Estrogen Alternatives Ease Menopause Symptoms

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — In the wake of the Women's Health Initiative, "it's easier to get OxyContin out of a doctor's office than Prempro," Melissa A. McNeil, M.D., joked at the annual meeting of the American College of Physicians.

But how then is a physician to manage the vasomotor symptoms of menopause? Dr. McNeil of the University of Pittsburgh said that, although many remedies have advocates, few have been evaluated in controlled studies. She offered several evidence-based suggestions:

► **Time.** Tincture of time works for many women. Although 75% of menopausal women are troubled by hot flashes, for 30%-50% the symptoms improve within months, and hot flashes resolve for most women within 4-5 years.

The fact that hot flashes frequently resolve spontaneously leads to a large placebo effect—in the neighborhood of 25%—in studies of drugs and supplements.

► **Progestins.** There's good evidence from randomized, controlled trials for the efficacy of a number of progestins. Medroxyprogesterone and megestrol (Megace) both were reported to result in a 74% reduction in hot flashes. Depo-Provera was reported in one study to result in a 90% reduction in hot flashes. Uterine bleeding is a frequent side effect of progestin therapy, limiting its use in women with uterine cysts. Furthermore, there are no long-term safety data available.

The most significant bar to progestin therapy, however, comes from Women's Health Initiative results, which suggest that progesterone supplementation may confer an increased risk of certain cancers or adverse cardiovascular events, compared with estrogen alone.

► **Clonidine and methyldopa.** Studies of antihypertensive agents such as clonidine and methyldopa suggest a relatively small effect on hot flashes. Use of clonidine, in particular, is limited by side effects, including dry mouth, constipation, and drowsiness. Still, these drugs may be useful in women who need blood pressure treatment in addition to hot-flash relief.

► **Nonhormonal therapies.** Antidepressants, which are the most promising nonhormonal therapies for hot flashes, have become the mainstay of treatment.

In selecting a treatment for a patient's hot flashes, look for a twofer approach. 'If I'm treating depression, I'll go for an antidepressant.'

Venlafaxine, fluoxetine, and paroxetine all appear to result in 50%-65% reductions in hot flashes in controlled trials, although some of those trials studied breast cancer survivors, who may not be representative of the entire population of menopausal women.

One advantage of antidepressants is that their effect on hot flashes seems to begin relatively quickly—in about 1-2 weeks—compared with about a month for their effects on depression.

► **Gabapentin.** This drug appears to have a modest effect on hot flashes, with a reduction of about 50% in one small trial. About half the women in that trial experienced at least one adverse event, including dizziness, somnolence, palpitations, or peripheral edema.

► **Nutritional supplements.** Although these supplements have received a lot of coverage in the lay press, scientific evidence of their efficacy in treating hot flashes is lacking. Soy phytoestrogens engendered a great deal of enthusiasm a few years back, and several small studies seemed to indicate effectiveness, but more recently a larger controlled trial found no effect on hot flashes. Mixed evidence of effectiveness has been found for vitamin E and black cohosh, but most studies have been small and unblinded. Evening primrose oil, ginseng, and wild yam cream have all been shown to be ineffective.

In selecting a treatment for a patient's hot flashes, Dr. McNeil said that she always looks for a twofer. "If I'm treating depression, I'll go for an antidepressant," she said. "If they have chronic pain I think about gabapentin. And if they have hypertension I might use clonidine. If they're straight out of the starting block, I'd think about venlafaxine as my starting point."

Dr. McNeil said she had no conflicts of interest related to her presentation. ■