Light and Melatonin Can Reset Circadian Rhythm

By Jane Salodof MccNeil  Senior Editor

Scottsdale, Ariz. — Before traveling from California to South Africa, Dr. Alon Y. Avidan prepared for the time change by spending afternoons in his office, out of the sun. After he arrived in South Africa, he slept between 3 a.m. and 7 a.m. every morning and took a walk for an hour or more in bright sunlight.

“In a few days, I was on South African time,” he told those attending a meeting on sleep medicine sponsored by the American College of Chest Physicians.

Light therapy can be highly effective in correcting jet lag and other circadian rhythm disorders, according to Dr. Avidan, medical director of the University of California, Los Angeles, neurology clinic and associate director of UCLA’s sleep disorders center.

Melatonin, a dietary supplement with no approved medical indications, is another useful treatment when delayed sleep is a problem, he said, and ramelteon (Rozerem) shows promise. Although ramelteon is approved only for insomnia, Dr. Avidan said he prescribes it off label to patients with the type of circadian rhythm disorder that causes night owls to complain they can’t fall asleep at normal bedtime or wake up early in the morning.

Often they are tired all day, but not at night, which detracts from their quality of life. “Circadian-related disruption leads to insomnia, hypersomnia, or both,” he said, and it can cause impairment of social, occupational, or other areas of functioning.

Sunlight is the most powerful external time cue for regulating and synchronizing the body’s circadian rhythms with the environment, Dr. Avidan said. It promotes wakefulness as input from the retina goes to the suprachiasmatic nucleus (SCN) of the hypothalamus, which contains a circadian clock.

To oppose ends, the pineal gland releases melatonin in response to darkness. Melatonin promotes sleep, but levels of it decrease with aging. Compensating with the dietary supplement has been shown to help advance the circadian clock, according to Dr. Avidan.

For patients with delayed sleep, he recommended exposure to bright light—such as 10,000 lux—in the early morning and taking 0.5 mg of melatonin 5-7 hours before the patient’s habitual sleep time, or 12-14 hours before the time a person wishes to awake.

In response to an audience question, Dr. Avidan said several small studies not yet published suggest ramelteon also can advance sleep time. It acts on the melatonin receptors MT1 and MT2, he noted, and described ramelteon as “a true drug.”

When using ramelteon off label for a circadian rhythm disorder, he prescribes a 4-mg dose (which is half the 8-mg dose approved for insomnia).

Altered Brain Response Seen in IBS Patients

Patients with irritible bowel syndrome have altered brain responses to the anticipation of pain and to pain itself, which might make them more sensitive to painful stimuli, reported Dr. Steven M. Berman and his colleagues from the Center for the Neurobiology of Stress at the University of California, Los Angeles.

During expectation of pain, irritable bowel syndrome patients generate higher levels of tonic noradrenergic activity, producing a bias toward interpretation of network activity as pain, and are inefficient at reducing such activity when discrimination of nonpainful stimulation should be maximized, they said (J. Neurosci. 2008;28:149-59).

Functional magnetic resonance imaging (fMRI) was used to measure the blood oxygen level-dependent response to anticipated and delivered rectal distention in 14 female IBS patients and 12 healthy controls (mean age 36 years). When controls were anticipating a painful stimulus, brain activity decreased in several regions, but there was less of this anticipatory deactivation in the IBS patients. When IBS patients perceived a painful stimulus, fMRI perfusion was performed using a computer-driven pump and rectal balloon. Four to six sessions of 16 inflations were performed. Each inflation was preceded by an anticipatory cue. During rectal distention, increases in activity in the insula, dorsal anterior cingulate cortex, and dorsal brainstem were more extensive in IBS patients than in controls.

The results show that during expectation of experimental abdominal/pelvic discomfort, female IBS patients are less anxious and less likely to develop a bias to downregulate activity within the CNS network activated by potentially aversive stimuli, the authors noted.

—Kate Johnson

POLYSOMNOGRAPHY STUDY: MIGRAINE LINKED TO DISTURBED SLEEP IN CHILDREN

By Patrice Wendling  Chicago Bureau

Chicago — Sleep apnea was observed in more than half of children with migraine in a study presented at the annual meeting of the American Academy of Neurology.

Polysomnography revealed sleep apnea in 56% of children with migraine, compared with 10% of those with nonmigraine headache in a study of 90 children aged 5-19 years with headache and sleep complaints.

The association between sleep apnea and migraine was significant, with an odds ratio of 2.1, Dr. Martina Vendrame, chief resident, Temple University Hospital, Philadelphia, and colleagues reported.

Two-thirds of the children with migraine also had frequent arousal during sleep.

Children with chronic migraine, defined as 15 days or more of migraine per month, took longer to fall asleep, had a shorter total sleep time, woke more frequently during the night, and had shorter REM and slow-wave sleep.

“Clinicians should ask all children with headaches and their parents about sleep problems,” including snoring, awakenings during sleep, and daytime sleepiness, Dr. Vendrame told reporters during a press briefing at the meeting. If concerns are raised, patients should be referred to ENT specialists for evaluation and treatment of sleep problems.

Two-thirds of children in the study identified with sleep apnea were evaluated by ENT specialists, and half underwent tonsillectomy. Of these, 80% had some benefit, including reduced migraine frequency, she said. Dr. Vendrame acknowledged the presence of headache could contribute to sleep disturbances, as children suffering from headache will often take daytime naps. In addition, it is widely accepted that headache and sleep disorders share common pathophysiologic mechanisms. Previous studies have evaluated the relationship between headache and sleep disturbances, but this is the first to use polysomnography in children, she said.

The study comprised 60 children with migraine, 11 with chronic daily headaches, 6 with tension headaches, and 13 with nonspecific headaches.

Children with chronic daily headache had shorter total sleep time, longer sleep latency, shorter REM sleep, and a higher arousal index.

When assessing patient sleep during the night, 50% of migraine patients had tension headaches, 50% suffered from teeth grinding, versus 2.4% of children with non-tension headaches (OR 1.95).

When asked if the study was biased by having a population of children who already had reported headaches, Dr. Vendrame told reporters at a press briefing at the meeting. If concerns are raised, patients should be referred to ENT specialists for evaluation and treatment of sleep problems.

The study was conducted at the Christopher Hospita l for Children, Drexel University, Philadelphia; and the authors had no conflicts of interest to disclose.