Perimenopausal Depression Link to Hot Flashes Affirmed

BY PATRICE WENDLING
Chicago Bureau

TUCSON, ARIZ. — When a female patient presents with hot flashes, consider screening her for depression, Dr. Marlene Freeman advised at a psychopharmacology conference sponsored by the University of Arizona.

The risk of depression is known to increase during perimenopause, and epidemiologic studies have shown that women in early perimenopause have greater rates of persistent mood symptoms (15%-18%) than do premenopausal women (8%-12%).

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But a recent study found that the onset of perimenopausal depression was associated only with hot flashes, and not with many of the risk factors that are conventionally suspected, such as parity, previous depression, family history, smoking, duration of perimenopause, endocrine measures, vitamin or mineral supplements, exercise, or medical illnesses (Am. J. Psychiatry 2004;161:2238-44).

"We don't know if all women are going to have a tough time during perimenopause, but for some it can be an exquisitely high-risk time," said Dr. Freeman, director of the Women's Mental Health Program at the University of Arizona, Tucson.

In general, history of major depressive episodes is important to predict future episodes, because some patients with depression have patterns of recurrence. But psychosocial factors—such as aging parents, children leaving home, marital issues, and the individual woman's feelings about growing older and leaving the reproductive years—also may factor into whether a woman experiences depressive symptoms or episodes, Dr. Freeman said.

Selective serotonin reuptake inhibitors are an attractive potential option for mood and somatic symptoms of perimenopause, particularly given the controversy surrounding the use of hormone therapy.

Dr. Freeman and her colleagues recently conducted a small, open-label, 8-week study in which 20 perimenopausal women with major depression were treated with escitalopram (Lexapro) 10 mg/day for 2 weeks, with the option of either decreasing the dosage or increasing to a maximum of 20 mg/day. Side effects caused two patients to drop out of the study, which was supported by Lexapro maker Forest Pharmaceuticals Inc.

An intent-to-treat analysis of 18 patients showed that 16 patients experienced a 50% or greater decrease in scores on the Hamilton Rating Scale for Depression, and 13 experienced a 50% or greater decrease in scores on the Greene Climacteric Scale used to quantify somatic symptoms. Paired t tests showed that the differences in pre- and posttest scores were significant for both of the primary measures.

Other studies have shown that extended-release paroxetine (Paxil) and venlafaxine (Effexor) have been successful in reducing hot flashes in women, she said. Open-label data showed that citalopram (Celexa) was efficacious as a monotherapy for perimenopausal and postmenopausal women with depression, and as an adjunct therapy for women who had remained depressed after 4 weeks of estrogen therapy with estradiol (J. Clin. Psychiatry 2003;64:473-9). ■

Eszopiclone Aids Sleep, but Has No Effect on Hot Flashes

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Perimenopausal women who took eszopiclone for 1 month experienced significant improvements in sleep problems brought on by hot flashes, results from a randomized trial have found.

However, the drug had no apparent effect on the number or severity of daytime and nighttime hot flashes, Rob Mariani, Ph.D., reported during a poster session at the American Psychiatric Association's Institute on Psychiatric Services.

"I think this is another example of how you can improve the quality of your life in great part by improving how well you can sleep at night, especially in perimenopausal women who complain of sleep difficulties," said Dr. Mariani, senior medical liaison for Sepracor Inc., which markets eszopiclone under the brand name Lunesta. The nonbenzodiazepine drug was approved by the Food and Drug Administration in 2004 for the treatment of insomnia.

Dr. Mariani went on to note that most of the published studies in the area of menopause and sleep "indicate that there are really not any significant sleep architecture changes in patients at menopause or perimenopausal age. Yet at the same time, women who are perimenopausal and postmenopausal complain about a significant number of sleep problems, especially those who have vasomotor symptoms."

In a study funded by Sepracor Inc., Dr. Mariani and his associates enrolled 410 perimenopausal women aged 40-60 years who met the Stages of Reproductive Aging Workshop criteria for early menopausal transition, late menopausal transition, and early postmenopause, and who reported sleep latency of 30 minutes or more and total sleep time of 6 hours or less per night at least three times a week for 1 month.

Investigators randomized 201 women to receive 3 mg eszopiclone and 209 to receive placebo nightly for 4 weeks. Study end points included sleep latency, wake time after sleep onset, total sleep time, awakenings due to hot flashes, daytime hot flashes, and physician global evaluations.

Scales used included the Greene Climacteric scale, the Montgomery Asberg Depression Rating scale, and the Menopause Quality of Life scale.

Compared with the women in the placebo group, those who took eszopiclone had significant changes in median sleep latency (reduction from baseline of 18.6 minutes vs. 8.1 minutes) and in median wake time after sleep onset (reduction of 30.6 minutes vs. 16 minutes). The increase in median total sleep time was greater among women who took eszopiclone (48.9 minutes per day vs. 29.7 minutes).

Although eszopiclone did not affect the frequency or duration of daytime hot flashes, it did yield significant benefits in the physician global evaluation of menopause symptoms, the Montgomery Asberg Depression Rating scale score, the Greene Climacteric scale score, and in the vasomotor and physical domains of the Menopause Quality of Life scale. ■

Extra Vitamin D Cuts Fall Risk in Elderly Women, Not Men

BY KATE JOHNSON
Montreal Bureau

Elderly women, particularly those who are less active, can significantly reduce their risk of falling by taking a daily supplement of vitamin D, according to a new study. However, the supplement does not protect men in the same age group.

Daily supplementation with 700 IU of cholecalciferol and 500 mg of calcium citrate malate reduced the odds of falling by 46% in ambulatory older women and by 65% in less active women, noted Dr. Heike A. Bischoff-Ferrari of University Hospital Zurich, and colleagues.

The supplementation is not only "very inexpensive, well tolerated, and simple" but also has similar or greater benefit than more expensive and time-intensive interventions, added the authors (Arch. Intern. Med. 2006;166:424-30).

The findings are from a secondary analysis of a 3-year double-blind placebo-controlled study that looked at the effect of cholecalciferol-calcium on bone mineral density. Primary results of the study noted a 60% reduction of osteoporotic fractures with the supplement, compared with placebo. The secondary analysis examined the risk of falling during the study period for 199 men and 246 women aged 65 years or older.

One explanation for this gender difference in treatment effect could be that lower muscle strength in women makes them more susceptible to falls.

Multivariate analysis controlled for age, gender, baseline body mass index, dietary calcium, baseline plasma 25-hydroxyvitamin D (25-OHD) levels, baseline plasma intact parathyroid hormone levels, activity level, baseline smoking status, baseline alcohol use, baseline comorbid conditions, baseline creatinine clearance and length of follow-up.

Overall, cholecalciferol-calcium supplementation did not significantly reduce the risk of falling compared with placebo, with 49% of men and 55% of women reporting at least one fall during the study period. However, multivariate analysis revealed that, compared with placebo, supplementation significantly reduced the odds of falling in women (odds ratio [OR] 0.54) and particularly in less active women (OR 0.35).

The treatment did not have the same effect on men, however, regardless of whether they were less active (OR 0.96) or more active (OR 1.01).

Baseline levels of 25-OHD, creatinine clearance or parathyroid hormone did not impact the effect of the supplement.

The gender difference in the effect of vitamin D supplementation has not been previously described because generally men have not been included in previous studies, noted the authors. One explanation for this gender difference in treatment effect could be that decreased muscle strength in women, compared with men, makes them more susceptible to falls, the investigators suggested. Vitamin D supplementation increases muscle strength thus protecting against falls.

They noted that length of treatment was another important factor in the study because the benefit of supplementation "increased with time and occurred primarily after 12 months of treatment." Short-term benefits of supplementation have been noted in other studies, but "may be explained by a combination of older age, increased frailty, and significantly lower baseline 25-OHD levels in their participants," they observed.

The fact that low baseline levels of 25-OHD did not enhance treatment effects in this study "may be explained by the rather high mean baseline 25-OHD levels observed in our study participants, which is likely owing to vitamin D fortification in dairy products and activity level of our healthy and relatively young community-dwelling older participants," the investigators noted. ■