Gabapentin, Antidepressants Target Hot Flashes

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CHICAGO — Gabapentin and four newer antidepressants significantly reduce hot flash activity, according to a meta-analysis of 10 placebo-controlled studies that was presented as a poster at the annual meeting of the American Society of Clinical Oncology.

As a group, the antidepressants—paroxetine (Paxil), venlafaxine (Effexor), fluoxetine (Prozac), and sertraline (Zoloft)—decreased absolute hot flash scores 26% more than was seen with their corresponding placebo arms ($P = .0001$), reported Dr. Charles L. Loprinzi, professor of oncology at the Mayo Clinic, Rochester, Minn., and his coauthors.

Three trials showed that gabapentin (Neurontin) decreased absolute hot flashes 35%-38% more than did their corresponding placebo arms ($P = .0001$).

The newer antidepressesants all relieve hot flashes, but the efficacy is not identical among them.

DR. LOPRINZI

"This current pooled analysis does support that both newer antidepressants and gabapentin are useful for relieving hot flashes in women. It suggests, however, that the efficacy of newer antidepressants is not identical between the agents," the investigators wrote.

Among the antidepressants, they reported paroxetine and venlafaxine appear to decrease hot flashes more than do sertraline or fluoxetine.

The antidepressants—with the exception of venlafaxine—are selective serotonin reuptake inhibitors that are primarily indicated for treatment of major depressive disorder, obsessive compulsive disorder, and panic disorder.

Paroxetine and sertraline are also indicated for the treatment of social anxiety disorder and posttraumatic stress disorder. Venlafaxine is a mixed serotonin and norepinephrine inhibitor that is indicated for the treatment of major depressive disorder.

Several researchers, including Dr. Loprinzi, have speculated that serotonin modulation plays a role in the effectiveness of these antidepressants against hot flashes.

Gabapentin is indicated for the treatment of postherpetic neuralgia and as an adjunctive treatment of partial seizures in patients with epilepsy. The drug inhibits neuronal calcium currents in vitro, which is hypothesized to play a role in the effectiveness of the drug against neuropathic pain.

Dr. Loprinzi and others have speculated that "similar upregulation of the gabapentin binding site could be involved in the hypothalamus as a result of oestrogen withdrawal, leading to increased activity of the neurotransmitters in the hypothalamus. Gabapentin might exert its effect on hot flashes by this mechanism" (Lancet 2005;366:818-24).

For the analysis, the researchers collected individual patient data (for 10 previous studies assessing the efficacy of paroxetine (2 studies), venlafaxine (1 study), fluoxetine (1 study), sertraline (3 studies), and gabapentin (3 studies).

The change in hot flash activity from baseline to week 4 for each agent was calculated using both weighted and unweighted approaches. The size of the study was used for weighting. Regression models and linear random effects were used to adjust for the effects of age, breast cancer history, and tamoxifen use on hot flash activity.

Data from 1,341 patients indicated that paroxetine, venlafaxine, fluoxetine, and sertraline decreased absolute hot flash scores, respectively, 41%, 33%, 13%, and 3%-18% more than did their corresponding placebo arms. Results were similar for the weighted and unweighted effect size approaches. Adjustment for age, breast cancer history, and tamoxifen use did not have an impact on the findings.

Dr. Loprinzi reported that he has served as a consultant to Concert Pharmaceuticals Inc. Several of his coauthors reported financial relationships with other pharmaceutical companies, including Wyeth, JDS Pharmaceuticals (now owned by Noven Pharmaceuticals Inc.), Depomed Inc., and GlaxoSmithKline. ■