Sleepiness Versus Sleeplessness: Shift Work and Sleep Disorders

This ACADEMIC HIGHLIGHTS section of The Journal of Clinical Psychiatry *presents the highlights of the teleconference series "Differential Diagnosis and Management of Daytime Sleepiness and Nighttime Wakefulness" held April 5, 7, and 22, 2004, and supported by an unrestricted educational grant from Cephalon, Inc. This meeting report was prepared by Physicians Postgraduate Press, Inc.*

*The chair was **Thomas Roth**, Ph.D., Henry Ford Hospital Sleep Center, Detroit, Mich. The faculty were **Karl Doghramji**, M.D., Department of Psychiatry and Human Behavior and the Sleep Disorder Center, Thomas Jefferson University, Philadelphia, Pa.; **Paul Doghramji**, M.D., Brookside Family Practice, Pottstown, Pa.; **Jonathan R. L. Schwartz**, M.D., Integris Sleep Disorders Center of Oklahoma, Oklahoma City; and **James K. Walsh**, Ph.D., Sleep Medicine and Research Center, St. Luke's Hospital, Chesterfield, Mo.*

Faculty Disclosure

In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME activity were asked to complete a full disclosure statement.

*The information received is as follows: **Dr. Roth** is a consultant for and has received grant/research support and honoraria from Cephalon, Sepracor, Merck, Lundbeck, Aventis, Neurocrine Biosciences, Pfizer, and Sanofi-Synthelabo. **Dr. Karl Doghramji** has received grant/research support from Cephalon, GlaxoSmithKline, Sanofi-Synthelabo, and Wyeth; and is member of the speakers or advisory boards for Cephalon and Forest. **Dr. Paul Doghramji** is a member of the speakers or advisory boards for Sanofi-Synthelabo, Cephalon, Eli Lilly, and Sepracor. **Dr. Schwartz** is a consultant for AstraZeneca, Altana Pharma, Cephalon, Boehringer Ingelheim, and Pfizer; has received grant/research support from AstraZeneca, Cephalon, Resmed, Sepracor, and GlaxoSmithKline; and has received honoraria from and is a member of speakers or advisory boards for AstraZeneca, Altana Pharma, Cephalon, MedPointe, Aventis, Genentech, Orphan Pharmaceuticals, Boehringer Ingelheim, and Pfizer. **Dr. Walsh** has received research support from Upjohn, Lorex, Searle, Pfizer, Abbott, American Cyanamid, Hoffman-LaRoche, Merck, Bristol-Myers Squibb, Wyeth, Orphan Pharmaceuticals, Takeda, Ancile, Neurocrine Biosciences, Cephalon, Sanofi-Synthelabo, Lundbeck, and Sepracor; is a consultant for Alza, Bristol-Myers Squibb, Pharmacia, Whitehall-Robbins, Lorex, Searle, Wyeth, Abbott, Eli Lilly, Pfizer, Sanofi-Synthelabo, Cephalon, American Cyanamid, CoCensys, Neurocrine Biosciences, Takeda, Sepracor, Ancile, Lundbeck, Proctor & Gamble, McNeil, Elan, Aventis, Respironics, Merck KgaA-Darmstadt, Restiva, King, GlaxoSmithKline, and Merck; and has received honoraria from Searle, Cephalon, Upjohn, Abbott, Wyeth, Sanofi-Synthelabo, Elan, and Pfizer.*

The opinions expressed herein are those of the authors and do not necessarily reflect the views of the CME provider and publisher or the commercial supporter.

Characteristics of Normal Sleep

Thomas Roth, Ph.D., began the meeting by stating that the need for sleep is a basic physiologic drive in humans, but sleep itself is fragile and not fully understood. Dr. Roth went on to describe the processes of normal sleep. Three processes are thought to regulate sleep and wakefulness: a homeostatic process, a circadian process, and an ultradian process.[1] Altering any of these processes, such as forcibly changing one's circadian rhythm when working rotating shifts, can have a negative impact on the amount and quality of sleep.

The homeostatic process of regulating sleep on any given night is determined by the amount of time the individual has slept in the recent past. The body inherently needs 8 hours of sleep per 24 hours, and if that amount is not provided at night, daytime sleepiness with a tendency to fall asleep during the day can be the result. One way in which this process can be seen, Dr. Roth explained, is through a Multiple Sleep Latency Test (MSLT). Participants sleep in a sleep laboratory for a night, and they are then given 5 nap opportunities during the course of the next day and are told not to resist the urge to fall asleep. Those participants who experienced a reduction in sleep the previous night will fall asleep during the nap opportunities much more quickly than those who have experienced no such reduction.[2]

According to Dr. Roth, another way to see homeostatic sleep balance at work is through electroencephalogram (EEG) results. In the early hours of sleep, slow-wave activity is predominant, and that type of activity decreases as sleep progresses. Sleep-deprived individuals, though, experience slow-wave activity into the later hours of nocturnal sleep, which appears to be, in part, the body's way of making up for lost slow-wave time.

Most people are familiar with the concept of the circadian rhythm, another hypothesized sleep process. This process regulates sleep and wakefulness during the 24-hour day, i.e., within one light-dark cycle.[3] Although the physiology of the circadian clock has yet to be completely explained, its effects are well documented. For example, the circadian cycle is closely tied to body temperature. In humans, body temperature is at its lowest from 3 a.m. to 5 a.m., has another low period midday from 1 p.m. to 3 p.m., and peaks in early evening from 5 p.m. to 8 p.m. Humans tend to want to sleep when their body temperature is low and tend to be most alert when it peaks.[4]

The ultradian rhythm controls rapid eye movement (REM) and non-REM cycles of sleep. This cycle usually lasts between 90 and 120 minutes and repeats 3 to 6 times every night. This process appears to be tied to the homeostatic process, since slow-

wave activity decreases as REM sleep increases.

Dr. Roth concluded by reiterating the need for more study on sleep, its regulation, and the consequences of disruptions to sleep such as those caused by shift work.

REFERENCES

1. Roth T, Roehrs T. Sleep organization and regulation. Neurology 2000;54 (suppl 1):S2–S7
2. Roth T, Roehrs T, Carskadon M, et al. Daytime sleepiness and alertness. In: Kryger MH, Roth T, Dement WC, eds. Principles and Practice of Sleep Medicine. Philadelphia, Pa: WB Saunders; 1994: 40–50
3. Harrington ME, Rusak B, Mistlberger RE. Anatomy and physiology of the mammalian circadian system. In: Kryger MH, Roth T, Dement WC, eds. Principles and Practice of Sleep Medicine. Philadelphia, Pa: WB Saunders; 1994:286–300
4. Roehrs T, Roth T. Transient and short-term insomnia. In: Kryger MH, Roth T, Dement WC, eds. Principles and Practice of Sleep Medicine. Philadelphia, Pa: WB Saunders; 1994:486–493

Excessive Sleepiness, Insomnia, and Shift Work Sleep Disorder in the Psychiatric Setting

Karl Doghramji, M.D., began his presentation by pointing out that the prevalence of disturbed sleep among patients with psychiatric conditions is quite high. For example, Sweetwood and colleagues[1] found the prevalence of overall sleep disturbance—i.e., trouble with falling asleep, staying asleep, waking up too early, sleeping too much, and napping during the day—to be 58% among male psychiatric outpatients versus 21% among healthy controls. In addition, of almost 1900 depressed subjects in a European survey,[2] 73% reported tiredness and 63% reported sleep problems during the previous 6 months.

Clearly, therefore, psychiatrists often see sleep disturbances in their practices, including insomnia, sleepiness, tiredness, fatigue, and daytime somnolence. These symptoms can be related to underlying psychiatric disorders, such as depression, but they can also be the consequence of other influences, such as poor sleep hygiene, medical conditions, and circadian rhythm disorders such as shift work sleep disorder.

The recognition and management of these sleep disturbances are of paramount importance, according to Dr. Doghramji, because the impact of these symptoms can be serious. Excessive daytime sleepiness, for example, is linked to slower response time, instability of attention, deterioration of performance, and cognitive slowing. Daytime sleepiness also negatively affects memory and the ability to distinguish between what is essential and nonessential in daily tasks.[3,4]

Although sleep disturbances appear to be common, Dr. Doghramji predicted that they may be underreported in both psychiatry and other types of medical practices. Few patients with insomnia specifically visit physicians and complain of insomnia. Additionally, daytime sleepiness can go unrecognized by physicians and patients alike. A vast discrepancy has been documented between subjects' awareness of sleepiness despite a high likelihood of falling asleep during daytime activities.[5] If patients do not realize that they are sleepy during the day, they cannot accurately report such episodes to their doctors. Such observations underline the importance of keeping a high index of suspicion for sleepiness in clinical settings, and for developing strategies for identification and quantification of sleepiness in patients.

Dr. Doghramji reported that a number of subjective tools can be used to identify sleepiness (Table 1). With the Stanford Sleepiness Scale,[6] patients rate the degree of sleepiness they feel at several different times during the day on a scale of 1 to 7, with 1 being most alert ("feeling active, vital, alert, or wide awake") and 7 being the least alert ("no longer fighting sleep, sleep onset soon; having dreamlike thoughts"). However, this scale may not be very accurate in assessing sleepiness since patients are often not aware of their level of sleepiness. Therefore, the Epworth Sleepiness Scale (ESS)[7] was developed. The ESS assesses a person's likelihood of falling asleep during the course of the day in normal, everyday situations (Table 2). The person rates 8 items on a scale of 0 to 3, where 0 = would never doze or fall asleep and 3 = high chance of dozing or falling asleep. If the test-taker scores a 10 or higher, he or she is advised to seek the counsel of a physician to determine the cause of the excess sleepiness.

Dr. Doghramji also noted that some psychiatric scales can be used to identify other sleep symptoms that are similar to excessive sleepiness. One such symptom is excessive fatigue, which is usually regarded as an overwhelming and sustained exhaustion associated with a decreased capacity for physical and mental work and which is incompletely relieved by rest or sleep. For example, the retardation factor of the Hamilton Rating Scale for Depression (HAM-D)[8] assesses the degree of retardation or anergy in psychiatric patients. The fatigue/inertia subscale of the Profile of Mood States[9] is also commonly used to assess levels of fatigue and sleepiness in patients.

Objective tests have also been developed to assess sleepiness and sleep disorders. These tests can be more efficacious and sensitive in assessing sleepiness than subjective rating scales and are used in specialized settings such as sleep disorders clinics. One of the most common sleep tests is the MSLT, as described by Dr. Roth. In a variant of the MSLT, the Maintenance of Wakefulness Test,[10] patients are asked to stay awake during the nap opportunities. The results of this test may be more directly proportional to the level of wakefulness during everyday situations because patients are asked to remain awake, just as they are required to be awake during the day at their jobs or other activities.

Table 1. Measures Used to Assess Sleepiness

Subjective tests
Stanford Sleepiness Scale[6]
Epworth Sleepiness Scale[7]
Hamilton Rating Scale for Depression[8] (retardation factor)
Profile of Mood States[9] (fatigue/inertia subscale)
Objective tests
Multiple Sleep Latency Test
Maintenance of Wakefulness Test[10]

Table 2. Items Assessed on the Epworth Sleepiness Scale[a]

Patient is asked to rate the chance of dozing in the following situations:
Sitting and reading
Watching television
Sitting inactive in a public place, such as a theater
As a passenger in a car for an hour without a break
Lying down to rest in the afternoon
Sitting and talking to someone
Sitting quietly after lunch (when no alcohol has been drunk)
In a car, while stopped in traffic

[a]Based on Johns.[7]

Table 3. Factors Contributing to Shift Work Sleep Disorder

Increasing age
Possible existence of underlying sleep disorders such as sleep apnea or narcolepsy
Self-treatment or self-medication on the part of the patient (long naps, caffeine to stay awake, alcohol to sleep)
Direction in and degree to which shift changes occur: slow or clockwise shift changes may be more easily tolerated than rapid or counterclockwise ones

A number of scales that assess insomnia are also available—the HAM-D,[8] for example, has a number of questions regarding insomnia—and are useful for the assessment of insomnia severity, but the most direct way to identify the presence or absence of insomnia is to ask. In order to assess its severity and impact, according to Dr. Doghramji, the physician should carefully and systematically ask the patient how long it takes him or her to fall asleep, how many awakenings he or she has during the night, and how often the patient wakes up earlier than desirable and is unable to fall asleep again. Patients should also be asked about the quality of their sleep. Some patients will sleep 8 hours but wake up feeling unrefreshed or that they did not get a "good night's sleep." For both insomnia and daytime sleepiness, an interview with the bed partner, when there is one, is essential. Bed partners are often much more aware than the patient of whether the patient's sleep has been disturbed or if the patient falls asleep during the day.

The differential diagnosis of insomnia and daytime sleepiness can be challenging in psychiatry, asserted Dr. Doghramji. A number of psychiatric disorders, such as depression and schizophrenia, have sleep problems as symptoms. The effects of many drugs and medications—those used for both medical purposes and recreation—can cause both insomnia and daytime sleepiness. Of course, a patient can also have a primary sleep disorder, such as narcolepsy or sleep apnea, or a circadian rhythm disorder such as shift work sleep disorder.

Shift Work Sleep Disorder

Dr. Doghramji went on to narrow his discussion to shift work sleep disorder. Individuals who work variable shifts must often change their bedtimes from one day to the next to accommodate their work schedule. Unfortunately, these changes can be to such an extent that the body is unable to adapt properly, so these individuals at times complain of both sleepiness during their waking hours and insomnia. Shift workers have also reported a number of psychological and psychiatric symptoms[11] as well as medical symptoms, including gastrointestinal difficulties.[12] Not all shift workers experience shift work sleep disorder, the diagnosis of which should be reserved for those workers who may be getting reprimanded on the job, falling asleep on the job, or having such difficulty sleeping that it interferes with social and occupational functioning.

Dr. Doghramji reviewed a number of factors that predispose people who work variable shifts to develop a sleep disorder (Table 3). One factor is age. The older one gets, the harder it becomes to adapt to shift changes. A second factor is the possible existence of underlying sleep disorders, such as sleep apnea or narcolepsy. In fact, the prevalence of sleep apnea symptoms has been reported to be high in populations who do shift work, such as bus drivers.[13]

A third factor includes the ways in which some patients try to self-medicate the effects of shift work. Many patients consume large quantities of caffeinated beverages to stay awake and alcohol to induce sleep, and many take long naps at the wrong times as well. These methods of dealing with shift-work disruptions in sleep can make the effects of shift work worse, not better, and may eventually lead to full-fledged shift work sleep disorder.

A fourth factor is the direction in which shift changes occur. Clockwise shifts may be more easily tolerated than counterclockwise shifts.[14,15] Rapidly rotating shifts may be more difficult for workers to adjust to than shifts that are nonvariable or rotate more slowly.[16]

The proper treatment for shift work sleep disorder, shared Dr. Doghramji, is to reinforce proper sleep hygiene and ensure that changes in sleep scheduling between one day and the next vary by no more than a few hours. Additionally, shift workers may benefit from short naps timed in such a way that they do not interfere with regular sleep. Shift workers may be treated with a combination of bright light therapy, stimulants, wake-promoting agents, and hypnotics to adjust their sleep patterns.

Conclusion

Dr. Doghramji concluded by emphasizing that insomnia and daytime sleepiness are common in psychiatric disorders. These conditions are consequential and, unfortunately, often underrecognized by psychiatrists as well as their patients. A number of both subjective and objective measures are available to quantify, define, and identify these symptoms in clinical practice.

REFERENCES

1. Sweetwood H, Grant I, Kripke DF, et al. Sleep disorder over time: psychiatric correlates among males. Br J Psychiatry 1980;136:456–462
2. Tylee A, Gastpar M, Lépine J-P, et al. DEPRES II (Depression Research in European Society II): a patient survey of the symptoms, disability and current management of depression in the community. Int Clin Psychopharmacol 1999;14:139–141
3. Alapin I, Fichten CS, Libman E, et al. How is good and poor sleep in older adults and college students related to daytime sleepiness, fatigue, and ability to concentrate? J Psychosom Res 2000;49:381–390
4. Leger D, Guilleminault C, Bader G, et al. Medical and socio-professional impact of insomnia. Sleep 2002;25:625–629
5. Rosenthal L, Nykamp K, Day R, et al. The detection of brief daytime sleep episodes. Sleep 1999;22:211–214
6. Hoddes E, Zarcone V, Smythe H, et al. Quantification of sleepiness: a new approach. Psychophysiology 1973; 10:431–436
7. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep 1991;14:540–545
8. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23: 56–62
9. McNair DM, Lorr M, Droppleman LF. Manual for the Profile of Mood States. San Diego, Calif: Educational and Industrial Testing Service; 1971
10. Doghramji K, Mitler MM, Sangal RB, et al. A normative study of the Maintenance of Wakefulness Test (MWT). Electroencephalogr Clin Neurophysiol 1997;103:554–562
11. Gordon NP, Cleary PD, Parker CE, et al. The prevalence and health impact of shiftwork. Am J Public Health 1986; 76:1225–1228
12. Segawa K, Nakazawa S, Tsukamoto Y, et al. Peptic ulcer is prevalent among shift workers. Dig Dis Sci 1987;32:449–453
13. Hui DS, Chan JK, Ko FW, et al. Prevalence of snoring and sleep-disordered breathing in a group of commercial bus drivers in Hong Kong. Intern Med J 2002; 32:149–157
14. Lavie P, Tzischinsky O, Epstein R, et al. Sleep-wake cycle in shift workers on a clockwise and counter-clockwise rotation system. Isr J Med Sci 1992;28:636–644
15. Knauth P. The design of shift systems. Ergonomics 1993;36:15–28
16. Åkerstedt T. Shift work and disturbed sleep/wakefulness. Occup Med 2003; 53:89–94

Primary Care Recognition and Assessment of Sleep Disturbances and Shift Work Sleep Disorder

According to Paul Doghramji, M.D., up to a third of the general population will experience insomnia with daytime dysfunction.[1] The 2002 Sleep in America Poll,[2] conducted by the National Sleep Foundation, found that 35% of respondents reported difficulty falling asleep or staying asleep, waking too early, or waking feeling unrefreshed every night or almost every night; another 23% reported one or more of these symptoms of insomnia a few nights a week (Figure 1).

However, continued Dr. Doghramji, few of the patients who present with symptoms of insomnia in primary care are diagnosed with or treated for insomnia. Hatoum and colleagues[1] surveyed 7500 members of managed care organizations, 3447 of whom responded. Of those who responded, 13.5% reported insomnia, i.e., difficulty initiating or maintaining sleep, and 32.5% reported insomnia with daytime dysfunction. However, only 5.5% of those reporting insomnia and 11.6% of those reporting insomnia with daytime dysfunction were receiving prescription medications for their insomnia; 11.2% and 21.4%, respectively, were self-medicating their sleep problems with over-the-counter agents. Another study[3] of patients of primary care clinics found that fewer than a third of patients with insomnia had received pharmacotherapy for it (an antidepressant or a benzodiazepine); those with current depression plus insomnia were more likely to receive treatment (38%) than those with insomnia alone (13%).

One reason for the underdiagnosis and undertreatment of insomnia may be that few patients visit their primary care physician specifically for insomnia or other sleep problems. Hatoum and colleagues[1] found that only 0.9% of survey respondents reported visiting a physician because of sleep problems. Many patients will mention being tired or fatigued but will not always associate these symptoms with sleep problems. The challenge for the primary care physician at that point is to identify the cause of the patient's tiredness, whether it be from lack of sleep, a medical condition, or a psychiatric condition.

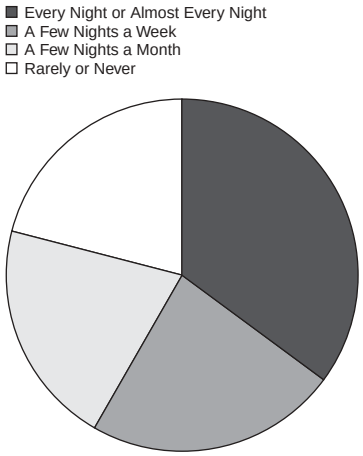
Consequences of Insomnia

The consequences of insomnia can be grave. For example, falling asleep at inappropriate times can lead to potentially life-threatening automobile crashes, industrial accidents, and the like. Poor motor, mental, and cognitive function at home, school, and work can have a detrimental impact on the patient's quality of life and performance in these areas and, therefore, on the patient's self-confidence and sense of well-being. Simon and VonKorff[3] found a high degree of functional impairment in primary care patients with insomnia; both disability ratings (Figure 2) and the amount of time spent in bed or with limited activity due to illness (Figure 3) were significantly higher in the group with insomnia versus the group without insomnia. Simon and VonKorff[3] also found that patients with insomnia—whether trouble getting to sleep or staying asleep—had significantly higher health care costs during the 3 months before and the 3 months after the screening interview ($p = .02$).

Differential Diagnosis of Insomnia in Primary Care

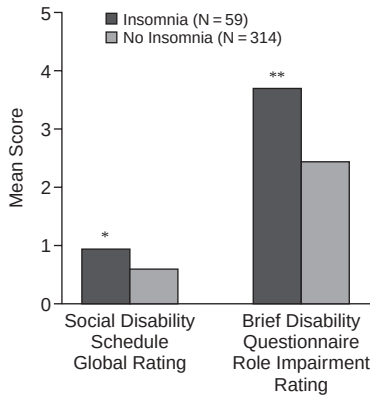
Dr. Doghramji stated that patients typically visit their primary care provider for 1 of 3 reasons: an acute visit for a particular reason, a follow-up visit for a chronic condition, or a complete physical examination. At any type of visit, patients may complain of tiredness and fatigue, although they rarely report being sleep-deprived. Therefore, it is important for the primary care provider to have sleep problems in mind when assessing patients who report tiredness or fatigue or related symptoms. The physician should ask such a patient about sleep habits and problems, such as if the patient goes to bed at the same time every night, if the patient has difficulty falling asleep or

Figure 1. Respondents to the 2002 Sleep in America Poll Who Reported 1 Symptom or More of Insomnia (N = 1010)[a]



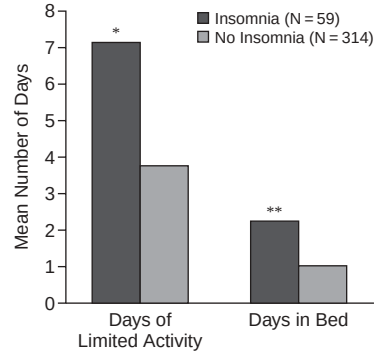
[a]Data from the National Sleep Foundation.[2]

Figure 2. Functional Impairment in Primary Care Patients With and Without Insomnia: Disability Rating Scale Scores[a]



[a]Data from Simon and VonKorff.[3]
*p = .002.
**p < .001.

Figure 3. Functional Impairment in Primary Care Patients With and Without Insomnia: Days Spent Impaired Due to Illness[a]



[a]Data from Simon and VonKorff.[3]
*p = .002.
**p = .003.

staying asleep, or if the patient awakens unrefreshed. A bed partner may also be able to report whether the patient snores or is restless while asleep. Dr. Doghramji then reviewed some of the possible causes of insomnia, emphasizing the need to differentiate among medical causes, psychiatric causes, and primary sleep disorders (Table 4).

Shift Work Sleep Disorder in Primary Care

Dr. Doghramji noted that our society runs 24 hours a day, 7 days a week, and that many people in the United States must therefore work shifts other than a regular daytime schedule. According to the U.S. Bureau of Labor Statistics,[4] 14.5% of almost 100 million full-time workers surveyed worked shifts. Some examples of shift workers include truck drivers, factory workers, power plant workers, hospital workers, and emergency workers such as firemen and police officers. Other shift workers are employed at places that are open 24 hours a day, such as diners, convenience stores, supermarkets, and gas stations, to serve others who work shifts.

Dr. Doghramji reported that shift work can result in shift work sleep disorder (Table 5). The consequences of insomnia or excessive sleepiness due to shift work sleep disorder are the same as discussed earlier, such as impaired functioning and occupational performance.

Of course, not everyone who works shifts suffers from a sleep disorder, noted Dr. Doghramji. Ohayon and colleagues[6] interviewed 817 hospital staff members who worked fixed daytime schedules (N = 442), rotating daytime shifts (N = 323), and 24-hour shifts or fixed nighttime schedules (N = 52). Of those working rotating daytime shifts, 29.7% reported disrupted sleep 2 nights a week or more, and 20.1% reported difficulties initiating sleep, significantly more than in the fixed daytime schedule group. Almost a fourth of the group working shifts or nighttime schedules met the diagnostic criteria for a circadian rhythm disorder ($p \leq .01$ vs. the fixed daytime schedule group).

Dr. Doghramji was then asked about his strategy for treating sleep disorders such as those caused by shift work, specifically whether he treats the disturbed sleep or the daytime sleepiness or both. Dr. Doghramji replied that he first suggests that the patient discontinue shift work if possible. If the patient must continue to work shifts, Dr. Doghramji would then recommend that he or she try to work the same shift every day and keep weekend sleep schedules as close to weekday schedules as possible. By minimizing irregularities in one's sleep cycle, he said, the patient may be able to keep his or her circadian clock steady.

At times, Dr. Doghramji continued, he and the patient might decide that a medication would be useful to combat this problem. For example, for a patient whose body clock consistently says that it is time to be awake when the patient is trying to go to sleep, a sleeping medication such as one of the benzodiazepine receptor agonists may be an appropriate treatment. Wake-promoting agents may also be appropriate for patients who experience excessive daytime sleepiness as a result of shift work sleep disorder.

Conclusion

In his summary, Dr. Doghramji emphasized the importance of the primary care provider's understanding that most patients will not complain of sleep disorders even though many of them do, in fact, have sleep disorders and that the consequences of sleep disorders can be serious. The primary care provider should therefore seize any opportunity during an acute event, a follow-up visit, or an annual physical examination to

Table 4. Possible Causes of Insomnia

Medical causes
Chronic obstructive pulmonary disease
Asthma
Gastroesophageal reflux disease
Chronic pain
Cardiovascular disease
Thyroid disorders
Menopause
Benign prostatic hypertrophy
Medications, both prescription and over the counter
Psychiatric and psychological causes
Anxiety disorders
Depressive disorders
Bipolar disorder
Major life events
Substance or alcohol abuse
Primary sleep disorders
Obstructive sleep apnea
Restless legs syndrome
Periodic limb movement disorder
Narcolepsy
Parasomnias
Circadian sleep problems such as shift work sleep disorder

Table 5. Diagnostic Criteria for Shift Work Sleep Disorder[a]

Patient must experience disruptions in sleep due to his or her shift work schedule; patient must also meet the criteria for circadian rhythm sleep disorder:
1. Sleep disruption resulting from dysfunction of the circadian timing system or a mismatch between endogenous circadian timing and exogenous sleep-wake schedule
2. Impairment in social, occupational, or other functioning or subjective distress resulting from insomnia or excessive sleepiness
3. Sleep problems not accounted for by another sleep or psychiatric disorder
4. Sleep problems not accounted for by substance use or medical condition

[a]Based on the DSM-IV-TR.[5]

ask about sleep and determine whether sleep problems are present and, if so, what the cause might be—medical condition, psychological condition, shift work schedule, or others.

REFERENCES

1. Hatoum HT, Kania CM, Kong SX, et al. Prevalence of insomnia: a survey of the enrollees at five managed care organizations. Am J Manag Care 1998;4:79–86
2. 2002 Sleep in America Poll. Washington, DC: National Sleep Foundation; 2002. Available at: http://www.sleepfoundation.org/img/2002SleepInAmericaPoll.pdf. Accessed May 24, 2004
3. Simon GE, VonKorff M. Prevalence, burden, and treatment of insomnia in primary care. Am J Psychiatry 1997; 154:1417–1423
4. Bureau of Labor Statistics, US Department of Labor. Table 5. Shift usually worked: full-time wage and salary workers by occupation and industry, May 2001. Available at: http://www.bls.gov/news.release/flex.t05.htm. Accessed May 25, 2004
5. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC: American Psychiatric Association; 2000
6. Ohayon MM, Lemoine P, Arnaud-Briant V, et al. Prevalence and consequences of sleep disorders in a shift worker population. J Psychosom Res 2002;53:577–583

Pharmacologic Management of Insomnia

James K. Walsh, Ph.D., spoke about trends in the pharmacologic treatment of insomnia and the effectiveness and safety of medications available for the treatment of insomnia.

Medication Usage and Trends

Dr. Walsh stated that the percentage of people in the United States who use medication to help them sleep is very small, and most people who use hypnotic medications do so for a short period of time. However, for some people it is necessary to use hypnotic medications regularly for a year or more.

Pharmacotherapy is indicated for many types of insomnia, most notably transient insomnia, including shift work sleep disorder, jet lag sleep disorder, adjustment sleep disorder, and environmental sleep disorder. Also, many patients with chronic insomnia would benefit from pharmacotherapy. Types of chronic insomnia include primary insomnia and insomnia secondary to medical or psychiatric disorders. Often, these patients need treatment specifically for their insomnia in addition to treatment for the primary condition.

From 1987 to 1996, there was a shift toward less pharmacologic management of insomnia,[1] although Dr. Walsh believes that this may have reversed in the past few years. Prescriptions for the treatment of insomnia declined by 24% during that period, and while prescriptions of hypnotics declined by 54%, prescriptions of sedating antidepressants for the treatment of insomnia rose by 146%.

Benzodiazepine Receptor Agonists

Dr. Walsh reported that meta-analyses[2,3] of several benzodiazepine receptor agonists (BZRAs) show that they are efficacious in reducing sleep latency, increasing total sleep time, reducing the number of awakenings overnight, and improving sleep quality. However, in the majority of studies included in these meta-analyses, the medications were only administered for 1 or 2 weeks. Six-week studies with estazolam[4] and triazolam[5] found that they reduced sleep latency and improved total sleep time, and gains were maintained over the study period.

In the first truly long-term efficacy trial of a BZRA,[6] 3 mg of eszopiclone was administered on a nightly basis over a period of 6 months. Eszopiclone significantly improved sleep latency, increased total sleep time, and decreased awakenings after sleep onset compared with placebo. These improvements were maintained throughout the study period.

Daytime sedation is often a concern with medications such as eszopiclone that have an intermediate or longer duration of action. Patients given eszopiclone rated their daytime alertness significantly better than those given placebo,[6] indicating that the agent may not treat only the nighttime symptoms of insomnia, but the daytime symptoms as well.

The available data suggest that BZRAs are effective for the treatment of insomnia even in nonresearch settings. In one study,[7] individuals were asked to take into account all the positive and negative effects of the medication that they were taking for their sleep problem and decide whether they would take that medication again

for the same purpose. Of the patients taking BZRAs, between 74% and 84% said that they would. Sixty-one percent of patients taking over-the-counter medications agreed.

Dr. Walsh explained that, like any medication, the BZRAs can have adverse effects, and that patients and physicians should be aware of this. Typically, the most common side effects of the BZRAs are drowsiness, dizziness, and headache. However, more serious side effects can sometimes occur.

One occasional side effect of BZRA usage is rebound insomnia. If a patient has been on a medication for several days or weeks, on the first night he or she does not take the medication, sleep quality may be significantly worse than it was at baseline. Rebound insomnia can be avoided simply by using low doses of medication and tapering the dose when it is discontinued.

Long-acting hypnotic medications can cause residual daytime sedation in some patients. If this happens, Dr. Walsh recommends switching to a short-acting drug. If a patient is particularly anxious or hyperaroused during the day, a long-acting medication may not be problematic, but some patients may not be able to tolerate the residual sedation caused by the long action.

Dr. Walsh emphasized that it is important to prescribe the lowest effective dose of these medications, because the side effects are highly dose-dependent. Doses higher than those recommended are generally no more effective and increase the risk of adverse effects.

Two other medications, zaleplon and zolpidem, are frequently prescribed for the treatment of insomnia. Although they are not chemically benzodiazepines, they act on similar receptor sites and are BZRAs. The primary hypnotic effect of zaleplon is to reduce sleep latency. It is a short-acting drug, and it does not increase total sleep time. Zolpidem, however, reduces sleep latency and increases total sleep time. Five-week studies have been performed with both zaleplon[8] and zolpidem,[9] and both medications maintained their efficacy throughout the course of each study.

Because zaleplon and zolpidem bind to receptors more selectively than the benzodiazepines, Dr. Walsh explained, the selectivity of zaleplon and zolpidem is hypothesized to lead to better side effect profiles than the benzodiazepines. However, more data are needed to support this claim. The side effects most frequently reported with zaleplon and zolpidem have been headache, nausea, and dizziness.

Sedating Antidepressants

Although the benzodiazepine receptor agonists have been well-studied, less is known about the sedating antidepressants, which include trazodone, amitriptyline, doxepin, and mirtazapine. Most information on the sedative properties of these antidepressants comes from experience with depressed individuals; Dr. Walsh explained that a dearth of information exists about the efficacy and safety of these agents in the treatment of insomnia that is not associated with depression.

The sedating antidepressants are associated with anticholinergic effects, hypotension, dry mouth, weight gain, and other side effects.[10] Dr. Walsh said that even though these medications are commonly used for the treatment of insomnia, there is no strong scientific basis for their use.

Conclusion

Dr. Walsh concluded his presentation by discussing some of the treatments for insomnia that are currently being developed. Many of these agents involve mechanisms of action other than the benzodiazepine receptors, and include GABA agonists, GABA reuptake inhibitors, corticotropin-releasing hormone antagonists, and 5-HT_2 antagonists.

REFERENCES

1. Walsh JK, Schweitzer PK. Ten-year trends in the pharmacological treatment of insomnia. Sleep 1999;22:371–375
2. Holbrook AM, Crowther R, Lotter A, et al. Meta-analysis of benzodiazepine use in the treatment of insomnia. CMAJ 2000;162: 225–233
3. Nowell PD, Mazumdar S, Buysse DJ, et al. Benzodiazepines and zolpidem for chronic insomnia: a meta-analysis of treatment efficacy. JAMA 1997;278: 2170–2177
4. Lamphere J, Roehrs T, Zorick F, et al. Chronic hypnotic efficacy of estazolam. Drugs Exp Clin Res 1986;12:687–691
5. Stepanski E, Zorick F, Kaffeman M, et al. Effects of the chronic administration of triazolam 0.50 mg on the sleep of insomniacs [FRENCH]. Nouv Presse Med 1982;11:2987–2990
6. Krystal AD, Walsh JK, Laska E, et al. Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. Sleep 2003;26:793–799
7. Balter MB, Uhlenhuth EH. The beneficial and adverse effects of hypnotics. J Clin Psychiatry 1991;52(suppl 7):16–23
8. Walsh JK, Vogel GW, Scharf M, et al. A five week, polysomnographic assessment of zaleplon 10 mg for the treatment of primary insomnia. Sleep Med 2000;1: 41–49
9. Scharf MB, Roth T, Vogel GW, et al. A multicenter, placebo-controlled study evaluating zolpidem in the treatment of chronic insomnia. J Clin Psychiatry 1994; 55:192–199
10. Settle EC Jr. Antidepressant drugs: disturbing and potentially dangerous adverse effects. J Clin Psychiatry 1998;59 (suppl 16):25–30

Pharmacologic Management of Daytime Sleepiness

Jonathan R. L. Schwartz, M.D., discussed the steps for treating a patient with excessive daytime sleepiness. These include correctly diagnosing the patient's problem, setting treatment goals, initiating treatment, and following up with the patient.

Determining the Cause of Excessive Daytime Sleepiness

Dr. Schwartz stated that, although primary sleep disorders such as narcolepsy and obstructive sleep apnea are typically recognized as causes for excessive sleepiness, there are a number of other causes of excessive daytime sleepiness that are frequently seen in clinical practices (Table 6). These include idiopathic hypersomnia, post-traumatic hypersomnia, and circadian rhythm disorders such as shift work sleep disorder. Also, the side effects of medications, including psychiatric

Table 6. Possible Causes of Excessive Daytime Sleepiness

Primary sleep disorders
Narcolepsy
Sleep apnea
Idiopathic hypersomnia
Posttraumatic hypersomnia
Circadian rhythm disorders
Shift work sleep disorder
Jet lag sleep disorder
Delayed sleep phase disorder
Medication side effects
General medical condition
Residual symptoms of a sleep disorder currently being treated

medications or medications for chronic pain, and combinations of medications, may cause excessive daytime sleepiness. Patients who are currently being treated for a sleep disorder may sometimes remain excessively sleepy during the day. Patients who use nasal continuous positive airway pressure (CPAP) at night for obstructive sleep apnea may remain sleepy during the day,[1,2] and the ongoing hypersomnolence can be effectively treated with medication.[3]

Dr. Schwartz emphasized that, although medications are helpful in the treatment of daytime sleepiness, nonpharmacologic treatment is necessary in addition to pharmacologic treatment to provide a patient with optimum care for the sleep disorder. Many patients with a sleep disorder get insufficient sleep, have poor sleep hygiene, or have a secondary sleep disorder. These patients may experience partial symptom relief when treatment is begun but later worsen if they are not properly counseled.

Treatment Goals for Patients With Excessive Daytime Sleepiness

Dr. Schwartz noted that treatment goals for daytime sleepiness have not yet been well defined. Although a consensus statement[4] for the treatment of narcolepsy has been published and revised, there is no true consensus for the proper treatment of excessive daytime sleepiness. Many physicians base their choice of treatment on previous therapeutic successes and/or failures. But without a standard by which to judge medication use, they may use too low a dosage of medication to optimally treat the patient, perhaps being limited by side effects they have seen in previous patients.

Dr. Schwartz believes the goal of therapy for excessive daytime sleepiness should be to significantly improve daytime alertness to allow the best return to normal functioning at work, school, home, and in social interactions. The ideal treatment would have no or minimal side effects and use a dosing regimen that enhances adherence. Because adherence is inversely proportional to the number of doses that must be taken each day, a once-a-day dosing schedule is best. Because of the risk of decreased compliance, prescribing a medication that requires more than 2 doses a day should be avoided if possible.

A frequent problem in the treatment of daytime sleepiness is that many physicians do not adequately communicate their expectations for treatment to the patient. The patient may have a totally different set of expectations from the physician, and without communication, the patient does not understand the full benefit that he or she is expected to gain from the treatment.

When a patient is diagnosed with one or more sleep disorders, the physician should help the patient set treatment goals and expectations. He or she should explain what the medications can and cannot do, and that wake-promoting medications are not a replacement for getting enough sleep. Sleepy patients should always be advised to avoid driving or other potentially dangerous activities when sleepy.

Medications Used in the Treatment of Daytime Sleepiness

Dr. Schwartz went on to say that amphetamines were first used in the 1930s to treat narcolepsy. Methylphenidate became available in the late 1950s, and then pemoline became available in the 1970s. The most recent medication introduced for the treatment of excessive sleepiness, modafinil, became available in 1999.

Amphetamines. The amphetamines have a long record of clinical efficacy, but few large-scale controlled studies have been performed,[5] which has made it difficult to document the benefit-to-risk ratio.

Methylphenidate. Methylphenidate also has a long record of clinical efficacy in the treatment of excessive sleepiness. Although there are data regarding these agents in the treatment of other conditions, there is still a lack of data for its efficacy in sleep disorders.[5]

Pemoline. Pemoline, which was used as a first-line stimulant treatment for some time, is currently rarely used due to a significant risk of hepatotoxicity.[6] Hepatotoxicity, although rare with pemoline, can still be fatal.

Modafinil. Modafinil is the newest and the most-studied medication for the treatment of excessive sleepiness. It is the only FDA-approved medication for the treatment of patients with sleep apnea who remain sleepy during the day despite CPAP therapy at night and for the treatment of patients with shift work sleep disorder. Large multicenter studies[7–9] have documented a favorable benefit-to-risk ratio for modafinil, and its efficacy and safety is supported by open-label experience.

γ-Hydroxybutyric acid. γ-Hydroxybutyric acid (GHB), also known as sodium oxybate, is currently indicated only for the treatment of cataplexy. It is a liquid medication and is dosed at bedtime and in the middle of the night. GHB has also been reported to improve daytime alertness in patients with narcolepsy.[10,11]

Follow-Up Care of Patients Being Treated for Daytime Sleepiness

Dr. Schwartz advised that physicians should follow up with their patients during the first few weeks of treatment to assess efficacy and adherence to medication schedules and to look for potential side effects. It is also important to make sure that the medication does not worsen a sleep disturbance or cause insomnia or mood changes. After the initial follow-up,

additional follow-ups should be performed at least every 6 months to gauge the effectiveness of the medication and to screen for any other sleep disorders that the patient may have developed while being treated.

When treating a patient with the traditional stimulants amphetamine and methylphenidate, physicians should watch carefully for side effects. The most common ones are related either to the nervous system (e.g., headache, tremor, anxiety, or mood disturbance), or to the cardiovascular system (e.g., blood pressure problems, arrhythmia, exacerbation of angina). Patients may develop a tolerance for these medications, especially when given at high doses.

If a patient fails to respond to medication, the physician should reassess him or her for other possible sleep disorders, poor sleep hygiene, and insufficient sleep.

Conclusion

According to Dr. Schwartz, the first step in managing excessive daytime sleepiness in a patient is to determine its cause or causes, whether it is narcolepsy, obstructive sleep apnea with residual somnolence, shift work sleep disorder, medication-induced sleepiness, or some other etiology. The second step includes initiating therapy, reviewing the goals of therapy with the patient, and stressing sleep hygiene. The third step is to follow up with the patient to make sure that the treatment plan is effective and side effects are minimal. Ongoing follow-up is essential to ensure optimal outcome.

REFERENCES

1. Engleman HM, Martin SE, Deary IJ, et al. Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. Lancet 1994;343:572–575
2. Sforza E, Kriger J. Daytime sleepiness after long-term continuous positive airway pressure (CPAP) treatment in obstructive sleep apnea syndrome. J Neurol Sci 1992; 110:21–26
3. Schwartz JRL, Hirshkowitz M, Erman MK, et al, for the United States Modafinil in OSA Study Group. Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea: a 12-week, open-label study. Chest 2003;124:2192–2199
4. American Academy of Sleep Medicine Standards of Practice Committee. Practice parameters for the treatment of narcolepsy: an update for 2000. Sleep 2001;24: 451–466
5. Fry JM. Treatment modalities for narcolepsy. Neurology 1998;50(suppl 1): S43–S48
6. McCurry L, Cronquist S. Pemoline and hepatotoxicity [letter]. Am J Psychiatry 1997;154:713–714
7. US Modafinil in Narcolepsy Multicenter Study Group. Randomized trial of modafinil as a treatment for the excessive daytime somnolence of narcolepsy. Neurology 2000;54:1166–1175
8. Beusterien KM, Rogers AE, Walsleben JA, et al. Health-related quality of life effects of modafinil for treatment of narcolepsy. Sleep 1999;22:757–765
9. Mitler MM, Harsh J, Hirshkowitz M, et al, for the US Modafinil in Narcolepsy Multicenter Study Group. Long-term efficacy and safety of modafinil (PROVIGIL®) for the treatment of excessive daytime sleepiness associated with narcolepsy. Sleep Med 2000;1:231–243
10. Mamelak M, Scharf MB, Woods M. Treatment of narcolepsy with gamma-hydroxybutyrate: a review of clinical and sleep laboratory findings. Sleep 1986;9 (1, pt 2):285–289
11. Scharf MB, Brown D, Woods M, et al. The effects and effectiveness of gamma-hydroxybutyrate in patients with narcolepsy. J Clin Psychiatry 1985;46:222–225

Drug names: *amitriptyline (Elavil and others), doxepin (Sinequan, Zonalon, and others), estazolam (Prosom and others), methylphenidate (Concerta, Ritalin, and others), mirtazapine (Remeron and others), modafinil (Provigil), pemoline (Cylert and others), sodium oxybate (Xyrem), trazodone (Desyrel and others), triazolam (Halcion and others), zaleplon (Sonata), zolpidem (Ambien).*

Disclosure of off-label usage: *The chair has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented that is outside U.S. Food and Drug Administration–approved labeling. If you have questions, contact the medical affairs department of the manufacturer for the most recent prescribing information.*

To cite a section from this ACADEMIC HIGHLIGHTS, follow the format below:
Doghramji K. Excessive sleepiness, insomnia, and shift work sleep disorder in the psychiatric setting, pp 1008–1010. In: Roth T, chair. Sleepiness Versus Sleeplessness: Shift Work and Sleep Disorders [ACADEMIC HIGHLIGHTS]. J Clin Psychiatry 2004;65:1007–1015

For the CME Posttest for this article, see pages 1024–1026.