Caffeine Associated With Improved Cognition in Apnea Patients

In 2003, physicians at the Intermountain Sleep Disorders Center in Salt Lake City described ataxic breathing, central apnea, sustained hypopnea, and other abnormalities in three patients on long-acting opioid therapy for pain (Chest 2003;123:632-9).

Several studies of the complication have been published, but most accounts are anecdotal. Some reports focus on patients on methadone maintenance, while others address the growing number of people taking opioids for chronic pain. (See box.)

Emerging Evidence

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Methadone Used for Pain Linked to Sleep Apnea

The sleep-disordered breathing seen in baby boomers being treated for chronic pain is severe.

BY JANE SALODOF McNEIL
Southwest Bureau

D r. Amanda A. Beck and her colleagues were puzzled by some of their patients at the University of New Mexico’s Sleep Disorders Center in Albuquerque. The patients took methadone, but they did not have histories of drug abuse. They were middle-class baby boomers under treatment for chronic pain, and their nighttime breathing problems were severe.

They needed a variable positive airway pressure device, the VPAP Adapts, recently approved for the treatment of central sleep apnea, mixed sleep apnea, and periodic breathing. “We are getting this very complicated sleep-disordered breathing, which used not to be in our lexicon,” Dr. Beck, director of adult services, said at a university-sponsored psychiatric symposium, where she described her center’s experience as a red flag for methadone prescribers.

Central sleep apnea increases the risk of apneic and hypopneic events that reduce or block airflow, resulting in partial or complete lack of oxygen. The condition is an unexplained phenomenon. Dr. Beck said, “We ordered breathing, which used not to be in our lexicon.”

In another study that Dr. Webster presented at the same meeting, he compared polysomnography data on 73 opioid-naive primary care patients who had been referred for sleep studies with data on 139 asymptomatic chronic pain patients taking opioids. In both groups, 16% of the patients had severe sleep apnea.

Obstructive sleep apnea was more common in the primary care patients at 89%, vs. 77% of cases in the pain group. Central sleep apnea, a more severe condition, occurred more in the pain patients: 32%, vs. 6% of the primary care cases.

As a result of his ongoing research, Dr. Webster has become a campaigner for more conservative use of methadone. “No one was aware this was a problem. Most pain practices would not ordinarily order sleep studies,” he said in an interview with this newspaper.

Dr. Webster emphasized that he is not opposed to methadone use for pain management. “But patients and physicians need to understand it is not like other opioids.”

Recent reports have also associated methadone with poor sleep quality in adolescents with pain on treatment programs (J Adolesc Health 2009;44:422-6).

Patients with a mean apnea-hypopnea index of 63 episodes per hour, indicating severe sleep apnea, performed significantly worse on an assessment battery that included tests of speed of information processing, executive functioning, memory skills, verbal skills, and attention and working memory domains.

Caffeine intake was assessed using a detailed instrument that has been shown to characterize usual caffeine consumption based on 24-hour recall. Daily caffeine intake in cognitively impaired patients was one-sixth that of non-cognitively impaired patients (30 mg vs. 180 mg). Dr. Norman said previous findings that obstructive sleep apnea patients consume three times the caffeine of nonapnic individuals on a daily basis led to speculation that those with sleep apnea were self-medicating with caffeine to counteract daytime sleepiness. Caffeine has been shown to enhance cognition, and the findings of the current study suggest that this is an additional effect experienced by those who use caffeine for that purpose.

—Sharon Worcester

Methadone Prescribing on the Rise

Not without irony, Dr. Webster said, “We think it is safe because it is legal.” Physicians turned to methadone for treatment of pain in part because they believed it was safer than other opioids and less likely to bring regulatory complications. When Oxycodone abuse became a public issue, they saw methadone as a drug with little street value or abuse potential.

“Physicians think it is safe because it has been used for addiction so many years,” he said.

Health insurers also appear to have played a role. Methadone is the cheapest opioid by far. One estimate puts the monthly cost to pharmacists as $8 for an oral dose of 5 mg taken three times a day, based on wholesale prices. In comparison, chronic pain therapy with generic sustained-release morphine would cost $101.50; MS Contin, $113.50; OxyContin, $176.50; and Duragesic, $154 (Am. Fam. Physician 2005;71:1333-8).

Confronted with such steep price differences, some health plans reportedly have made methadone their drug of choice when an opioid is prescribed for pain. In many cases, Dr. Beck said, that is why methadone is being prescribed to older pain patients with comorbidities and other medications that can interact with methadone.

It is really irresponsible of insurers and HMOs, of anyone who sets up a formulary that [designates] the most dangerous in its entire category as the first-line agent to be used. I think that is unconscionable,” she said.

Formularies also are responsible for an increase in methadone prescribing by primary care physicians who are not familiar with its unique characteristics, according to Dr. Howard A. Heit, a chronic pain specialist certified in addiction medicine who practices in Fairfax, Va. “Are we forcing doctors to use a medication that they don’t have the knowledge to use, which could be fraught with major complications, which will cost more in the long run?” he asked during an interview.

Dr. Heit served on a U.S. Substance Abuse and Mental Services Administration panel that reported in 2004 on nationwide increases in methadone-related deaths. The panel cited as a likely factor a fivefold increase from 1998 to 2002 in the volume of methadone distributed through pharmacies. The risk of apnea was not considered because it was not an issue at that time, he said.

Psychosomatic Medicine

Preventing Methadone Associated Deaths

Several factors may contribute to the increase in methadone-related deaths and complications with an advisory. (See related story, p. 2.)

A U.S. study reported that 84% of 225 patients at maintenance programs had central sleep apnea, mixed sleep apnea, and periodic breathing. A fivefold increase from 1998 to 2002 in the volume of methadone distributed through pharmacies. The risk of apnea was not considered because it was not an issue at that time, he said.

That article spurred Dr. Lynn R. Webster to order sleep studies on patients prescribed opioid therapies at the Lifetree Pain Clinic in Salt Lake City. Dr. Webster, medical director of the clinic and an affiliated research center, presented polysomnography data on 152 patients at the American Academy of Pain meeting in February 2006.

“We are getting this very complicated sleep-disordered breathing, which used not to be in our lexicon.”

Dr. BECK

Three-fourths of the patients had an abnormal apnea-hypopnea index, including 42% with obstructive sleep apnea, 12% with central sleep apnea, and 21% with mixed obstructive and central sleep apnea. One-third of the patients had been prescribed methadone and long-acting opioids; 4% took only methadone, according to the abstract.

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