WHI Casts Doubt on Hormones for Hot Flashes

BY MITCHEL L. ZOLER
Philadelphia Bureau

BETHESDA, MD. — Now that results from the Women's Health Initiative have shot down hormone therapy as a way to prevent coronary events, dementia, and urinary incontinence in postmenopausal women, the only indication left standing has been relief of menopausal symptoms, especially vasomotor symptoms such as hot flashes.

But even this application is on shaky ground thanks again to results from the Women's Health Initiative (WHI).

One problem with using estrogen plus progestin, or estrogen alone to manage vasomotor symptoms is that a comprehensive quality of life assessment in the WHI showed no clinically significant benefit from hormone therapy, Jennifer Hays, Ph.D., said at a conference on the Women's Health Initiative, sponsored by the Department of Health and Human Services.

This result carries the caveat that the WHI hormone study enrolled only women who were willing to accept randomization to placebo, which means that women with the worst symptoms were probably not included.

A second problem is that 56% of women in the WHI who had hot flashes when they started hormone therapy experienced a recurrence 8-12 months after stopping hormone therapy.

The finding that symptoms recurred after hormone therapy stopped is "very important," said Dr. Hays, a developmental psychologist at Scott & White Hospital in Temple, Tex., and a principal investigator for WHI. "We now talk about treating women with estrogen for a short term, but what happens when women get taken off?"

Despite this drawback, hormone therapy is "clearly still the best treatment for vasomotor symptoms," commented Dr. Robert Brzyski, an ob.gyn. at the University of Texas Health Science Center, San Antonio, and another WHI principal investigator.

That symptoms recurred after therapy stopped is important. Women are treated with estrogen short term, but what happens when they get taken off?

The prevalence of menopausal symptoms when women entered the WHI hormone study was related to age. Among women aged 50-54 years, the most common symptom was hot flashes, reported by about 23% of women.

Vaginal dryness, headache, and mood swings were each reported by 10%-15% of women, and joint pain was noted by 20%. The prevalence of all symptoms at entry, except joint pain, was lower with increased age. For example, among women aged 55-59 years, the prevalence of hot flashes was 15%.

After 1 year of treatment with estrogen and progestin, about 85% of women with hot flashes reported that this symptom had significantly improved, compared with about 58% of women in the placebo group, a statistically significant difference. Improvement in vaginal dryness was reported by about 75% of women treated with estrogen plus progestin, compared with about 55% in the placebo group, also a significant difference, Dr. Hays said at the meeting.

But serial surveys that measured health-related quality of life using the RAND 36-Item Health Survey failed to identify any clinically meaningful improvements after 1 or 3 years of estrogen-plus-progestin treatment, compared with placebo. A similar quality of life assessment using the RAND 36 failed to show any clinically meaningful improvements in women treated with estrogen only, compared with placebo.

The incidence of menopausal symptoms in women who stop hormone therapy was examined by studying the 9,351 women who were still taking their prescribed estrogen plus progestin or placebo regimen when the treatment phase of this trial was stopped in July 2002. This group comprised 56% of the participants originally enrolled, and included 4,558 in the hormone arm and 4,793 in the placebo group.

During the first 8-12 months after stopping, hot flashes occurred in 56% of women who had this symptom when they began hormone therapy, compared with a 21% incidence in women who had hot flashes when they entered the placebo arm of the study (JAMA 2005;294:183-93).

In women who had hot flashes at any time before entering the WHI study, the symptom occurred after treatment stopped in 22% of women who had been on estrogen plus progestin, compared with 4% of women from the placebo group.

The results suggest hormone therapy only postpones certain menopausal symptoms, and may eventually make the symptoms worse, Dr. Hays noted in an interview.

Several management options are alternatives to hormone therapy for menopausal symptoms, including drugs such as clonidine or selective serotonin reuptake inhibitors, treatment with various supplements or herbal agents, or modified forms of hormone therapy that involve different dosages, duration of treatment, or formulations, or routes of administration. But these alternatives are all are limited by a lack of information on their safety and efficacy, said Dr. Margery Gass, an ob.gyn. at the University of Cincinnati and a principal investigator for the WHI. ■

Eszopiclone May Put to Rest Perimenopause Sleep Disruptions

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.

The drug had no effect on the number or severity of daytime and nighttime hot flashes, however, Rob Mariani, Ph.D., reported in 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 Lunesta. The nonbenzodiazepine drug was approved by the Food and Drug Administration in 2004 for the treatment of insomnia.

Dr. Mariani noted 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.

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). ■

Discontinuing OCs May Not Lower SHBG in Some Women

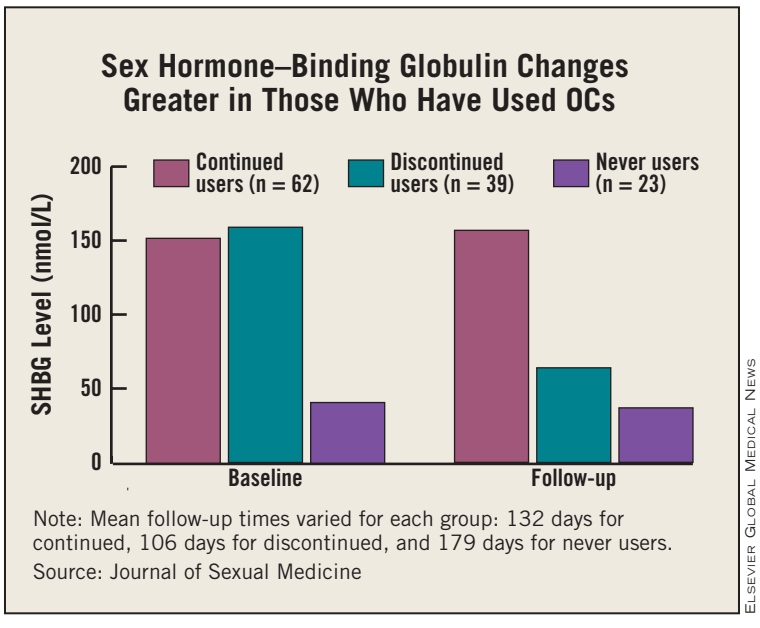
Women with sexual dysfunction maintained elevated levels of sex hormone–binding globulin even after they discontinued use of oral contraceptives, according to Dr. Claudia Panzer of Boston University Medical Center and her colleagues.

In a retrospective study of sex hormone–binding globulin (SHBG) levels before and after discontinuation of oral contraceptive use, researchers examined 124 premenopausal women with sexual health complaints. The women were divided into three groups: "continued-users," 62 women (mean age 32 years) who had been on OCs for more than 6 months and continued taking them; "discontinued-users," 39 women (mean age 33 years) who had been on OCs for longer than 6 months and discontinued them; and "never-users," 23 women (mean age 36 years) who had never taken OCs.

SHBG was a significant four times higher in the continued-user group, compared with the never-user group (152 nmol/L vs. 41 nmol/L). But despite a decreased level of SHBG in the discontinued-user group, the level remained significantly higher than in the never-user group for more than 120 days, according to the investigators (J. Sex. Med. 2006;3:104-13). (See graphic.)

SHBG elevation induced by OCs may lead to long-term sexual, metabolic, and mental health changes, the investigators said.

—Mark S. Lesney



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