

Sleep HealthCenters® Newsletter

David P. White, MD, Editor July 2005

Dear colleague,

In this issue of the Sleep HealthCenters® Newsletter, we discuss insomnia, one of the most common complaints presented in physician offices. Dr. John Winkelman discusses the differential diagnosis and treatment of insomnia, and the importance of assessing the underlying causes of insomnia for effective treatment. If insomnia persists after treating underlying causes, alternatives such as cognitive behavioral therapy or medication are also discussed.

In the CEO Section, we introduce the expansion of the Sleep HealthCenter affiliated with Hallmark Health to include clinic services. We also welcome Dr. Kelly Carden, Medical Director of the Malden Sleep Center, and Ms. Rosellen Sullivan, Director of Business Development.

If you have any questions about sleep disorders or our services, please feel free to contact us.

Sincerely,

David P. White, MD
Corporate Medical Director
Sleep HealthCenters® LLC




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1-877-SLEEPHC
1-877-753-3742

The Diagnosis and Treatment of Insomnia

By John Winkelman, M.D., Ph.D.

Dr. Winkelman is Medical Director of the Sleep HealthCenter® Affiliated with Brigham and Women's Hospital. He is board certified in Sleep Medicine, Psychiatry and Neurology. Dr. Winkelman is an Assistant Professor of Psychiatry at Harvard Medical School, and is on the Medical Advisory Board of the Restless Legs Syndrome Foundation.



Insomnia is one of the most common complaints heard in physicians' offices. Most individuals with insomnia will describe brief or intermittent periods of sleeplessness, usually associated with identifiable precipitants. However, roughly 10% of all adults have chronic, unremitting sleep problems. We are now recognizing that chronic insomnia is associated with a number of adverse consequences for both mental and physical health, as well as quality of life. Recent data demonstrates that those with insomnia have an elevated future risk of diabetes, depression, anxiety, and substance abuse disorders. These may be mediated by the physiological and cognitive hyperarousal which has been documented in chronic insomniacs.


Treatment of insomnia begins with the differential diagnosis and assessment of this complaint, as it is preferable to find and treat underlying conditions causing insomnia than to use empiric therapies. A mnemonic covering the differential diagnosis of insomnia (DREAM PCH) is listed in Table 1.

At times, despite our efforts to identify an underlying cause of insomnia, no clear etiology can be identified. Furthermore, treating an identified cause may not always fully or even partially reduce sleeplessness. In such cases, empiric therapy of insomnia with either cognitive behavioral therapies (CBT) or pharmacotherapy is indicated.

CBT addresses the counterproductive habits, beliefs and emotions which may produce or perpetuate insomnia. It includes restriction of time in bed, avoidance of stimulating activities in the bedroom setting or close to bedtime, teaching of relaxation techniques, elimination of catastrophic beliefs regarding the consequences of sleeplessness, and improvement in sleep hygiene. Multiple studies have demonstrated the efficacy of CBT in the treatment of insomnia, and brief forms of CBT now exist which can be employed in the busy primary care office.

Multiple pharmacotherapies also exist which have demonstrated efficacy in the treatment of insomnia. The only FDA-approved pharmacotherapies (listed in Table 2) bind to the benzodiazepine receptor on the GABA receptor complex. Some of these agents are selective, and bind primarily to the alpha-1 receptor ("non-benzodiazepines"), and other older agents bind non-selectively to alpha-1, alpha-2 and alpha-3 receptors. The clinical significance of this receptor selectivity has not been clearly established, though it appears that the sedative, amnestic, and anticonvulsant properties of these drugs are due to their effects at the alpha-1 receptor. More importantly, benzodiazepine receptor agonists differ in their duration of action, primarily due to the intrinsic half life of the drug.

Although these agents have well established efficacy in insomnia, there is reluctance to prescribe them among many in the medical field due to concerns about the potential for abuse and tolerance, and about potential side effects. In addition, until recently, the package inserts on all such agents recommended short term treatment with benzodiazepine receptor agonists, further constraining physicians' prescribing patterns, and leading many insurance carriers to limit prescriptions to 10 pills per month. With additional recent research about this class of medications, a more balanced assessment of the benefits and risks of these medications is now available. (continued on page 2)


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In this issue of the Sleep HealthCenters® Newsletter...

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- ▶ CEO Corner:
 - Sleep HealthCenters® Expands Malden Sleep Center to Include Clinic Services
 - Sleep HealthCenters® Welcomes New Staff, Dr. Kelly Carden, Medical Director of the Malden Sleep Health Center Affiliated with Hallmark Health, and Ms. Rosellen Sullivan, Director of Business Development
- ▶ Research Activities

Sleep HealthCenters® is a network of sleep medicine clinics and labs staffed by experts in the field of sleep medicine. Our integrated care system provides all the services needed to diagnose and treat patients with the entire array of sleep disorders, including obstructive sleep apnea, insomnia, narcolepsy and restless legs syndrome. Sleep HealthCenters® has locations throughout eastern Massachusetts and is affiliated with the Brigham & Women's Hospital, Beth Israel Deaconess Medical Center, McLean Hospital, Faulkner Hospital, and Hallmark Health.

Sleep HealthCenter® locations include South Weymouth, Newton, Bedford, Malden, Boston, and Jamaica Plain.

For more information, please contact our scheduling office at: 1-877-SLEEPHC (1-877-753-3742) or visit our website at www.sleephealth.com.

Referral forms are available on our website.

Sleep HealthCenters® Newsletter

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Certain risks of benzodiazepine receptor agonists appear to be inevitable with currently available medications, including amnesia and psychomotor impairment. These risks are related to the intrinsic activity of these specific drugs and are present during the period of time in which the drug is active in the nervous system. For this reason, careful attention to the half-life and dose of the prescribed agent is essential, as excessively long durations of action are counterproductive for patient health and safety and add liability to physicians. Other risks of benzodiazepine receptor agonists, such as abuse, have been more carefully defined, and appear to be present in a minority of users, and in particular, generally limited to those with previous histories of drug or alcohol abuse. Similarly, falls in the elderly appear to be a risk of insomnia itself. Thus, it is unclear whether use of a hypnotic in the elderly will decrease or increase the risk of falls.

Concerns about the development of tolerance to benzodiazepine receptor agonists remain one of the largest impediments to prescription of these drugs. This issue is of particular salience as many patients seen in practice have chronic insomnia and might thus be appropriate for long-term treatment if it were not for this concern. However, recent data has addressed the paradox of a chronic medical problem and only short-term studies. Treatment with eszopiclone, a selective benzodiazepine receptor agonist, was recently shown to reduce sleep onset latency and wake time after sleep onset, improving total sleep time, compared to placebo, without tolerance over six months of nightly use.

TABLE 2

FDA Approved Medications Used to Treat Insomnia:

Nonselective Benzodiazepine-Receptor Agonists Commonly Used as Hypnotics		
Agent (brand name)	Dose range	Half-life
Flurazepam (Dalmane)	15-30 mg	50-100 hr
Estazolam (Prosom)	1.0-2.0 mg	10-20 hr
Temazepam (Restoril)	7.5-30 mg	4-18 hr
Triazolam (Halcion)	0.125-0.25 mg	2-3 hr
Selective Benzodiazepine-Receptor Agonist Hypnotics		
Agent (brand name)	Dose range	Half-life
Eszopiclone (Lunesta)	1-3 mg	5.5-8 hr
Zolpidem (Ambien)	5-10 mg	2-3 hr
Zaleplon (Sonata)	5-10 mg	1-2 hr

TABLE 1
Differential Diagnosis of Insomnia (DREAM PCH)

Underlying Disorder	Key Features	Treatments
Depression/Dysthymia	<ul style="list-style-type: none"> Can be associated with any insomnia complaint Depressed even after a good night's sleep Associated loss of interest/motivation 	<ul style="list-style-type: none"> Antidepressants +/- short-term hypnotic (SSRIs effective even with prominent insomnia)
Restless Legs Syndrome	<ul style="list-style-type: none"> Dysesthesia and/or motor restlessness in legs Relief with movement and worse at night 	<ul style="list-style-type: none"> Evaluate underlying causes esp Fe deficiency (keep ferritin > 40) ropinirole (.5-2.0 mg) or pramipexole (.25-.75 mg)
ETOH/Caffeine	<ul style="list-style-type: none"> May fall asleep, but awakenings followed by difficulty returning to sleep 	<ul style="list-style-type: none"> No caffeine after noon Limit alcohol in the evening
Anxiety Disorder	<ul style="list-style-type: none"> Can be associated with any insomnia complaint Anxiety regarding other things than sleep History of anxiety disorder, panic attacks, trauma 	<ul style="list-style-type: none"> Benzodiazepines, SSRIs or cognitive-behavioral therapy
Medication-related	<ul style="list-style-type: none"> SSRIs, steroids, bronchodilators, decongestants 	<ul style="list-style-type: none"> Taper or d/c med, if possible Add hypnotic (see below)
Pain/dyspnea	<ul style="list-style-type: none"> More difficulty staying, than falling, asleep Arthritis, fibromyalgia, GERD, COPD, CHF 	<ul style="list-style-type: none"> Treat underlying disorder if possible; if not, can add hypnotic (see below)
Conditioned Insomnia	<ul style="list-style-type: none"> Significant worry re sleeplessness Usually more difficulty falling, than staying, asleep Previous episodes of insomnia with stress Improved mood/anxiety after good night's sleep 	<ul style="list-style-type: none"> Short term: Hypnotics (see below) Longer term: Cognitive-behavioral therapy (see below) and hypnotics
Poor sleep "Hygiene"	<ul style="list-style-type: none"> Stressful activities too close to bedtime Variable bed/wake times Long periods in bed awake, watching the clock 	<ul style="list-style-type: none"> No daytime naps Regular exercise Restrict time in bed at night to 6 hrs Out of bed if awake > 30 minutes

This study led to elimination of the FDA short-term treatment recommendation in the eszopiclone label. Whether this lack of tolerance is a property of other selective and non-selective benzodiazepine receptor agonists is unknown. Similarly, the efficacy of non-GABA agents such as trazodone over long-term treatment is unknown.

In summary, insomnia is common in both general medical and specialty practices. A thorough assessment for underlying causes is essential, and treatment of these initially is the best practice. However, if insomnia persists after treatment of putative underlying causes, or if these cannot be determined or treated effectively, independent treatment of insomnia is usually indicated. Cognitive behavioral therapies are very effective for many patients, and should be applied. A variety of medications, with a broad range of half-lives, are FDA approved for the treatment of insomnia. New pharmacologic agents are also available which have demonstrated persistent efficacy over six months of nightly use.

For a fully referenced version of this article, visit the Sleep HealthCenters® website at www.sleephealth.com.



CEO Corner

Paul S. Valentine
President and Chief Executive Officer

We are pleased to announce that Sleep HealthCenters® continues to expand to provide quality sleep medicine services throughout Massachusetts. In May, we expanded our Malden Sleep HealthCenter affiliated with Hallmark Health to include a new four-room clinic enabling us to provide comprehensive services from diagnosis to treatment and follow-up for patients suspected of having sleep disorders. The services include physician consults, CPAP set ups, patient monitoring and education. The facility is located at 100 Hospital Road on the third floor of the Malden Medical Center.

We are proud to welcome the newest member of our medical team, Kelly A. Carden, M.D., the Medical Director of the Malden Sleep Center. Dr. Carden is board certified in Internal Medicine, Pulmonary Disease, Critical Care Medicine and Sleep Medicine. She completed a Sleep Medicine Fellowship at Harvard Medical School and is a clinical researcher at the Brigham and Women's Hospital. Dr. Carden conducts her clinic sessions in both the Malden and Newton facilities.

To keep up with the growing demand for sleep medicine services, we are delighted to welcome Rosellen Sullivan, the Director of Business Development, to our management team. Ms. Sullivan will help Sleep HealthCenters® expand its service area beyond eastern Massachusetts to areas north, south and west of Boston. Ms. Sullivan has extensive experience in the health care industry and was previously Vice President of Sales at Hospitals-online.com, an allied health recruiting site. She was also the Director of Business Development at Morrison Management Specialists, providing food nutrition services to hospitals, and she was the Vice President of Corporate Sales for Cross Country Inc., the largest healthcare temporary staffing agency in the United States.

Please contact us if you are interested in a tour of the Malden facility or if you would like additional information on the services we offer. If you have a patient that you would like us to see, you may contact our scheduling office at 1-877-SLEEPHC (1-877-753-3742). We look forward to continuing to service your patients at our new Malden clinic as well as our other sleep medicine centers.

Research Activities

Sleep HealthCenters® and their related research affiliations are actively recruiting patients for the following studies:

Apnea Positive Pressure Long-Term Efficacy Study (APPLES)

A NIH-funded study examining the long-term effects on quality of life, neurocognitive function, sleepiness and mood of using Continuous Positive Airway Pressure (CPAP) to treat sleep apnea. The Sleep HealthCenter® affiliated with Brigham and Women's Hospital is recruiting patients age 18 or older who suspect they may have sleep apnea but have not been previously treated with CPAP or surgery. Subjects will be enrolled for six months (maximum of 7 months) and will receive extra medical attention as well as monetary compensation. Study contact: Denise Clarke 617-527-3501 ext. 146.

Heart Failure and Cheyne-Stokes Respiration

A research study investigating a new mode of positive pressure therapy for the treatment of Cheyne-Stokes respiration during sleep. The Sleep HealthCenter® affiliated with Brigham and Women's Hospital is recruiting patients age 21-80 with congestive heart failure (LVEF < 40%). The study involves one home study and up to four overnight studies in our sleep lab. Study contact: Mary MacDonald 617-527-3501 ext. 162.

Restless Legs Syndrome

A research study of a new drug is being tested (in the form of a patch) for Restless Legs Syndrome. The Sleep HealthCenter® affiliated with Brigham and Women's Hospital is recruiting individuals age 18-75 who suffer from Restless Legs Syndrome (achy, creepy-crawly sensations in the legs, which get worse at night). Males and females are eligible. Participation in this study requires 14 clinic visits over an 8-month period. There will be no overnight stays. Up to \$600 for participation. Study contact: Lindsay Johnston 617-527-3501 ext. 115.

