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optimizing self-treatment of occasional sleep disturbances/sleeplessness introduction

Throughout recorded history, philosophers, poets and scientists around the world have mused over the origins of sleep and its importance to physical and mental health.¹ Indeed, people have pursued remedies to manage sleep for as long as sleep has been recognized as a priority for humans. As far back as 2800 B.C., the Chinese used ginseng root for its sedative properties, while the ancient Greeks used remedies made from geese and snakes, as well as opiates from poppies for sleep therapy.¹

Despite the long history of interest in sleep, the science of sleep, sleep disorders and their treatment is relatively recent, prompted in the 1950s with the discovery of rapid eye movement and the stages of sleep.² Today, the search for a good night's sleep continues, with an estimated 50 to 70 million Americans not having satisfactory sleep,² and more than one-quarter of Americans reporting not getting enough sleep occasionally.³ In a recent poll by the National Sleep Foundation (NSF), 87% of respondents reported having at least one of the following sleep problems at least a few nights/days a week: difficulty falling asleep, waking up in the middle of the night, waking up too early or waking up feeling un-refreshed.⁴ More than six in 10 said they woke up during the night (64%) and/or woke up feeling un-refreshed (61%) at least a few nights/days a week.⁴ Given this broad impact of sleep disturbances, it is important that pharmacists appreciate the impact of occasional disturbance/sleeplessness and understand the role of sleep hygiene and over-the-counter (OTC) medications for the management of this common problem.

The insights of Thomas Roth, Ph.D., are featured in this publication. Dr. Roth is a Professor of Psychiatry at Wayne State University School of Medicine in Detroit, Michigan, and Clinical Professor of Psychiatry at the University of Michigan College of Medicine in Ann Arbor. Dr. Roth also currently serves as the Director of the Sleep Disorders and Research Center at the Henry Ford Hospital in Detroit. Dr. Roth has been Chairman of the National Center on Sleep Disorders Research advisory board for the National Institutes of Health and the World Health Organization's worldwide project on sleep and health. His research focuses on normal and pathological sleep processes, and he has published extensively in this area.

the importance of getting adequate sleep

Sleep is a vital physiological function that is essential to well-being. Sleep provides an opportunity for the brain to process information by creating new learning and memory pathways in the brain. Sleep also regulates the release of certain hormones which control metabolism and other vital physiological functions.⁵

The impact of short-term, acute sleep loss varies from person to person and depends on a number of factors, including sleep and circadian influences (amount and distribution of prior sleep, length of time awake, circadian time); arousal system influences (e.g., being active, exposure to bright light, noise); individual characteristics (age, individual sensitivity); and how the impact is measured (e.g., length of the test, difficulty and complexity of the test, etc.).⁶ Commenting on this, Dr. Roth explained that the impact of sleep loss is influenced significantly by "the nature of the task—that is, if the person is trying to do something complicated as opposed to something simpler, like watching TV."

Occasional lack of adequate sleep may affect next day behavior and performance including sleepiness, alertness, short-term memory/cognitive function, mood and ability to concentrate.⁶ Mood changes such as

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“Sleep and rest are not one and the same. Sleep is a biological necessity. All animals sleep. Sleep is a biological imperative, so you will always make up sleep. The question is when that happens—when driving a car, when you’re in bed. Your body has to make up sleep.”
- Dr. Thomas Roth

irritability and difficulty controlling emotions are commonly reported with lack of sleep, and are among the earliest indicators of sleep loss.^{5,6} In one study, a modest daily restriction of sleep by two hours per night for one week was associated with significant increase in sleepiness and a reduction in psychomotor performance.⁷ In another study, one night of total sleep deprivation resulted in lowered waking activity in parts of the brain associated with alertness, attention, and higher order cognitive processes.⁸ Importantly, Dr. Roth noted, the changes observed with acute sleep loss “accumulate across time.”

the causes of insomnia and occasional sleeplessness

Insomnia, the most common sleep disorder, is defined as difficulty falling or staying asleep, or as having nonrestorative, poor quality sleep despite adequate opportunity and circumstance to sleep.^{2,5,9} Insomnia is associated with daytime consequences as well, including fatigue, decreased alertness, emotional changes and reduced performance.² Although insomnia can be primary (i.e., existing in isolation), most cases of insomnia occur with another medical or psychiatric condition,¹⁰ sleep circadian rhythm disorders or as a result of medications.⁵ Dr. Roth emphasized that “insomnia is comorbid about 85% to 90% of the time.” The most common comorbidity in insomnia is major depression, occurring in up to 20% of patients diagnosed with insomnia.² In fact, as Dr. Roth noted, “insomnia is the biggest risk factor for depression that there is. Many studies have demonstrated that patients with insomnia up to a five-fold risk of developing depression.”¹¹

In contrast to chronic insomnia (which occurs more than three times per week and persists for more than 30 days), many adults experience occasional sleep disturbances, which may be referred to as short-term insomnia, adjustment insomnia, stress-related insomnia, or transient psychophysiological insomnia.¹² Short periods of difficulty falling or staying asleep are somewhat common and do not necessarily occur hand-in-hand with a major medical condition.^{5,9} Stressful life experiences (e.g., job loss, death of a family member) or normal life transitions (e.g., anticipation of weddings, holidays) can disturb sleep and make it difficult to fall asleep or remain asleep.⁹ Other common life circumstances that can disturb sleep include jet lag (i.e., traveling across time zones), shift work, or other major schedule changes.⁹ Indeed, several days may be required for the body’s circadian rhythms to adjust to a new time zone.¹³

“The prevalence of insomnia in the U.S. is 10% to 25%. In contrast, occasional sleep difficulties occur in nearly everyone at some point in their lives. Chronic insomnia; is typically associated with other medical conditions, a comorbid medical or psychiatric disorder, while acute sleep disturbances/sleeplessness are more commonly associated with stress and acute events (jet lag, stress, etc.). But both transient sleep disturbances and chronic insomnia have significant morbidity associated with them.”
- Dr. Thomas Roth

management of occasional sleep difficulty/sleeplessness

Sleep hygiene is defined as various practices that are necessary to have normal, quality nighttime sleep and full daytime alertness.¹⁴ Establishing good sleep hygiene, as noted in the healthy tips, is essential to managing occasional sleep disturbances. Simple adjustment of the routines and rituals around sleep can have an impact on a person’s ability to fall asleep and get a full night’s rest. The NSF’s recommendations for healthy sleep are summarized in **Table 1**.¹⁵

Table 1.

National Sleep Foundation Healthy Sleep Tips¹⁵

- 1. Maintain a regular bed and wake time schedule including weekends.** Our sleep-wake cycle is regulated by a “circadian clock” in our brain and the body’s need to balance both sleep time and wake time. A regular waking time in the morning strengthens the circadian function and can help with sleep onset at night. That is also why it is important to keep a regular bedtime and wake time, even on the weekends when there is the temptation to sleep-in.
- 2. Establish a regular, relaxing bedtime routine such as soaking in a hot bath or hot tub and then reading a book or listening to soothing music.** A relaxing, routine activity right before bedtime conducted away from bright lights helps separate your sleep time from activities that can cause excitement, stress or anxiety which can make it more difficult to fall asleep, get sound and deep sleep or remain asleep. Avoid arousing activities before bedtime like working, paying bills, engaging in competitive games or family problem-solving. Some studies suggest that soaking in hot water (such as a hot tub or bath) before retiring to bed can ease the transition into deeper sleep, but it should be done early enough that you are no longer sweating or over-heated. If you are unable to avoid tension and stress, it may be helpful to learn relaxation therapy from a trained professional. Finally, avoid exposure to bright light before bedtime because it signals the neurons that help control the sleep-wake cycle that it is time to awaken, not to sleep.
- 3. Create a sleep-conducive environment that is dark, quiet, comfortable and cool.** Design your sleep environment to establish the conditions you need for sleep—cool, quiet, dark, comfortable and free of interruptions. Also make your bedroom reflective of the value you place on sleep. Check your room for noise or other distractions, including a bed partner’s sleep disruptions such as snoring, light and a dry or hot environment. Consider using blackout curtains, eye shades, ear plugs, “white noise,” humidifiers, fans and other devices.
- 4. Sleep on a comfortable mattress and pillows.** Make sure your mattress is comfortable and supportive. The one you have been using for years may have exceeded its life expectancy—about nine or 10 years for most good quality mattresses. Have comfortable pillows and make the room attractive and inviting for sleep but also free of allergens that might affect you and objects that might cause you to slip or fall if you have to get up during the night.
- 5. Use your bedroom only for sleep and sex.** It is best to take work materials, computers and televisions out of the sleeping environment. Use your bed only for sleep and sex to strengthen the association between bed and sleep. If you associate a particular activity or item with anxiety about sleeping, omit it from your bedtime routine. For example, if looking at a bedroom clock makes you anxious about how much time you have before you must get up, move the clock out of sight. Do not engage in activities that cause you anxiety and prevent you from sleeping.

6. Finish eating at least two to three hours before your regular bedtime.

Eating or drinking too much may make you less comfortable when settling down for bed. It is best to avoid a heavy meal too close to bedtime. Also, spicy foods may cause heartburn, which leads to difficulty falling asleep and discomfort during the night. Try to restrict fluids close to bedtime to prevent nighttime awakenings to go to the bathroom, though some people find milk or herbal, non-caffeinated teas to be soothing and a helpful part of a bedtime routine.

7. Exercise regularly. It is best to complete your workout at least a few hours before bedtime.

In general, exercising regularly makes it easier to fall asleep and contributes to sounder sleep. However, exercising sporadically or right before going to bed will make falling asleep more difficult. In addition to making us more alert, our body temperature rises during exercise, and takes as much as six hours to begin to drop. A cooler body temperature is associated with sleep onset. Finish your exercise at least three hours before bedtime. Late afternoon exercise is the perfect way to help you fall asleep at night.

8. Avoid caffeine close to bedtime. It can keep you awake.

Caffeine is a stimulant, which means it can produce an alerting effect. Caffeine products, such as coffee, tea, colas and chocolate, remain in the body on average from three to five hours, but they can affect some people up to 12 hours later. Even if you do not think caffeine affects you, it may be disrupting and changing the quality of your sleep. Avoiding caffeine within six to eight hours of going to bed can help improve sleep quality.

9. Avoid nicotine (e.g., cigarettes, tobacco products). Used close to bedtime, it can lead to poor sleep.

Nicotine is also a stimulant. Smoking before bed makes it more difficult to fall asleep. When smokers go to sleep, they experience withdrawal symptoms from nicotine, which also cause sleep problems. Nicotine can cause difficulty falling asleep, problems waking in the morning, and may also cause nightmares. Difficulty sleeping is just one more reason to quit smoking. And never smoke in bed or when sleepy!

10. Avoid alcohol close to bedtime.

Although many people think of alcohol as a sedative, it actually disrupts sleep, causing nighttime awakenings. Consuming alcohol leads to a night of less restful sleep.

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In addition to lifestyle changes and behavioral approaches, a number of OTC and prescription medications are available to treat occasional sleeplessness. All OTC sleep medications contain diphenhydramine or doxylamine (**Table 2**), which are the only two Food and Drug Administration (FDA)-approved OTC medications indicated for difficulty falling asleep. Originally approved as a prescription antihistamine in 1946, diphenhydramine was subsequently approved in 1982 for OTC use to treat occasional sleeplessness.^{16,17} Diphenhydramine demonstrated efficacy for this indication in two well-controlled studies nearly three decades ago,^{19,20} and remains the most extensively studied OTC sleep aid.

In addition to single active ingredient products, a number of combination products contain a pain reliever, such as acetaminophen or ibuprofen, and a sleep-aid (**Table 2**).²³⁻²⁵ These products are indicated for the relief of occasional sleeplessness accompanied by minor aches and pains. While these products may be useful for patients who have sleep difficulty and pain, Dr. Roth notes that persons “who only have difficulty sleeping do not need a combination product.” Natural sleep supplements, such as chamomile, valerian or natural melatonin are also available in the supplement portion of the sleep-aid aisle. However, these products have not been evaluated rigorously and are not regulated by the FDA.²¹

“Diphenhydramine and doxylamine are the only two OTC drugs approved for occasional sleeplessness. They should only be used occasionally, not every night. People whose problem lasts for more than two weeks should be referred to a physician for further evaluation.” - Dr. Thomas Roth

Table 2. OTC Medications For Occasional Sleeplessness

| Medication | Use | Dosage |
|--|--|--|
| Diphenhydramine hydrochloride (HCl) or citrate ¹⁸ | For relief of occasional sleeplessness | Adults and children 12 years and older: Take diphenhydramine HCl 50 mg by mouth at bedtime as needed. Take diphenhydramine citrate 76 mg by mouth at bedtime as needed. |
| Doxylamine succinate ²² | Helps to reduce difficulty in falling asleep | Adults and children 12 years and older: Take 25 mg before bedtime; do not exceed 25 mg each day. |
| Diphenhydramine citrate or HCl & ibuprofen ^{23,24} | For relief of occasional sleeplessness when associated with minor aches and pains | Adults and children 12 years and over: Take 76 mg diphenhydramine citrate/400 mg ibuprofen at bedtime. Do not take more than 76 mg diphenhydramine citrate/400 mg ibuprofen in 24 hours. Adults and children 12 years and over: Take 50 mg diphenhydramine HCl/400 mg ibuprofen at bedtime. Do not take more than 50 mg diphenhydramine HCl/400 mg ibuprofen in 24 hours. |
| Diphenhydramine HCl & acetaminophen ²⁵ | Temporary relief of occasional headaches and minor aches and pains with accompanying sleeplessness | Adults and children 12 years and over: Take 50 mg diphenhydramine HCl/1,000 mg acetaminophen at bedtime. Do not take more than 50 mg diphenhydramine HCl/1,000 mg of this product in 24 hours. |

Pharmacists are encouraged to counsel patients on several key points regarding the appropriate use of OTC sleep-aids. Patients should be aware that the approved dose of diphenhydramine HCl as a sleep-aid is 50 mg at bedtime (not to exceed 50 mg in 24 hours),^{17,18} which is twice the dose indicated to treat allergies (i.e., 25 mg every four to six hours). In order to have access to proper directions and labeling, patients may be directed to diphenhydramine products that are marketed as sleep-aids rather than for allergy management. Patients who prefer products that do not require water for administration may be directed to sleep-aids that are available in liquid formulations in addition to tablets or capsules. The use of other drugs containing diphenhydramine or other antihistamines should be discouraged while using OTC sleep-aids,¹⁸ and patients taking combination pain relief/sleep-aid products should be aware that the product may contain acetaminophen or ibuprofen. Finally, patients whose sleeplessness persists continuously for more than two weeks should be referred for medical evaluation.¹⁸

conclusions

Despite the vital role sleep plays in our physical and mental health, one in four Americans suffer from occasional sleep disturbances/sleeplessness. Establishing good sleep hygiene practices is essential for improving sleep. In addition, a number of OTC medications are

available to treat occasional sleeplessness. Pharmacists can help patients optimize self-management of occasional sleeplessness by providing recommendations for good sleep hygiene and guiding appropriate product selection and use of OTC sleep-aids.

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