Insomnia: Epidemiology, Characteristics, and Consequences

Thomas Roth, PhD

Chief, Division of Sleep Medicine
Sleep Disorders and Research Center
Henry Ford Hospital
Detroit, Michigan

Timothy Roehrs, PhD

Director of Research
Sleep Disorders and Research Center
Henry Ford Hospital
Detroit, Michigan

Insomnia is a symptom of difficulty initiating and maintaining sleep or experiencing nonrefreshing sleep and is associated with daytime consequences. Although insomnia is typically secondary to a medical, psychiatric, circadian, or sleep disorder, it can also be a primary disorder. Primary insomnia is estimated to occur in 25% of all chronic insomnia patients. It is hypothesized to be a disorder of hyperarousal, which has been supported by research on the autonomic nervous system and hypothalamic-pituitary-adrenal axis function. Chronic insomnia is prevalent in 10% of the adult population. Age, sex, medical and psychiatric disease, and shift work all represent an increased risk of chronic insomnia. The morbidity of insomnia varies as a function of etiology. While transient insomnia produces sleepiness and impairment in psychomotor performance, chronic insomnia is associated with absenteeism, frequent accidents, memory impairment, and greater health care utilization. The most consistent impact of insomnia is a high risk of depression.
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Several characteristics make insomnia unique in medicine. One such characteristic is that insomnia is both a symptom and a disorder. The *International Classification of Sleep Disorders* and the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (1,2) define insomnia as a symptom complex consisting of difficulty falling asleep, or staying asleep, or nonrefreshing sleep, in combination with some form of daytime sequelae. This symptom complex can be secondary to another condition or it can be an independent disorder (ie, primary insomnia). The high prevalence of comorbidities associated with chronic insomnia attests to the fact that it is typically a condition that is secondary to other disorders (3). Most commonly, secondary insomnia is associated with psychiatric disorders, especially affective disorders (4). The special relationship between insomnia and depression has recently received significant research attention.

Insomnia is also frequently associated with medical disorders, especially those producing pain or dyspnea (5,6). Some drugs used to treat medical and psychiatric disorders cause insomnia (7). Drug treatment has recently become more of an issue in psychiatric conditions because, unlike in the past when most psychotherapeutic agents were sedating, current medications are minimally sedating and in some cases alerting (8). Insomnia can also be associated with behavioral disorders (9), including a state termed *conditioned insomnia*, as well as with poor sleep habits. These conditions are especially

responsive to behavioral treatment. Finally, insomnia can be associated with circadian rhythm disorders or primary sleep disorders. Among the most common circadian rhythm disorders leading to insomnia are shift-work sleep disorders and the phase advance syndrome seen in the elderly. Multiple primary sleep disorders, such as restless legs syndrome (RLS), periodic limb movement disorder (PLMD), and sleep-related breathing disorder, also produce insomnia. Among the primary sleep disorders is primary insomnia, which consists of the insomnia symptoms discussed above but not associated with any other disorder. In clinical practice, primary insomnia is typically a diagnosis of exclusion, and both electroencephalographic and endocrine function signs are associated with it (10, 11). Although the prevalence of primary insomnia is not currently well defined, one study found it to be present in 25% of patients with chronic insomnia at a sleep clinic (12).

KEY POINT

One of the goals of treating transient insomnia is to prevent the evolution to chronic insomnia. The other is to reverse sleep disruption to prevent the accompanying deterioration of daytime performance.

DIMENSIONS OF INSOMNIA

Although experts distinguish between transient and chronic insomnia, they disagree about the specific time requirement. Transient insomnia is defined as sleep problems that last days to weeks; chronic insomnia lasts from months to years. Transient and chronic insomnia differ in terms of consequence etiology and overall therapeutic approach. The consequences of transient insomnia parallel those of sleep deprivation (ie, sleepiness and associated performance decrements). In contrast, the morbidity of chronic insomnia is broader and varies as a function of diagnostic category. Unlike chronic insomnia, which is a primary disorder or secondary to another disorder, transient insomnia can be caused not only by another disorder, but also by changes in the sleep environment, the timing of sleep, and acute stress. Interestingly, data exist to support the notion of individual differences in the vulnerability to transient insomnia (13,14)—that the sleep of some individuals is disturbed when exposed to certain factors, while in others it is not. Further, it is hypothesized that chronic insomnia can evolve from bouts of transient insomnia. One of the goals of treating transient insomnia is to prevent this evolution to chronic insomnia. The other is to reverse the sleep disruption and thereby prevent the accompanying deterioration of daytime performance (15).

Another important dimension of insomnia is the nature of the sleep symptom. As previously mentioned, insomnia is defined as difficulty with sleep initiation, sleep maintenance, or sleep quality. While it is important to recognize that in most patients these symptoms coexist or vary across time, for some individuals they are specific and can be of use in the diagnostic process. The clearest example of this would be insomnia in association with circadian rhythm disorders. Individuals who exclusively have sleep onset problems typically have a phase delay, while individuals who exclusively have sleep offset problems (ie, early morning awakenings) typically have a phase advance.

Another critical dimension is the characteristic of the sleep disturbance. Individuals with prolonged periods of wakefulness before, after, or during sleep are likely to have a behavioral, psychiatric, or circadian disorder. In contrast, patients whose symptoms are primarily frequent, brief nocturnal awakenings, sleep fragmentation, or nonrefreshing sleep are more likely to be suffering from a medical or primary sleep disorder.

The severity of insomnia is a primary consideration in developing a treatment plan; however, determining severity is difficult. The most obvious consideration is the magnitude and frequency of the sleep problem. While important, it should be kept in mind that insomniacs are not good at estimating the magnitude of their sleep problems, and there are considerable individual differences in this ability. Another factor in assessing severity is the extent of daytime consequences. Unfortunately, it

is often difficult to determine to what degree sleep disturbance caused the daytime problem and to what degree the daytime behavior caused the sleep disturbance. For example, an elderly patient reports that his sleep is highly disturbed and as a result finds himself having to take multiple naps. Are the naps causing the insomnia, is the insomnia causing the daytime napping, or is it both? Similarly in an individual with insomnia who reports that his sleep problem makes him depressed, the question is, what is cause and what is effect? These issues clearly demonstrate the need for a rather extensive sleep—and often medical and psychiatric—history in patients with chronic insomnia.

The final dimension of insomnia is its diagnosis. As mentioned, 6 major diagnostic categories have been established for chronic insomnia: medical, psychiatric, circadian, behavioral, pharmacologic, and primary sleep disorder. The prevalence of each relative to the overall prevalence of insomnia is not well understood. Several studies have attempted to define their relative prevalence (12,16); however, these were clinic-based samples and do not represent the true prevalence in the general population. Also, the relative prevalence varies as a function of population (17). Thus, for example, phase advance is more common in the elderly, while phase delay is more common in adolescents. Similarly, the elderly are more vulnerable to movement disorders (eg, RLS, Parkinson's) but not psychiatric disorders. Clearly, population-based research is needed on the relative prevalence of insomnia disorders and their associated risk factors in the general population.

KEY POINT

Results of the multitude of studies documenting the prevalence of insomnia indicate that clear risk factors exist for chronic insomnia. The factors most commonly identified are age, gender, medical disease, psychiatric disease, and shift work.

EPIDEMIOLOGY OF INSOMNIA

While a multitude of studies have documented the prevalence of insomnia, the results vary dramatically as a function of the definition of insomnia and the population examined. Some conclusions can be derived from the literature despite the variability in approaches to this question. Although they employed different survey techniques, populations, and questions, all of the major studies estimate that chronic insomnia occurs in about 10% of the adult population (**Figure**) (18–21). The prevalence of occasional or transient insomnia is higher than chronic insomnia, but prevalence is variable from study to study. This variability reflects 2 factors: (a) the prevalence of transient insomnia is impacted more by the study criteria used to define it; and (b) the prevalence of transient insomnia is more variable from population to population and from time to time. Thus, for example, studies done after a catastrophic event (September 11, a hurricane) show higher prevalences than those conducted at other times (22). A final conclusion that can be derived from these studies is that clear risk factors exist for chronic insomnia. The factors most commonly identified are age, gender, medical disease, psychiatric disease, and shift work. We may understand the mechanisms for the higher risk associated with some of these variables, but we are less certain about others. The greater risk observed in the elderly can be traced to changes in sleep processes, circadian factors, and an increased incidence of medical disease. However, the higher prevalence of insomnia seen in women (especially the elderly) is not well understood. Similarly, the increased risk associated with medical disorders is better understood than that associated with psychiatric disorders.

A final issue in the epidemiology of insomnia is its chronicity. While few studies address this issue, the research that has been conducted shows insomnia to be a long-term problem with little spontaneous remission. Katz and McHorney (23) found that among individuals with severe insomnia, 85% continued to report that their insomnia was of moderate or severe intensity in a 2-year follow-up. The unremitting nature of insomnia has significant implications for its treatment. The notion that sleep-promoting agents should be used only on a

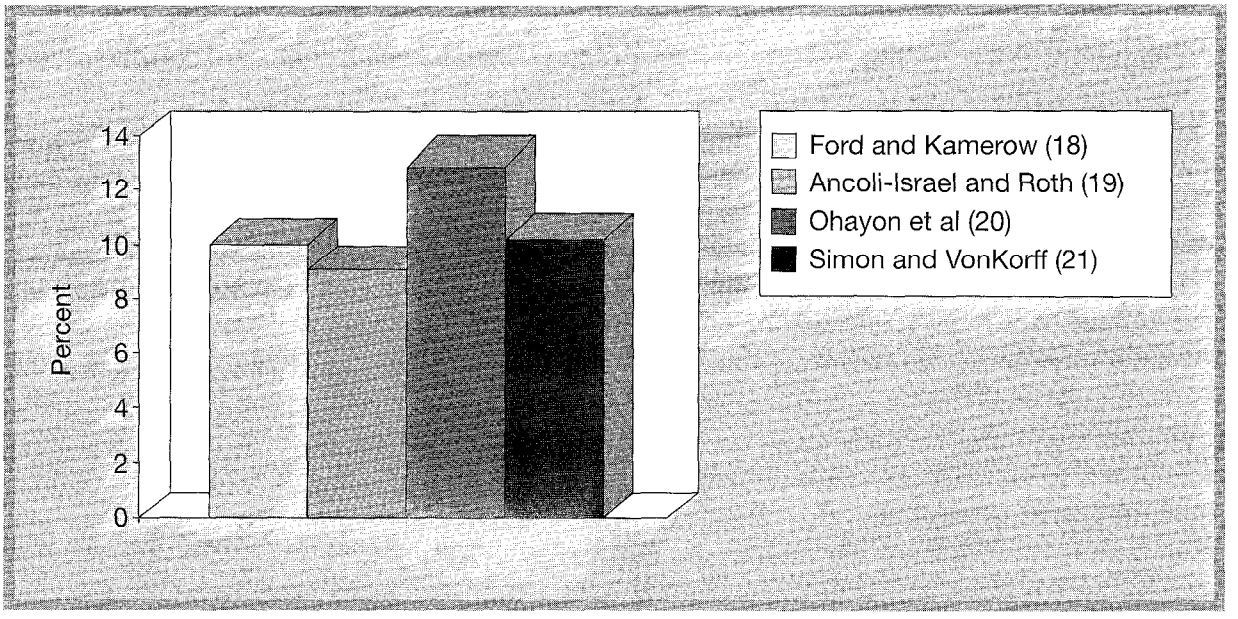

Figure. *Prevalence of insomnia. These major studies estimate that chronic insomnia occurs in about 10% of the adult population.*

short-term basis is at odds with the chronic nature of insomnia. In fact, the data on the use of hypnotics suggest that therapy for chronic insomnia is increasing. The chronic nature of insomnia calls for more information about both its natural course and efficacy of long-term therapies.

KEY POINT

The notion that sleep-promoting agents should be used only on a short-term basis is at odds with the chronic nature of insomnia. Data on the use of hypnotics suggest that therapy for chronic insomnia is increasing.

CONSEQUENCES OF INSOMNIA

One facet of insomnia that has been neglected over the years is its consequences. While we have expanded our knowledge of sleep loss and sleep fragmentation in normal volunteers (24–26), we know less about their consequences in the context of an insomnia complaint. Experimental studies of total and partial sleep deprivation as well as sleep fragmentation consistently show an increase in sleepiness and impairments on measures of psychomotor function. The effect of sleep loss on daytime sleepiness has been demonstrated using objective measures (the Multiple Sleep Latency Test), as well as on a number of sleepiness and mood scales (27). This effect on sleepiness is linear, at least over 1 night of sleep deprivation, and its impact accumulates across days. Similarly, performance on a variety of psychomotor tests (eg, reaction time, vigilance, divided attention) has been shown to deteriorate as a function of degree of sleep deprivation and sleep fragmentation. While sleep loss seems to affect multiple aspects of human performance, it exerts its greatest effect on the ability to sustain attention. Thus the most frequently reported performance effects are an increase in lapses. A lapse is a period of nonresponsivity on the part of the subject and is believed to be a manifestation of a microsleep. These impairments have certainly been described as a consequence of transient insomnia and some of its subtypes. In other words, transient insomnia essentially is a special case of sleep deprivation and shows the expected daytime consequences.

Chronic insomnia is more complex. Some of the causes of chronic insomnia produce daytime sleepiness and impaired psychomotor performance while others do not. Among the secondary insom-

nias, rheumatoid arthritis has been shown to produce sleep fragmentation and a subsequent increase in fatigue, but not in objectively measured daytime sleepiness (28). While not investigated systematically, increased fatigue/daytime sleepiness has been reported to be present in other medical causes of sleep-disruption insomnia. Among the primary sleep disorders, PLMD and sleep-related breathing disorders have been shown to produce increased objective daytime sleepiness (29). On the other hand, chronic insomnia patients do not exhibit more daytime sleepiness. In fact, studies have shown that individuals with chronic insomnia are significantly more alert, as evident in a higher mean latency on the Multiple Sleep Latency Test, than controls without insomnia (30). This greater alertness despite decreased sleep times (ie, sleep loss) has lent support to the hypothesis that insomnia is a disorder of hyperarousal (31,32). Studies of both the autonomic nervous system as well as the hypothalamic-pituitary-adrenal (HPA) axis have shown increased arousal in insomniacs. For example, Vgontzas et al (32) reported a significant correlation between the degree of sleep difficulty and hypersecretion of cortisol. Thus, a commonly held view of chronic insomnia is that the underlying pathophysiology in many chronic insomnia patients is an abnormality in the HPA axis. (33). The issue then is whether in the absence of sleepiness there is any morbidity associated with insomnia.

KEY POINT

The most common comorbidity of insomnia is psychiatric disorders; among these, depression is the most common finding for insomniacs.

Increasingly, research on the consequences of insomnia has focused on morbidities that are not mediated by increased sleepiness. Patients with insomnia have been shown to have higher rates of absenteeism, increased rates of accidents, decreased productivity, decreased quality of life, and impaired memory function (21,34,35). Only some studies have controlled for age, sex, and medical and psychiatric comorbidities; another important consideration is that all of these studies were cross-sectional. Thus it is difficult to determine when in the evolution of chronic insomnia these effects manifest themselves. Further research is needed to determine the direct contribution of insomnia to these comorbidities, to what extent these effects can be attributed to insomnia, and whether treating insomnia reverses these morbidities. Given the consequences, it is not surprising that insomnia leads to increased health care utilization—an increase that is present even after controlling for age, sex, and medical and psychiatric disease.

The most common comorbidity of insomnia is psychiatric disorders; among these, depression is the most common finding for insomniacs. Population as well as clinic-based studies have demonstrated a high rate of psychiatric comorbidities in patients with chronic insomnia. The prevalence of psychiatric diagnoses is about 40% to 50% (36–38) and anxiety or an affective disorder is most frequently found. It has traditionally been assumed that insomnia is secondary to the psychiatric disorder; however, given the chronicity of insomnia, it is possible that in some cases the insomnia preceded the psychiatric disorder. In fact, it is possible that insomnia represents a significant risk for the development of a subsequent psychiatric disorder. In a large-scale European population-based study, it was found that insomnia more often precedes rather than follows incident cases of a mood disorder (39). This effect is even more pronounced for relapses of the mood disorder. In contrast, in chronic insomnia patients with a comorbid anxiety disorder, the first occurrence of anxiety or a relapse precedes insomnia in most instances (**Table**). To further understand the relation of sleep and psychiatric disorders, several longitudinal studies have examined the evolution of psychiatric disorders among insomnia patients. These studies have used follow-up periods from 1 to 40 years, with the majority using a 1- to 3-year follow-up period. In all these studies, insomnia was found to be a substantial risk for the development of a depressive disorder (40,41). Typically the relative risk was about 5 (range 2–40) and in all cases it was

TABLE. INSOMNIA AS A POSSIBLE PREDICTOR OF MOOD DISORDER AND RELAPSE

	Mood Disorder		*Anxiety Disorder*	
	First Episode (%)	*Relapse (%)*	*First Episode (%)*	*Relapse (%)*
Insomnia appears before	41.0	56.2	18.0	23.2
Insomnia appears at same time	29.4	22.1	38.6	42.5
Insomnia appears after	28.9	21.6	43.5	34.3

statistically significant. While some studies also reported an increased risk for anxiety or drug abuse, neither of these were consistently found. Finally, longitudinal studies in subjects with affective disorders show that among depressed patients, those whose sleep improves show a more rapid antidepressant response and those whose insomnia persists have a shorter time to relapse (42,43). What is clearly needed are clinical trials to assess the impact of insomnia therapy on incidence of depression as well as the time to relapse in depressed patients who are in remission.

The question then arises as to whether insomnia causes depression, vice versa, or both. The most likely outcome is that insomnia and depression have a common pathology that makes the individual vulnerable to both conditions. As was previously noted, data have shown that both the diagnosis of insomnia and the severity of the sleep disturbance are related to the hypersecretion of cortisol. The overactivation of the HPA axis has also been reported in patients with depression. This abnormality might represent the common risk factor, and therefore it is quite possible that both disorders would respond to the same therapeutic intervention (eg, corticotropin-releasing hormone antagonists).

In managing chronic insomnia patients, it is important to understand the nature of the consequences of insomnia. The most common daytime complaint reported by insomnia patients is fatigue. Unfortunately, this term is employed in several different ways in the medical literature. Fatigue is often used synonymously with sleepiness. In the literature on hours of service and transportation, sleepiness and fatigue are used interchangeably. This type of fatigue is reversed by recovery sleep. A second use refers to muscular fatigue, for example, in certain medical and, especially, neurological disorders. This type of fatigue is reversed by extended rest (sleep is not necessary). The term fatigue is also used to reflect mental fatigue, which is the case with patients with affective disorders. This type of fatigue is not responsive to either sleep or rest. The challenge for the clinician dealing with insomnia is that all 3 types of fatigue can be, and often are, present in insomnia patients.

SUMMARY

Insomnia is a common problem with a prevalence of about 10%. It can occur as an independent disorder or secondary to other conditions. The most common comorbidity found among insomnia patients is a psychiatric disorder. Further research is needed to understand the evolution to chronic insomnia, the causes of which are not fully understood. In managing chronic insomnia patients, clinicians must understand the nature of the consequences of insomnia. Fatigue in various manifestations is the most common daytime complaint and presents the greatest challenge in treating insomnia patients.

Address correspondence to: Thomas Roth, PhD, Sleep Disorders and Research Center, Henry Ford Hospital, 2799 West Grand Blvd, CFP-3, Detroit, MI 48202. Phone: (313) 916-5171. Fax: (313) 916-5167. E-mail: troth1@hfhs.org.

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Dialogue Box

EDITORIAL BOARD

Please elaborate further on how transient insomnia differs from chronic insomnia.

ROTH

Transient insomnia is what most people have. It is basically involuntary sleep loss—like that experienced during the days when you were a house officer—and the consequence of it is sleepiness the next day and impairment of performance. People with chronic insomnia are not sleepy at all. In fact, if anything, they're superalert.

EDITORIAL BOARD

Is this superalertness a compensatory mechanism on their part to sleep deprivation?

ROTH

I certainly wouldn't view it as an adaptive phenomenon because it has negative consequences, including reduced productivity, impaired memory function, and mental fatigue. Moreover, it has been found that many of these patients have an overactivation of the HPA axis with hypersecretion of cortisol. This abnormality may very well be the basis for their 5- to 6-fold increased risk for developing depression.

EDITORIAL BOARD

So the HPA abnormalities precede the insomnia and not vice versa?

ROTH

That certainly seems to be the case. If I wake you up 22 times tonight, how are you going to feel tomorrow morning? You'd be drinking coffee and trying hard not to fall asleep. Conversely, if I were to wake up a patient with primary insomnia, that patient not only wouldn't get sleepy, he or she actually might become hyperaroused. The natural response to a sleep deficit is to compensate for it. Thus, if an apneic patient gets awakened every minute, that patient will get sleepy. If a house officer is on call all night, he or she becomes sleepy. On the other hand, primary insomnia patients, when they're up all night, hypersecrete cortisol and become more "wakeful."

Dialogue Box

EDITORIAL BOARD

Are those individuals who become hyperalert when sleep deprived born with this trait or do they develop the overactivation of the HPA axis in response to changes in their sleep environment?

ROTH

For all we know they're born that way. Recognize that most surgical residents completing a 5- or 6-year residency always exhibit the same response to sleep deprivation—that is, every time they stay up all night, they become sleepy. The rare house officer who seems to remain hyperalert despite only getting 3 hours of sleep very likely is selected from the 2% to 3% of the general population born with the central nervous system abnormalities seen in primary insomnia. These findings include not only HPA axis abnormalities but also certain electroencephalographic patterns as well as changes in the ventrolateral preoptic area.

EDITORIAL BOARD

Are these changes unique to the patient with chronic insomnia?

ROTH

No, they're also seen in patients with depression.

EDITORIAL BOARD

Does insomnia cause depression?

ROTH

I don't think insomnia causes depression nor do I think depression causes insomnia. Rather, I think they're both caused by a common pathology. In fact, there are a number of ongoing clinical trials investigating the role of corticotropin-releasing hormone (CRH) antagonists in the treatment of insomnia and depression. It would not surprise me if in 10 years CRH antagonists were to assume a prominent role in the management of both of these common conditions.

EDITORIAL BOARD

As opposed to being a genetic trait, can the hyperarousal state of which you speak be "learned"? This seems to be implied when one considers the entity referred to as "psychophysiologic" insomnia.

ROTH

I don't use that term. I greatly prefer using the *DSM-IV* term, "primary insomnia." Primary insomnia is best viewed as chronic insomnia which, after thorough investigation, is found not to arise from a medical, psychiatric, circadian, behavioral, pharmacologic cause, or from an otherwise defined primary sleep disorder, such as RLS or sleep apnea. I don't like the term "psychophysiologic insomnia" because it seems to me to imply certain assumptions that may or may not be true. Psychophysiologic is a word that can mean anything you want it to mean—for some people it means simply "hyperarousal," to others, it may imply "learned" hyperarousal and I'm not convinced that that is indeed the case.

EDITORIAL BOARD

What are your feelings regarding the role of melatonin in the management of advanced sleep phase disorder?

ROTH

I think its value has been a bit overstated. Based on clinical trials, melatonin appears to be more effective for phase delay sleep disorder as opposed to phase advance disorder. The most promising treatment for phase advance (and we tend to see phase advance mostly in elderly people) is light therapy. If a 75-year-old woman

Dialogue Box

walks into our clinic and complains that she always wakes up at 5:00 in the morning, the very first question we ask is "when do you get sleepy in the evening?" If she says she gets sleepy in the evening at 9:00 and gets up at 5:00 AM, our job is to move her clock to a point where that's acceptable. The best way to move patients' clocks is with light. We tell the patient to sit and watch television, use light, and to minimize light during the night when they go to bed. In addition to not being as effective as light in phase advance patients, melatonin is not a particularly safe compound and can constrict coronary arteries.

EDITORIAL BOARD

Do you favor the use of benzodiazepine receptor agonist (BZRA) hypnotic agents, such as zolpidem or zaleplon, as adjuncts to antidepressant therapy in depressed patients with insomnia as a major complaint?

ROTH

Studies are available that show that improved sleep in depressed patients is associated with a more rapid response to antidepressant therapy and that in those patients whose insomnia persists despite antidepressant therapy there seems to be a shorter time to relapse. In light of this, it is incumbent that treatment of insomnia not be overlooked as a valuable adjunct to antidepressant therapy in the patient with depression. Although improving the patient's sleep can be accomplished just as effectively with behavioral therapies, pharmacologic management with one of the newer BZRA agents would obviously be just as effective and in many practices likely more practical. In my view, both strategies should be routinely employed in the patient's sleep management. For example, when treating hypercholesterolemia, primary care doctors don't simply prescribe a statin, they also counsel the patient on diet. In the same vein, when prescribing a hypnotic, it is also just as important to counsel the patient on the principles of good sleep hygiene and behavior.

EDITORIAL BOARD

What sleep behavior and hygiene measures have you found most useful?

ROTH

The only form of sleep therapy that works consistently is sleep restriction therapy, which calls for patients to reduce their time in bed and make their sleep more efficient. Other useful elements of sleep hygiene are regularity of bedtimes, not napping, and avoidance of alcohol and caffeine. One element of sleep behavioral therapy that I'm not such a big fan of is advising the patient who can't fall asleep to get up in the middle of the night and read a book in the light. This has always seemed to me to run the risk of moving the patient's circadian clock to another time and potentially further compounding the sleep problem.

EDITORIAL BOARD

For patients who have been chronically taking a BZRA agent for a self-limited problem, such as a selective serotonin reuptake inhibitor–induced insomnia, how difficult is it to discontinue the hypnotic once the secondary cause of the insomnia is removed?

ROTH

For most patients, not very hard at all. In studies at our institution, when we tried to stop the medication, compared with placebo, the patients didn't ask for any more pills.

EDITORIAL BOARD

Were you able to simply stop the hypnotic or was tapering required?

Dialogue Box

ROTH

It really depends on the patient. As with most things in clinical practice, it is important to know and understand the patient and make the required adjustment. In some patients we simply discontinued the hypnotic and in others we chose to wean. For example, in some patients using zolpidem 7 nights a week, we initially reduced its frequency of use to 5 nights a week for a few weeks and tapered down from there.

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Do you think the need for tapering is more a reflection of the patient or more a reflection of the medication?

ROTH

It's absolutely a reflection of the patient. In the patient with insomnia, we have found that the BZRA agents have virtually no abuse potential. Tim Roehrs at my institution has conducted numerous studies that have helped to look at this issue and has found that patients with insomnia simply don't escalate the dose. Even if you give these patients 1, 2, or 3 pills that they can take at night, they only take 1, they don't take 2 or 3. If you give patients the opportunity to take sleeping pills during the day, they don't take them. Patients take these medications only when they have a sleep problem and, even then, only at the dose required to remedy their sleep problem.

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