Managing Insomnia
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Introduction

Between 50 and 70 million Americans of all ages report experiencing sleep-related problems.1 Insomnia is the most prevalent sleep disorder in the general population. It is defined as the subjective perception of difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity for sleep and results in varying degrees of daytime functional impairment.2-4 This newsletter will discuss the treatment strategies available to manage insomnia and will highlight various pharmacotherapy options.

Epidemiology and Impact

About 30 to 50 percent of the adult population experiences symptoms of insomnia within a given year and around ten percent actually have chronic insomnia.2,5-6 Chronic insomnia is defined as insomnia symptoms that occur at least three days per week and last 30 days or longer.3,4,7-8 Insomnia can also be classified as either primary or secondary. Primary insomnia is difficulty sleeping that has no known pathogenesis. Secondary or comorbid insomnia is much more common and it occurs due to an underlying condition (e.g., medical conditions, psychiatric disorders, other sleep disorders, substance abuse).2,4,6-8

In general, risk factors for insomnia include increased age, female sex, comorbid psychiatric disorders (e.g., depression, anxiety), comorbid medical conditions (e.g., chronic pain, respiratory conditions, neurological disorders), and shift work. Among psychiatric illnesses linked to insomnia, major depression has the strongest association; with a lifetime prevalence of approximately 31% in adults with insomnia compared to less than 3% in those without a sleep disorder.4,5,8,9 Sleep disturbances are a common symptom of depression. Unemployment and lower socioeconomic status have also been linked with higher rates of sleep disturbances. In addition, various medications may cause insomnia as a side effect.2,8

Insomnia can have significant consequences. It may be responsible for mood changes, impaired memory and concentration, and impaired daytime functioning. Insomnia may also affect professional performance, hinder social interactions, and decrease quality of life. Comorbid conditions can precipitate or worsen insomnia, which in turn may worsen the underlying condition. Insomnia may also be a factor in some automobile and industrial accidents. Chronic insomnia has a significant economic impact on society as direct costs (physician visits, medications, therapy) and indirect costs (e.g., work absenteeism, loss of productivity) have been estimated at tens of billions of dollars annually.4,7-8

Diagnosis

As with any other medical concern, diagnosing insomnia begins with a thorough medical history and physical examination. A comprehensive sleep history should include sleep habits, sleep environment, substance use (prescription and nonprescription medications, alcohol, nicotine, caffeine intake), and comorbid conditions. Assessing family, social, and occupational histories can help identify precipitating or exacerbating factors for insomnia.
Interviewing a bed partner or caregiver may provide additional information and a one to four week sleep diary may also be helpful. Polysomnography is useful if sleep-disordered breathing or periodic limb movement disorder is suspected or if insomnia fails to respond to treatment.\textsuperscript{2,3,7-9}

**Treatment of Insomnia**

Treatment is recommended if a patient has chronic insomnia that negatively impacts sleep quality, health, comorbidities, or daytime functioning.\textsuperscript{2} Treating co-morbid conditions, identifying and modifying behaviors that impair sleep, and limiting medications or substances that negatively affect sleep should be part of every treatment plan. When insomnia is comorbid with other medical conditions, psychiatric disorders, or other sleep conditions, those underlying conditions must be treated before the insomnia can be addressed effectively.\textsuperscript{2,3,9} For example, the patient whose insomnia is caused or exacerbated by untreated obstructive sleep apnea (OSA) should have the OSA addressed and treated (e.g., weight loss, changing sleep position, continuous positive airway pressure or CPAP). Another example is depression, where disturbed sleep and complaints of insomnia may be symptoms of the depression. In such patients, as the depression is adequately treated and remits, the sleep complaints may also resolve. If the insomnia symptoms persist despite adequate management of the underlying condition, then the insomnia needs to be treated.

Goals of treatment for insomnia include improving sleep quality and/or time, reducing daytime functional impairment and insomnia symptoms, and improving cognition.\textsuperscript{2} Therapy is tailored to address the patient’s primary sleep complaint (e.g., difficulty falling asleep, difficulty staying asleep, difficulty with both sleep onset and maintenance) and a follow-up plan with a specific timeline for reassessment should be outlined at the beginning of therapy and adjusted as needed during treatment.

**Nonpharmacological Options for Insomnia**

Cognitive behavioral therapies (CBT) are a group of techniques that address factors that precipitate or exacerbate chronic insomnia. These interventions include sleep-hygiene education, stimulus-control therapy, sleep-restriction therapy, and relaxation therapy. Sleep-hygiene education focuses on environmental or extrinsic factors that worsen insomnia symptoms (e.g., irregular sleep schedules, late night exercise, drinking caffeine before bed). Stimulus-control focuses on eliminating maladaptive responses to bedtime (e.g., reading or watching television in bed). Sleep-restriction therapy temporarily induces sleep deprivation to increase sleep time and improve sleep efficiency. Relaxation therapy is based on the assumption that insomnia is associated with hyperarousal and includes techniques like progressive muscle relaxation and meditation. The cognitive component of CBT involves educating the patient about sleep needs, addressing unrealistic expectations, and discussing how anxiety worsens sleep quality. Studies have shown that anywhere from 50% to 80% of patients will respond positively to CBT and benefits may be seen beyond the completion of therapy. Several CBT techniques may be used in a single patient and these interventions may also be combined with pharmacotherapy when needed.\textsuperscript{2,4,6-9}

**Pharmacotherapy for Insomnia**

Several different classes of agents may be used to treat insomnia (Table 1).\textsuperscript{2,7,10} FDA-approved options include benzodiazepines (estazolam, temazepam, and triazolam), benzodiazepine-receptor agonists (eszopiclone, zaleplon, zolpidem), melatonin-receptor agonists (ramelteon), and antidepressants (doxepin). Flurazepam and quazepam are long-acting benzodiazepines approved for treating insomnia but they are associated with daytime drowsiness, dizziness, and an increased risk of falls. Although chloral hydrate, various barbiturates, and meprobamate are also FDA-approved for insomnia, they are not recommended due to adverse effects, low therapeutic index, and risk of tolerance and dependence. Other sedating, low dose antidepressants like amitriptyline and trazodone are often used but do not have strong evidence supporting efficacy and are not FDA-approved for insomnia. Antipsychotics have limited evidence and also have the potential for serious side effects so they should be avoided. Nonprescription medications (e.g., first-generation antihistamines, antihistamine/analgesic combinations, melatonin,
valerian) are widely used by patients for insomnia. Existing data to support their use is not robust and antihistamines have side effects that may increase the risk of falls, particularly in older patients. Nonprescription medications containing diphenhydramine and other sedating antihistamines are associated with rapid tolerance to the sedative effects. They should be used very cautiously in elderly patients and avoided in children for the purpose of sedation.\textsuperscript{7,10,11} Their anticholinergic activity may result in additional adverse effects in those populations, such as mental clouding and confusion in the elderly or agitation and excitement in children.

Regardless of the agent selected, the intent of pharmacologic therapy is to reduce sleep latency and wakefulness after sleep onset, increase total sleep time, improve overall sleep quality, and ultimately enhance daytime functioning. None of the available agents induces rapid eye movement (REM) sleep. Benzodiazepines and benzodiazepine-receptor agonists are all controlled substances with the potential for tolerance, dependence, and abuse. Physical dependence with benzodiazepines may develop after just a few days of use and withdrawal symptoms may occur with abrupt discontinuation of the agent or rapid dose reduction. Short and intermediate-acting agents are associated with more rapid development of tolerance and are most likely to cause rebound worsening of insomnia symptoms and withdrawal when discontinued.\textsuperscript{2,7,10,12} Although the benzodiazepine-receptor agonists are thought to have better safety profiles than traditional benzodiazepines, there are reports of abuse and dependency with these agents. Benzodiazepine-receptor agonists have also been associated with unusual behaviors during sleep, such as sleep walking and sleep eating disorders, and may cause residual sedation similar to long-acting benzodiazepines.\textsuperscript{7,10}

The frequency and duration of pharmacologic treatment depend on the patient and clinician but data supports both nightly and intermittent dosing. Most initial trials are two to four weeks in duration with reassessment of insomnia symptoms. Evidence supporting treatment beyond six months is limited and agents that were FDA-approved before 2005 are only recommended for short-term use (30 days or less).\textsuperscript{2,7,10,12}

<table>
<thead>
<tr>
<th>Drug\textsuperscript{†}</th>
<th>Usual Dose</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>Benzodiazepines (Schedule IV Controlled Substances)</strong></td>
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<tr>
<td>Estazolam (ProSom\textsuperscript{®})\textsuperscript{*}</td>
<td>1-2mg at bedtime</td>
<td>Short- to intermediate-acting, for sleep maintenance insomnia</td>
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<tr>
<td>Temazepam (Restoril\textsuperscript{®})\textsuperscript{*}</td>
<td>15-30mg at bedtime</td>
<td>Short- to intermediate-acting, for sleep maintenance insomnia, reduce dose to 7.5mg in elderly and debilitated patients</td>
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<tr>
<td>Triazolam (Halcion\textsuperscript{®})\textsuperscript{*}</td>
<td>0.25-0.5mg at bedtime</td>
<td>Short-acting, for sleep onset insomnia, reduce dose to 0.125mg in elderly and debilitated patients</td>
</tr>
<tr>
<td><strong>Benzodiazepine-receptor Agonists (Schedule IV Controlled Substances)</strong></td>
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<tr>
<td>Eszopiclone (Lunesta\textsuperscript{®})\textsuperscript{***}</td>
<td>2-3mg at bedtime</td>
<td>Intermediate-acting, for sleep onset and maintenance insomnia, no short-term use restriction</td>
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<tr>
<td>Zaleplon (Sonata\textsuperscript{®})\textsuperscript{***}</td>
<td>10-20mg at bedtime</td>
<td>Short-acting, primarily for sleep onset insomnia but may be used for maintenance insomnia</td>
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<tr>
<td>Zolpidem (Ambien\textsuperscript{®})\textsuperscript{**}</td>
<td>10mg at bedtime</td>
<td>Short- to intermediate-acting, for sleep onset insomnia, reduce dose to 5mg in elderly and with hepatic impairment</td>
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<tr>
<td>Zolpidem controlled-release (Ambien CR\textsuperscript{®})\textsuperscript{**}</td>
<td>12.5mg at bedtime</td>
<td>Controlled-release, for sleep onset and maintenance insomnia, reduce dose to 6.25mg in elderly and with hepatic impairment</td>
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<tr>
<td><strong>Melatonin-receptor Agonists</strong></td>
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<tr>
<td>Ramelteon (Rozerem\textsuperscript{®})\textsuperscript{***}</td>
<td>8mg at bedtime</td>
<td>Short-acting, for sleep onset insomnia, no short-term use restriction</td>
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Various treatment options are available for patients with insomnia and practice guidelines do not recommend any single treatment option as superior. Treatment plans should always be tailored to the individual patient, as no approach is appropriate for everyone. Nonpharmacologic or cognitive behavioral therapies (CBT) are considered first-line options in most patients as there are few adverse effects associated with the various techniques and benefits may be sustained beyond the completion of therapy. CBT may also be used in combination with pharmacotherapy when indicated. Medications with the most evidence for benefit are benzodiazepines, benzodiazepine-receptor agonists, melatonin-receptor agonists, and several sedating antidepressants (not all FDA-approved). Selecting the optimal pharmacotherapy for each patient should be directed by patient-specific factors (e.g., insomnia symptom pattern, past treatment responses, comorbidities, treatment goals, patient preference) as well as medication-specific factors (e.g., duration of action, contraindications, adverse effects, cost).

Additional Resources
American Academy of Sleep Medicine - http://www.aasmnet.org/
National Sleep Foundation - http://www.sleepfoundation.org/

References

To report medical fraud, contact the Medicaid Quality Assurance Bureau at NM Medicaid Fraud @ state.nm.us or (505) 827-3100. We appreciate your continued support of our efforts to encourage quality care for our Medicaid clients.

Questions and/or comments about this newsletter may be directed to Diana Moya, R.Ph. at (505) 827-3174 or DianaJ.Moya@state.nm.us. DUR newsletters are posted on the New Mexico Human Services Department website: http://www.hsd.state.nm.us/providers/utilization-review.aspx.