Effexor Eases Hot Flashes in Breast Ca Patients

Drug is more effective than clonidine, but does not match a single dose of medroxyprogesterone acetate.

BY JANE SALODOF MACNEIL
Southwest Bureau

ORLANDO, FLA. — Venlafaxine controls hot flashes more effectively than clonidine, but not as well as a single dose of medroxyprogesterone acetate, according to randomized, controlled trials presented in posters at the annual meeting of the American Society of Clinical Oncology.

Safety is the big unanswered question. The concern is whether MPA interferes with hormonal therapies such as tamoxifen.

In a trial organized by the German Breast Group, venlafaxine (Effexor) reduced frequency of hot flashes by 62% and severity by 67% in breast cancer patients. Clonidine reduced frequency by 22% and severity by 48%, reported Sibylle Loibl, M.D.

In a North Central Cancer Treatment Group trial, venlafaxine reduced hot flash frequency by 52% and median hot flash scores by 57% in the first 185 patients evaluated. A single 400-mg dose of medroxyprogesterone (MPA, Depo-Provera) achieved an 85% drop in frequency and reduced scores by 88%, reported Charles L. Loprinzi, M.D.

MPA also had a better side effect profile than venlafaxine, but the North American trial did not address safety in women at risk for breast cancer.

"The bottom line is, it [MPA] clearly works better. I think it is a reasonable option to give," Dr. Loprinzi, an oncologist at the Mayo Clinic, Rochester, Minn., said in an interview. "Whether is has a small effect on breast cancer risk of recurrence or developing or decrease is unknown."

Dr. Loibl, a gynecologist in Neu-Isenburg, Germany, told this newspaper that the superiority of MPA was not surprising. "But we want to treat, especially breast cancer patients, without hormonal therapy," she said, adding that she would consider it only if a woman has not gained relief after 4 weeks on venlafaxine.

The double-blind German trial randomized 80 breast cancer patients (median age 53) from April 2002 to October 2004, and was able to evaluate 69. All had at least two hot flashes per day at baseline. None used medication to treat hypertension or depression.

During the 5-week study, 34 patients took two 0.075-mg clonidine pills per day; 35 patients took venlafaxine in 37.5-mg pills, also twice a day. The primary end point was frequency of hot flashes at 5 weeks, but the researchers also reported that venlafaxine worked faster, reducing hot flashes significantly in the first week.

Side effects were comparable with both drugs and mostly occurred in the first week. Mouth dryness was the most common in both groups. Tiredness occurred in 25% of the clonidine group and 33% of patients on venlafaxine. About 25% of the venlafaxine patients experienced nausea, but Dr. Loibl said the incidence dropped nearly to zero after the first week.

Four patients stopped treatment early because of side effects, and seven disappeared from follow-up.

In the North American trial, almost two-thirds (63%) of the women had a history of breast cancer. The remaining 37% were afraid to take hormonal treatments because of breast cancer risk, according to Dr. Loprinzi.

All patients enrolled had at least 14 hot flashes a week. None were on antidepressants. Median age was in the mid-50s for all three arms of the 6-week study. The poster report on the study included data on a total of 195 patients.

One group of 94 patients started on a 37.5-mg daily dose of venlafaxine, which increased after 1 week to 75 mg. A second group of 94 patients received a single 400-mg dose of MPA.

A third group stopped accrual with seven patients because of enrollment difficulties. These patients received 500 mg of MPA every other week for 6 weeks. Their results were even better than the single-dose cohort, but their numbers were too small to compare meaningfully.

By the end of the trial, Dr. Loprinzi reported that 22 patients (24%) in the one-dose MPA arm were free of hot flashes compared with one patient (1%) on venlafaxine. In the MPA group, 90% reported residual hot flashes scores as 49% or less of baseline, compared with 63% of those on venlafaxine.

For the most part, MPA also was better tolerated, with patients reporting significantly less constipation, hot flash distress, abnormal sweating, and sleepiness, as well as significantly more satisfaction with hot flash control and trends toward less trouble with sleeping and orgasm.

"Based on efficacy, MPA wins. Based on acute toxicity, MPA wins. Based on cost, MPA is cheaper," Dr. Loprinzi said, balancing the price of a single dose of MPA against daily treatment with venlafaxine.

Safety is the big unanswered question. The concern is whether MPA interferes with hormonal therapies such as tamoxifen and aromatase inhibitors, Dr. Loprinzi said.

"There is not a definitive answer," he said. "You find circumstantial evidence on both sides of the fence."

His group recommended discussing risks and benefits with patients. Dr. Loprinzi said he believes that risk is minimal because MPA has a half-life of 50 days.

"It is a short-term thing," he said. "I think it allows women to gradually go through menopause." ■

Black Cohosh Flunks Phase III Trial

Black cohosh, a popular herbal remedy, failed to reduce hot flashes in a randomized, double-blind, placebo-controlled, phase III crossover trial presented in another poster at the meeting.

Barbara Pockaj, M.D., and her colleagues reported that the average decrease in hot flash scores was larger in placebo users (27%) than in those who received 20 mg of black cohosh daily (20%).

At the end of the 9-week study, 36 (37%) of the 97 patients completing the study preferred placebo, 31 patients (32%) favored black cohosh, and 30 patients (30%) had no preference. The other 19 patients evaluated in the study were listed as missing. The study included breast cancer patients and women with a perceived risk of breast cancer.

Toxicity results gave a slight edge to black cohosh, with no adverse events reported by 87% of patients on the herbal remedy and 77% on placebo.

None of the findings reached statistical significance, Dr. Pockaj of the Mayo Clinic in Scottsdale, Ariz., said in an interview.

"Based on this, I see no reason to take black cohosh," Dr. Pockaj said. "It has no effect at all, not even a suggestion."

Black cohosh is the leading hot flash treatment in Germany, said Dr. Loibl, whose German Breast Group study showed venlafaxine to be effective for hot flashes. "I am very happy that this trial has been done finally, because it shows it [black cohosh] has no effect," she told this newspaper.

Nonetheless, she predicted that physicians would continue to recommend the herbal remedy. Venlafaxine is not approved for hot flashes, whereas black cohosh is available over the counter, Dr. Loibl noted.

Presumed IBS May Be Missed Pelvic Floor Dysfunction

BY TIMOTHY F. KIRN
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CHICAGO — Many individuals diagnosed with irritable bowel syndrome could actually have pelvic floor dysfunction, a condition that can be much more remediable, according to a study conducted at the Mayo Clinic.

Considerable overlap exists in the symptoms of pelvic floor dysfunction and irritable bowel syndrome (IBS), particularly constipation-predominant irritable bowel syndrome, even though the Rome diagnostic criteria for functional bowel disorders considers the two distinctly separate entities, Christopher N. Andrews, M.D., the main investigator of the study, said in a poster presentation at the annual Digestive Disease Week.

The study showed that few patients who present with symptoms of straining, lumpy or hard stools, or a sensation of incomplete evacuation get a pelvic floor work-up as they should, because those with pelvic floor dysfunction probably could be helped by biofeedback training of the pelvic floor muscles, Dr. Andrews said in an interview.

The study included 450 patients being seen at the Mayo Clinic, Rochester, Minn.; 77% of participants were women. The patients either had diagnosed IBS or were undergoing a scintigraphic GI transit study. The patients filled out a symptom questionnaire to help the investigators determine whether they had symptoms the Rome criteria listed in conjunction with pelvic floor dysfunction. Study investigators reviewed the patients' medical records to see if the subjects had been given any anorectal defecation testing.

A total of 194 of the patients had at least two symptoms of pelvic floor dysfunction as outlined by the Rome criteria. But only 50 patients (11%) had undergone pelvic floor dysfunction testing, usually balloon-expulsion manometry. Of those 50 patients, 13 (26%) had an abnormal test result.

Patients with constipation-predominant IBS were more likely to get testing, but they were also more likely to have overlapping symptoms and an abnormal test result.

Of the 78 patients with constipation-predominant IBS, 76 had at least two symptoms of pelvic floor dysfunction. Of those patients, 24 (32%) underwent testing, and among those tested, 8 (33%) had an abnormal test result.

Anorectal defecation testing of patients with IBS-type symptoms is thought to have become more common at highly specialized centers in recent years, Dr. Andrews said in the interview. But if the rate of testing is so low at the Mayo Clinic, then it is probably not done often enough anywhere.

One problem that may discourage testing is that there are different tests but no real standards concerning which to use, he added.

The Rome criteria symptoms used to define pelvic floor dysfunction include: straining when defecating more than 25% of the time, lumpy or hard stools more than 25% of the time, incomplete evacuation more than 25% of the time, sensation of anorectal blocking more than 25% of the time, manual maneuvers to facilitate defecation more than 25% of the time, or one or fewer defecations per week. ■