxepin and mirtazapine is more likely to cause weight gain.

Combination therapy of a benzodiazepine, GABA receptor agonist, or ramelteon and a low dose sedating antidepressant is a fourth line option for patients diagnosed with insomnia. Simultaneous treatment from two medication classes may reduce unwanted side effects associated with high dose treatment with a single agent.

Finally, if a patient fails the above therapies, other sedating agents such as anti-epileptics, and atypical antipsychotics should be considered. Due to insufficient evidence in primary insomnia and potential side effects, these agents should be avoided in patients without a comorbid condition warranting their use. Such options include gabapentin, tiagabine, quetiapine, and olanzapine.

Although approved for the treatment of insomnia, the AASM recommends against using chloral hydrate, barbiturates, and "non-barbiturate, non-benzodiazepine" medications, given their low therapeutic index and high probability of developing tolerance and dependence. Use of over-the-counter (OTC) sedative agents as a self-remedy for insomnia is not recommended. Caution should be used with OTC agents because of lack of evidence supporting safety and efficacy. OTC sleep agents should be avoided in elderly patients due to significant side effects.

Monitoring

After one week of treatment, patients should be evaluated for drug efficacy, adverse effects, and adherence to both pharmacologic and nonpharmacologic therapies. All patients, even those solely receiving nonpharmacologic treatment, should maintain a sleep log. A sleep log will supply information for monitoring such as bedtime, sleep latency, number and duration of awakenings, wake after sleep onset, time in bed, total sleep time, sleep efficiency, and nap times. This sleep log, or diary, should be kept with entries beginning before treatment initiation to provide baseline conditions.

Duration

To date, duration of sedative hypnotic use is a controversial topic. Prior to 2005, the FDA class labeling of hypnotics recommended short-term treatment. After 2005, the duration of treatment was not addressed. Utilizing the lowest effective dose intermittently, and for the shortest duration, is well accepted as the best way to avoid tolerance and dependence in patients. A gradual taper after 2-3 months, or a period of time appropriate for the insomnia disorder, should be completed. Reevaluation after 2-3 weeks following the discontinuation of therapy will determine the course of therapy. If the patient remains symptomatic 2-3 weeks after medication cessation consider initiating an alternative agent from the described treatment algorithm. If the patient's symptoms are better following discontinuation or unchanged as compared to active treatment, the medication should be withdrawn indefinitely.

Sleep Apnea

Sleep apnea is characterized by the periodic cessation of breathing during sleep followed by a short arousal and resumption of breathing. Because of their fragmented sleep patterns, patients suffering from sleep apnea experience symptoms of insomnia. Patients diagnosed with sleep apnea should not be treated with the sleep aids utilized in insomnia patients. Sleep apnea patients avoid central nervous system (CNS) depressants. CNS depressants reduce the brain's reflex ability which generates the brief sleep arousals that reinitiates breathing.

Conclusion

Nonpharmacologic therapies benefit a majority of insomnia sufferers, and therefore are considered first-line treatment. Although several benzodiazepines, GABA receptor agonists, and antidepressants are approved for insomnia, there are no recommendations for the optimal duration of treatment. Medications used to treat sleep disorders do not come without significant safety concerns. Health care providers and patients should be aware of the potential for rebound insomnia, medication withdrawal, medication abuse, and sleep-related behavioral disorders. All in all, treatment for sleep disorders includes a combination of nonpharmacologic and pharmacologic therapies tailored to each patient and his or her symptoms and medication-related adverse effects.

References available upon request.

NEBRASKA DUR

DUR Director
Marcia Muetting, PharmD, RP
6221 S 58th Street, Suite A
Lincoln, Nebraska 68516
Phone (402) 420-1500
Fax (402) 420-1406
Email dur@npharm.org
Website www.durnebraska.org

Nebraska Medicaid
Health & Human Services
PO Box 95026
Lincoln, Nebraska 68509-5026
Phone (402) 471-9029
Fax (402) 471-9092
Email medicaid.pharmacy@dhhs.ne.gov
Website www.hhs.state.ne.us/med/medprog.htm