Sleep Apnea Increased Mortality in 14-Year Study

BY HEIDI SPLETE
Senior Writer

BALTIMORE — Moderate to severe sleep apnea significantly increased the risk of all-cause mortality, according to 14 years of follow-up data from a large community sample.

"Sleep apnea is a disease of public health significance," said Nathaniel Marshall, Ph.D., of the University of Sydney, who presented results from the Busselton Health Study at the annual meeting of the Associated Professional Sleep Societies.

Previous studies have suggested that obstructive sleep apnea (OSA) increases the risk of death from cardiovascular disease, Dr. Marshall said. Until recently, however, the role of sleep apnea as an independent predictor of all-cause mortality has not been well studied, he added.

The Busselton Health Study is an ongoing community-based study in Busselton, Western Australia.

For the study, the researchers analyzed data from 400 community-dwelling adults aged 45-60 years. All of the participants were tested for OSA using a home sleep apnea monitoring device. Sleep apnea was quantified using the respiratory disturbance index (RDI), and moderate to severe apnea was defined as an RDI score of 15 or more respiratory disruptions per hour of sleep.

Complete data were available from 380 participants (278 men and 102 women) after an average of 13.4 years. The mortality rate was significantly higher (33.3%) among the 18 participants who had moderate to severe apnea (six deaths), compared with 6.5% among the 77 participants with mild OSA (five deaths) and 7.7% among the 285 participants without OSA (22 deaths).

Compared with people who did not have sleep apnea, the mortality hazard ratio was 6.24 for people with moderate to severe sleep apnea, after the researchers controlled for risk factors including age, gender, body mass index, mean arterial pressure (as a measure of blood pressure), smoking status, total cholesterol, HDL cholesterol, diabetes status, and physician-diagnosed angina.

"I was suspicious of the size of this effect," Dr. Marshall said. "If you put this same model into an odds ratio, you get an odds ratio of about 10." To put it another way, "sleep apnea has about the same effect on mortality as getting 18 years older," he said.

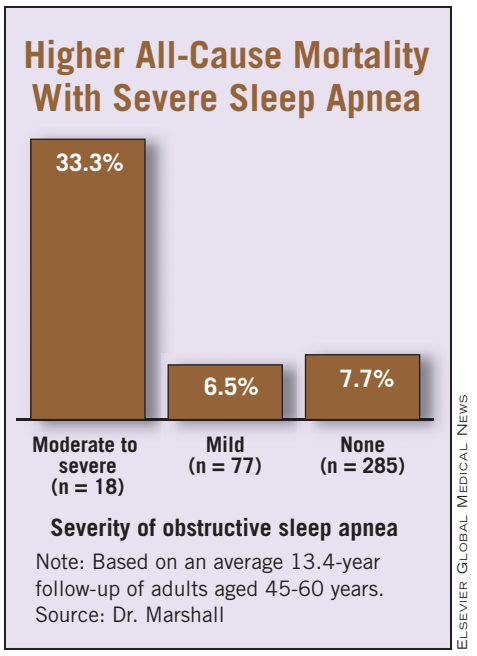
But the results reflect similar recent findings from two studies in the United States—the multicenter Sleep Heart Health Study and the Wisconsin Sleep Study—that also show significant independent associations between OSA and all-cause mortality.

The association between moderate to severe OSA and all-cause mortality in the Busselton Health Study persisted even in a partly adjusted model that did not control for blood pressure. That model was used for comparison because OSA is a known cause of hypertension, Dr. Marshall noted. However, the researchers found no significant association between mild sleep apnea and an increased risk of death, which is good news, he said.

The study was limited by a lack of information about any treatment of sleep apnea in the study group, but the community-based format of the study kept it free of clinical referral bias, Dr. Marshall explained.

The results suggest that sleep apnea could be added to the list of standard mortality risk factors. But the findings also emphasize the need for randomized controlled trials of sleep apnea treatments that are designed to identify reductions in mortality risk, Dr. Marshall noted.

Dr. Marshall reported that he had no financial conflicts to disclose. ■



ELSEVIER GLOBAL MEDICAL NEWS

Prolactin May Be Key Link Between Stress, Psoriasis

BY BRUCE JANCIN
Denver Bureau

KYOTO, JAPAN — Prolactin may be a key mediator in the pathway by which psychological stress triggers and exacerbates psoriasis, Dr. Ewan A. Langan said at an international investigative dermatology meeting.

This raises the intriguing prospect that prolactin may offer a novel future therapeutic target in psoriasis and other skin diseases that worsen in response to psychological distress, said Dr. Langan, who is with the University of Manchester (England).

Prolactin is a "remarkably versatile" neurohormone for which more than 300 distinct biologic actions have been identified. Several of these involve the skin, he noted.

For example, prolactin has been shown to promote keratinocyte proliferation and differentiation, angiogenesis, and a Th1 proinflammatory local cutaneous milieu marked by a T-cell–predominant infiltrate.

These just happen to be among the hallmarks of psoriasis, Dr. Langan observed at the meeting of the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

Dr. Langan presented what he described as the first-ever study to demonstrate that prolactin levels and prolactin receptor expression are increased in chronic psoriatic plaques, compared with the normal photo-protected skin of healthy controls.

The study involved 10 patients with early-onset chronic plaque psoriasis and 10 controls, all of whom surrendered skin biopsies that were subsequently analyzed immunohistochemically.

Both prolactin and prolactin receptors were detected in epidermal keratinocytes, dermal fibroblasts, and sweat glands of healthy controls.

By comparison, however, expression of prolactin and prolactin receptors was markedly upregulated throughout the epidermis in psoriasis plaques, especially in the basal layer, probably because of local cutaneous production.

No significant difference was noted between expression in the uninvolved skin of psoriasis patients and samples from normal controls.

The most likely scenario is that prolactin enhances interferon-γ–induced chemokine production in keratinocytes, thereby facilitating cutaneous T-cell infiltration, according to Dr. Langan.

Planned future studies will attempt to pin down the factors that regulate cutaneous prolactin and prolactin receptor production, he added. ■

Sodium Oxybate May Improve Sleep in Fibromyalgia Patients

BY SHERRY BOSCHERT
San Francisco Bureau

PHOENIX — Preliminary data on the off-label use of sodium oxybate suggest that it improved sleep in a randomized, placebo-controlled study of 151 patients with fibromyalgia who completed 8 weeks of treatment at 21 medical centers.

The study enrolled 195 patients who started with a drug washout period and were randomized to continue for 8 weeks on sodium oxybate 4.5 g/day or 6 g/day or placebo. Doses were split; patients took a half-dose at bedtime, then awoke 4 hours later for the other half.

Forty-four patients (23%) withdrew before completion, mostly from the higher-dose group and primarily because of side effects, including headache, dizziness, and nausea, Dr. Harvey Moldofsky reported at a meeting of the New Clinical Drug Evaluation Unit sponsored by the National Institute of Mental Health.

Both objective and subjective measures of sleep improved in the drug groups, compared with placebo—for those who finished the study—more so with the 6-g/day dose, said Dr. Moldofsky, president and director of the Centre for Sleep and Chronobiology, Toronto, and emeritus professor of medicine at the University of Toronto.

The study was funded by Jazz Pharmaceuticals, the company that makes sodium oxybate. Dr. Moldofsky is a consultant to and an advisory board member for the company.

Many patients with fibromyalgia have sleep disturbances, he noted.

Sleep polysomnography showed significant objective improvements in the high-dose group in the following areas: amount of time spent sleeping; sleep efficiency (the proportion of time spent sleeping, compared with time in bed); and the amount of deep, or slow-wave, sleep, he reported.

Subjective results from patient self-reports on several scales showed that they experienced improvements with either dose, compared with placebo, in pain and fatigue (Visual Analog Scale), daytime sleepiness (Epworth Sleepiness Scale), impaired sleep (Jenkins Scale), and daytime functioning (Functional Outcome of Sleep Questionnaire, SF-36 Vitality scale, and Fibromyalgia Impact Questionnaire).

The study provides a proof of concept, but more research is needed before the drug is used by patients with fibromyalgia, he said.

Besides headache, dizziness, and nausea, other side effects that occurred more frequently in the drug groups than in the placebo group included vomiting, nasopharyngitis, extremity pain, muscle cramp, nervous system disorders, restlessness, and incontinence or other renal/urinary disorders.

In 2002 sodium oxybate was approved in the United States to reduce cataplexy attacks in patients with narcolepsy, but the drug is under tightly restricted distribution from Jazz Pharmaceuticals alone — not from pharmacies.

The agent, more commonly known as gamma hydroxybutyrate, or GHB, entered the U.S. market as a dietary supplement in the early 1990s. It subsequently gained favor as a party drug, was used to perpetrate date rape because of its intoxicating effects, and caused many serious adverse events and some deaths from its use and misuse.

More research would be needed to determine whether the improvements in sleep seen in the current study were independent of subjective improvements in pain and functionality, Dr. Moldofsky said. ■