Nonhormonal Meds Aid Hot Flashes in Breast Ca

BY MARY ANN MOON

FROM THE JOURNAL OF CLINICAL ONCOLOGY

VITALS

Major Finding: Both venlafaxine and clonidine reduced the frequency and severity of hot flashes by approximately 45%, compared with placebo.

Data Source: A prospective, randomized, double-blind, multicenter clinical trial comparing 12 weeks of venlafaxine, clonidine, or placebo for control of hot flashes in 102 Dutch women with breast cancer.

Disclosures: No financial conflicts of interest were reported.

Venlafaxine and clonidine both outperformed placebo in controlling hot flashes among women with breast cancer in a randomized, placebo-controlled trial.

Effective treatments for hot flashes may improve these patients' ability to continue their anticancer therapies, said Dr. Annelies H. Boekhout of The Netherlands Cancer Institute, Amsterdam, and her associates.

The selective serotonin reuptake inhibitor venlafaxine (Effexor) and the antihypertensive clonidine "both are often prescribed treatments and are recommended in clinical guidelines in the management of hot flashes. However, a three-arm trial comparing clonidine, venlafaxine, and placebo in patients with breast cancer has not been conducted" until now, they noted.

In their double-blind study at three Dutch hospitals, 102 women with breast cancer who experienced at least two hot flashes per day were stratified by age, duration of symptoms, concurrent endocrine therapy, and previous chemotherapy, and randomly assigned to receive 75 mg of venlafaxine (41 patients), 0.1 mg of clonidine (41 patients), or matching placebo (20 patients) daily for 12 weeks.

The study participants completed daily diaries recording the frequency and severity of hot flashes. They also reported every week on adverse events such as reduced appetite, nausea, sleepiness, dizziness, fatigue, dry mouth, and constipation. In addition, they recorded their sleep quality, anxiety, depression, and sexual function at 4 weeks and at the conclusion of treatment.

A total of 22 subjects (22%) either dropped out of the study or were lost to follow-up. Two patients (5%) in the venlafaxine group and six (15%) in the clonidine group cited adverse effects such as somnolence, dizziness, and dry mouth as their reason for discontinuing. Another 9% of the study participants discontinued because of noncompliance, which "had some effect on the observed differences between treatments in this study."

Among the 35 women assigned to venlafaxine who completed the trial, there was a 42% decline in hot flashes during weeks 1-4, compared with the placebo group. Over the entire study period, the reduction in hot flashes was 41% with venlafaxine, compared with placebo, according to Dr. Boekhout and her colleagues.

Among the 28 women assigned to clonidine who completed the trial, hot flashes declined by only 26% during weeks 1-4 but then declined another 22% during the remainder of the study, for an overall reduction of approximately 45%.

Thus, both active agents decreased the frequency and severity of hot flashes compared with placebo, with no discernible difference between the two by week 12.

"A more rapid reduction of hot flashes suggests that venlafaxine is to be preferred over clonidine," Dr. Boekhout and her co-investigators said (J. Clin. Oncol. 2011 Sept. 12 [doi:10.1200/JCO.2010.33.1298]).

It is "advisable to treat patients to manage hot flashes with venlafaxine 37.5 mg daily in the first week and increase the venlafaxine dose to 75 mg if greater efficacy is desired."

A total of 14 patients (34%) in the clonidine group, 23 (56%) in the venlafaxine group, and 4 (20%) in the placebo group said that they wished to continue the study treatment at the end of the trial.

Women taking clonidine reported more symptoms of anxiety and women taking venlafaxine reported more symptoms of depression.

Sexual function and sleep quality did not differ between the two groups. However, the duration of this study may have been too short to permit adequate assessment of these adverse effects, according to the researchers. ■

VIEW ON THE NEWS

Small Numbers Mar Findings

The main weakness of this study was that "the patient numbers were too small to reliably identify suspected differences between the two active study arms," said Dr. Charles L. Loprinzi, Dr. Debra L. Barton, and Dr. Rui Qin.

The unbalanced randomization scheme and the unequal dropout rates, which likely were due to perceived toxicities, meant that only 35 patients were available for analysis in the venlafaxine group, 28 in the clonidine group, and 17 in the placebo group. To detect a10% difference between the two active drugs, 156 subjects would have been needed per study arm, and to detect a 5% difference, 620 would have been needed.

"With the currently reported sample size ... the power of detecting a 10% difference is only 29%," they noted.

For clinicians, they added, available data suggest that multiple nonestrogenic options are available for treating hot flashes. "Our suggestion is that these nonhormonal options be tried in the order in which they are listed (an antidepressant, then an antiseizure medication, then clonidine), unless there are contraindications to particular drugs in individual patients," they wrote.

DR. LOPRINZI, DR. BARTON, *and* DR. QIN *are at the Mayo Clinic in Rochester, Minn. Dr. Loprinzi reported ties to Pfizer. These remarks were taken from their editorial accompanying Dr. Boekhout's report (J. Clin. Oncol. 2011 Sept. 12 [doi:10.1200/JCO.2011.37.5865]).*

Endometriosis Treatment May Boost Migraine Risk

BY DAMIAN McNAMARA

FROM A MEETING OF THE NEW CLINICAL DRUG EVALUATION UNIT SPONSORED BY THE NATIONAL INSTITUTE OF MENTAL HEALTH

BOCA RATON, FLA. – Ovarian suppression to treat endometriosis might cause a woman to experience significantly more migraines, as well as more sleep disturbances, numbness, joint pain, hot flashes, and heart palpitations, a study revealed. Some women also experience more depression.

Migraines affect more than three times as many women as men in the United States. Decreases in hormone levels and sex steroids during the late luteal phase of the menstrual period, during the postpartum period, and during perimenopause, for example, can increase a woman's susceptibility to migraines. Researchers figured that treatments that intentionally lower a woman's estrogen levels to tackle endometriosis might, at the same time, increase her risk for more severe and more frequent migraines and depressive symptoms.

Dr. Julia K. Warnock said that gonadotropin-releasing hormone (GnRH) agonists will decrease estrogen and increase the risk of headaches, including migraines, and increase the risk for depressive symptoms. Some women tend to be more sensitive to mood-related hormonal changes, Dr. Warnock said at the meeting. She is professor of psychiatry and director of clinical research at the University of Oklahoma Health Science Center in Tulsa.

"As the patient transitions through the reproductive cycle, a number of [her] associated mood symptoms … are influenced by fluctuations in estrogen," said study coauthor Dr. J. Clark Bundren, an ob. gyn. in private practice in Tulsa.

"Proper supplementation of low dose estradiol in this population can improve migraine headache, anxiety, and depression," Dr. Bundren said.

Dr. Warnock and colleagues evaluated baseline hormone levels, depression, and physical symptoms for 56 women with endometriosis. Women completed the MENSI (Menopause Symptom Index) and the HAM-D (Hamilton Rating Scale for Depression).

Participants were then treated with 3.75 mg GnRH agonist via intramuscular injection daily for 28 days. They were reevaluated at 1 month, 2 months, and 5 months.

A significant increase in the frequency of headaches was observed at each follow-up, according to an item level chi square analysis of MENSI scores, compared with baseline. Total MENSI scores likewise significantly increased at 1, 3, and 5 months, according to a t-test of dependent samples.

Similarly, depressive symptoms significantly increased, compared with baseline, at months 1, 3, and 5, as reflected by the percentages of women who scored greater than 10 on the HAM-D.

"Psychiatrists should consider hormonal fluctuations in the treatment of women [with depression]," Dr. Warnock said, because decreases in estrogen levels can predispose some to worsening depression. Combination hormone and antidepressant treatment can have synergistic benefits.

"Together is better." This dual approach also can mean lower doses of antidepressants and therefore, lower risk of associated adverse events, Dr. Warnock added.

Regarding the well-publicized risks associated with hormone therapy, Dr. Bundren said, "Women on estrogen alone have a decreased risk of breast cancer, but it's not a simple message."

"It matters which estrogen, which patient, and how it's delivered," Dr. Warnock said. "In general, transdermal is better than oral. For women who are suffering, it's about their quality of life."

Potential limitations of the study include patient self-report of headache frequency on the MENSI, and a lack of assessment of progesterone or its metabolites.

The study was unfunded. Dr. Warnock and Dr. Bundren said they had no relevant disclosures. ■