Treatments for Sleepiness Vary in Cost, Side Effects

BY SHERRY BOSCHERT
San Francisco Bureau

SAN DIEGO — All three main treatments for problem sleepiness can perk patients up, but they differ in cost and side effects, Dr. Milton Erman said at a psychopharmacology congress sponsored by the Neuroscience Education Institute.

Caffeine is the cheapest, most accessible, and most widely used stimulant. The two other treatment options are prescription medications, which are more expensive: modafinil or CNS stimulants (most commonly amphetamines or methylphenidate).

Caffeine tolerance develops rapidly, however, and there's a moderate risk for dependence. Stopping a daily caffeine habit too quickly can trigger a "caffeine headache." Side effects from regular caffeine use include nervousness, irritability, insomnia, and GI problems, said Dr. Erman of the University of California, San Diego.

"Many of my insomniac patients tell me proudly that they aren't using caffeine" to indicate that caffeine can't be blamed for their insomnia, he said. Ironically, a bit of caffeine in the morning may be just what they need. "The problem with many of these insomniac patients is that they can't get going, get functioning in the morning," he said. Limited caffeine use in the morning may help them function better.

Use of CNS stimulants also leads to tolerance, and there is a high potential for dependence. Side effects include nervousness, headaches, insomnia, anorexia, GI problems, and mood changes. General CNS stimulants such as amphetamines have a high risk of abuse and hyperactivity because of their broad mechanism of action.

One experimental study of sleep deprivation that compared amphetamines with modafinil treatment to maintain wakefulness suggested that the two drugs are equally potent. In real life, however, "I think amphetamines are more potent," he said. Patients with narcolepsy who have used amphetamines in the past often aren't satisfied with the effects of modafinil.

Modafinil works more specifically on wakefulness circuits and has fewer side effects than other stimulants. Tolerance is not an issue—it maintains most of its efficacy over time—and use of the drug does not lead to dependence. Side effects include headache, nausea, dry mouth, insomnia, and hyperactivity.

The risk of headache relates to the dosing of modafinil. In early research on the drug, headache appeared primarily in patients who titrated up to a dose of 400 mg/day by the third day. In subsequent research that gave patients 7-9 days to titrate up to 400 mg/day, headache was much less of a problem, Dr. Erman said.

"Modafinil works quite well, particularly if we're not talking about the most severely hypersomnolent patients," such as narcoleptics who have become accustomed to taking stimulants, he said.

Dr. Erman is a speaker and consultant for, and has received research funding from, the company that makes modafinil, Cephalon Inc. Modafinil is approved to treat sleepiness from shift work, narcolepsy, and sleep apnea.

The most common cause of problem sleepiness is sleep apnea, which occurs in perhaps 10% of the population, he said. Restless leg syndrome can interrupt sleep and lead to daytime sleepiness. Narcolepsy is fairly uncommon. Insomnia can cause excessive sleepiness, but more often, insomniac patients are hypervigilant. "If anything, they are more alert" than they want to be, he said.

Secondary causes of sleepiness include chronic pain and any medical condition that causes pain or discomfort, which may interrupt sleep. Medications used to alleviate pain also can lead to daytime sleepiness because they affect breathing during sleep and increase the risk for sleep apnea.

Check to see if patients who complain of sleepiness are taking drugs that cause sedation or that disrupt sleep, Dr. Erman added, and consider alternative therapies.

Lifestyle issues, such as graveyard shift work, also contribute to excessive sleepiness,. The pace of U.S. culture commonly leads to chronic sleep deprivation that affects daytime function. "As a society, we really haven't dealt with this," he said. ■

PHQ-9 Detects Depression After Traumatic Brain Injury

BY JANE SALODOF MACNEIL
Southwest Bureau

SANTA ANA PUEBLO, N.M. — The Patient Health Questionnaire is a simple, reliable tool that any clinician can use to screen patients for depression after traumatic brain injury, Dr. Jesse R. Fann reported at the annual meeting of the Academy of Psychosomatic Medicine.

Dr. Fann and his colleagues at the University of Washington, Seattle, validated the nine-item questionnaire in a prospective cohort study with 135 patients who were also referred for structured clinical interviews.

These patients were among 478 patients enrolled at the time of analysis in a National Institutes of Health-supported study that is using the PHQ-9 to determine the prevalence of depression in people who have suffered traumatic brain injury.

"Various studies have estimated 25%-45% get depressed in the first year. The prevalence drops after the first year, but remains significantly higher than the general population," Dr. Fann, of the department of psychiatry and behavioral sciences, said in an interview about the poster.

Just why this population is more vulnerable to depression is not clear, Dr. Fann said. Brain lesions could be a factor, he said, but many patients also suffer from psychosocial stressors, such as unstable employment and social support or abuse of alcohol or other substances.

Dr. Fann said the standard of care at most hospitals and rehabilitation centers is not to screen traumatic brain injury patients for depression.

The investigators were especially interested in the PHQ-9 because it has been validated for other medical conditions and would be easy for nonpsychiatrists to use. "It takes 2-5 minutes," he said. "We did this over the phone. It can be filled out by the patients themselves with paper and pencil. Or it can be done face to face in an interview format."

The PHQ-9 asks whether patients had been bothered during the previous 2 weeks by each of nine symptoms of major depressive disorder in the DSM-IV. The multiple-choice answers range from "not at all" to "nearly every day."

"It has validity for major depression but also helps remind nonpsychiatrists what the DSM criteria are," Dr. Fann said.

The study found the optimal criterion for a positive screen on the PHQ-9 to be a patient reporting five or more of the nine symptoms for at least several days. The researchers specified that one of these five symptoms should be a cardinal symptom: either depressed mood or anhedonia.

When patients met the optimal criterion, the poster reported the PHQ-9 had a maximum sensitivity of 0.93, maximum specificity of 0.89, positive predictive value of 0.63, and negative predictive value of 0.99 in comparison to a Structured Clinical Interview for DSM-IV (SCID). The investigators also found correlations of 0.90 with the Hopkins Symptom Checklist Depression Subscale and 0.78 with the Hamilton Rating Scale.

Dr. Fann's group conducted the study at the Harborview Medical Center in Seattle, a level I trauma center serving the states of Washington, Idaho, Montana, and Alaska. They called participants at home to administer the PHQ-9 every month or two for a year after the patients were treated for a traumatic brain injury that was severe, moderate, or complicated mild. ■

Sodium Oxybate Reduces Daytime Sleepiness in Medicated Narcoleptics

BY DAMIAN MCNAMARA
Miami Bureau

MIAMI BEACH — Sodium oxybate significantly lessened daytime sleepiness and decreased frequency of sleep attacks in people with narcolepsy concurrently taking stimulants, compared with placebo, according to study findings presented at the annual meeting of the American Academy of Neurology.

Previous studies have shown that nightly administration of sodium oxybate (Xyrem, Orphan Medical) effectively treated cataplexy in people with narcolepsy (Sleep 2003;26:31-5; Sleep 2002;25:42-9).

The Food and Drug Administration approved the agent for treatment of cataplexy, a sudden loss of muscle tone associated with narcolepsy, in July 2002. Researchers in the two studies observed that the drug also decreased excessive daytime sleepiness.

To confirm this effect, Dr. Michael J. Thorpy conducted an 8-week, double-blind, placebo-controlled trial of adult narcolepsy patients from 42 sleep clinics in the United States, Canada, and Europe. Participants, after being weaned from anticataplectic medications, were randomized to receive 4.5 g, 6 g, or 9 g of sodium oxybate or placebo nightly.

The drug was administered in two equally divided doses at bedtime and 2.5-4 hours later. Sodium oxybate was increased weekly in 1.5-g increments up to the final dose, with the total treatment lasting 28 days.

There were 228 patients in the intent-to-treat population, half randomized to treatment and half to placebo. A total of 206 completed the 8-week study. The majority (78%) remained on steady doses of preexisting stimulant medications.

"I don't think we know the mechanism of action. We understand GABA-B [gamma-aminobutyric acid B] mechanism regarding nighttime sleep. Sodium oxybate affects a number of neurotransmitter systems, and tends to depress dopamine at night," Dr. Thorpy, director of the Sleep-Wake Disorders Center at the Montefiore Medical Center, New York, said in response to a question from the audience. Dr. Thorpy received support from Orphan Medical Inc., sponsor of the study.

Dr. Thorpy used the Maintenance of Wakefulness Test (MWT) as an objective measure of excessive daytime sleepiness, and the Epworth Sleepiness Scale (ESS) for a subjective assessment. Participants also kept diaries to record the incidence of sleep attacks. Changes in MWT scores at 8 weeks were significant, compared with baseline for patients receiving the final doses of either 4.5 g or 9 g. "Compared with placebo, patients treated with sodium oxybate showed a significant median increase in more than 10 minutes in MWT at the 9-g dose," Dr. Thorpy said.

Baseline ESS scores were "around 19, suggesting a lot of sleepiness," Dr. Thorpy said. The 6-g and 9-g treatment groups experienced statistically significant decreases in median ESS scores after 8 weeks, compared with baseline.

The weekly incidence of inadvertent naps was 14 to 18 overall at baseline. There were statistically significant reductions in these sleep attacks in the 6-g and 9-g groups, a mean of 6.5 fewer naps with treatment, compared with placebo. ■