Sleep Disorders

Sleep

Sleep is normally divided into two primary phases: rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep. Generally, individuals will cycle through three to five cycles of NREM and REM sleep in a single night.

REM sleep accounts for about one fourth of the total night’s sleep. The first REM period occurs about 80 to 120 minutes after the onset of sleep and lasts about 10 minutes. Later REM periods are longer (15 to 40 minutes) and occur mostly in the last several hours of sleep. The characteristics of REM sleep are shown in Table 1 and NREM sleep in Table 2. The different stages of sleep are shown in Table 3.

Age-related changes in regular sleep include a relative constant percent of REM sleep and a marked decrease in stage 3 and stage 4 sleep, there is an increase in wakeful periods during the night. These changes may be somewhat related to earlier bedtimes and daytime naps. In others, “jet lag” or idiosyncratic patterns, such as night owls, may develop different “biologic rhythms” by habitually going to bed late and sleeping late. Also there are those that work night hours and sleep during the day.

Sleep disorders generally include insomnia, snoring, narcolepsy, sleep apnea, and restless legs syndrome. A discussion on insomnia follows.

Insomnia

Prevalence

Insomnia is one of the most common patient complaints, ranking third behind headache and the common cold. It is the most prevalent of the sleep disorders and is defined by the National Heart, Lung, and Blood Institute as:
...the perception or complaint of inadequate or poor-quality sleep because of one or more of the following: difficulty falling asleep, waking up frequently during the night with difficulty returning to sleep, waking up too early in the morning, or undesirable snoring.

There are several categories of insomnia, including:

- **Transient.** Patients usually have no previous sleep complaints. Causes include acute stress, environmental disturbances, and time-zone changes. Usually lasts for only a few days and generally responds to non-pharmacologic treatment.

- **Short-term.** Lasts from about one to three weeks and usually is caused by more severe stressors, including loss of job, starting a new job, illness, death of a family member or friend, upcoming marriage/divorce, moving, financial difficulties, etc.

- **Long-term.** Lasts more than three weeks. May be caused by an underlying pathology, use/abuse of sedative, hypnotic or narcotics, illegal drugs, or alcohol. Undiagnosed pathology may include sleep-disordered breathing, narcolepsy, sleep apnea, obsessive pulmonary disease, need to urinate, restless legs syndrome, nocturnal myoclonus, cluster headache, Parkinson’s disease, pain from rheumatic disease, dental problems, angina, or peptic ulcer.

The prevalence of insomnia varies, but 10% to 40% of adults in the U.S. experience what they report as insomnia. Chronic insomnia is reported by about 10%. Patients complain of difficulty going to sleep, staying asleep, intermittent wakefulness, early morning waking, or any combination of these. The elderly may complain of insomnia because sleep becomes lighter and more easily disrupted with aging.

**Etiology**

Everyone has, at some time, been affected by insomnia. Insomnia can occur for a single night or may persist for several days, weeks, months, or years. An interesting characteristic is that it occurs with equal frequency in both genders until the mid-40s and then becomes more frequent in females. Age is associated with insomnia possibly due to greater medication use, circadian rhythm changes, and psychosocial and psychiatric factors.

Medications such as propranolol, antihypertensives, oral contraceptives, methyldopa, theophylline, thyroid supplements, corticosteroids, bronchodilators, anxiolytics, or antidepressants, and fluoxetine can cause insomnia. Also, the use of homeopathic remedies, some antiarthametics, and antihistamines can cause insomnia. A major cause of insomnia is caffeine, nicotine, and alcohol.

**Treatment (Non-pharmacological)**

Generally, there are a number of behavioral and social measures that can be tried prior to beginning therapy with medications, either without prescription or prescription. This may depend upon the severity and duration of insomnia and is a decision for the physician to make. Table 4 lists a number of non-pharmacologic measures that may help a patient to sleep.

**Treatment (Pharmacological)**

Table 5 lists a number of agents that have been used in the treatment of insomnia, along with doses and some pharmacokinetic data that may be of assistance. Alternative therapies include melatonin, Valerian, chamomile, hops, passion flower, skullcap, and germanium, with unknown safety and effectiveness.

Included in a list of compounded formulas that are not commercially available which have been used; various combinations can also be prepared. Ibuprofen, aspirin, acetaminophen, and other analgesics are sometimes combined with some of the agents listed in Table 5. Almost any dosage form can be prepared, including capsules, liquids, transdermal, injections, chewable troches, and others; please check with your compounding pharmacist for options for specific patients.

**TABLE 4: Non-pharmacological Measures that May Aid in Insomnia.**

- Drink a hot milk beverage at bedtime.
- Participate in stimulating activities during the daytime.
- Arise at a specific early hour each morning.
- Eliminate or decrease consumption of caffeine or alcohol containing beverages in the evening.
- Avoid heavy meals several hours before bedtime.
- Avoid naps during the day.
- Perform light exercise, such as leisurely walking, before bedtime.
- Designate a specific time for sleep.
- Relax by engaging in activities such as reading, watching television, or listening to relaxing music.
- Minimize external stimuli that might disturb sleep (e.g., light, noise).
- Limit excessive fluids in the evening.

**TABLE 5: Pharmacological Agents Used in the Treatment of Insomnia.**

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>BRAND</th>
<th>USUAL DOSE</th>
<th>ONSET</th>
<th>HALF-LIFE</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphenhydramine hydrochloride</td>
<td>Benadryl</td>
<td>25-50 mg</td>
<td>1-3 h</td>
<td>2-8 h</td>
<td>4-7 h</td>
</tr>
<tr>
<td>Diallylamine succinate</td>
<td>Decadryl</td>
<td>25 mg</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Dimeve</td>
<td>15 mg</td>
<td>11-20 h</td>
<td>74-90 h</td>
<td>7-8 h</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>Vistaril</td>
<td>25 mg</td>
<td>11-30 h</td>
<td>5-7 h</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Ativan</td>
<td>0.5 mg</td>
<td>16-60 h</td>
<td>15 h</td>
<td>6-8 h</td>
</tr>
<tr>
<td>Promethazine hydrochloride</td>
<td>Phenergan</td>
<td>25 mg</td>
<td>NA</td>
<td>9-16 h</td>
<td>2-6 h</td>
</tr>
<tr>
<td>Pyrimidine malate</td>
<td>NA</td>
<td>25 mg</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Sopor</td>
<td>75-150 mg</td>
<td>1-3 h</td>
<td>12-12 h</td>
<td>NA</td>
</tr>
<tr>
<td>Triazolam</td>
<td>NA</td>
<td>25-100 mg</td>
<td>1-3 h</td>
<td>7-8 h</td>
<td>NA</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Ambien</td>
<td>5-10 mg</td>
<td>10 h</td>
<td>1-7 h</td>
<td>6-7 h</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Ambien</td>
<td>5-10 mg</td>
<td>10 h</td>
<td>1-7 h</td>
<td>6-7 h</td>
</tr>
</tbody>
</table>

h = hours; m = minutes; NA = not applicable

**COMPONDFORMULAS**

- Diphenhydramine 25-mg Chewable Troches/Lozenges
- Diphenhydramine 25-mg and Ibuprofen 400-mg Capsules
- Diallylamine Succinate 25-mg Capsules
- Diallylamine Succinate 25-mg and Ibuprofen 400-mg Capsules
- Hydroxyzine Hydrochloride 25-mg Chewable Troches/Lozenges
- Lorazepam 2-mg/mL Oral Solution
- Lorazepam 2-mg/mL Nonaqueous Solution
- Lorazepam 1-mg or 2-mg Chewable Gummies
- Promethazine Hydrochloride 12.5-mg Chewable Gummies
- Promethazine Hydrochloride 25-mg Chewable Gummies
- Promethazine 12.5-mg/0.1-mL Transdermal Gel
- Tranxodone 15-, 50-, or 100-mg Capsules

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