Hormone Allergy May Cause Symptoms at Menses

BY JOHN R. BELL
Associate Editor

Progesterone and estrogen may provoke allergic antibody reactions in some women, which might in turn help explain various menstrual disorders, according to a prospective study.

Dr. Russell R. Roby and colleagues from the Roby Institute in Austin, Tex., found increased reactions to both hormones in patients with menstruation-related symptoms compared with control women (Am. J. Reprod. Immunol. 2006;55:307-13).

"Our data presented in this paper are the first to show the presence of IgM and IgE against different steroid hormones," they reported.

The investigators noted that acne, asthma, epilepsy, allergic rhinitis, and other disorders have been linked with menstrual cycle influences.

Their report "suggests the possibility of hormone allergy," they wrote, citing earlier investigations linking hormone reactions to endocrine disorders and periodic rashes.

The researchers sampled the blood of 270 patients from their clinic who reported a change in their menstrual symptoms over the course of 2 years and tested for IgM and IgG antibodies to progesterone.

They also obtained blood samples from 288 unaffected women to serve as a control group.

When blood was tested via enzyme-linked immunosorbent assay, the test patients had a mean optical density (a measure of antibody levels) of 0.17 for IgG and 0.32 for IgM.

In the control population, the mean optical density was 0.08 for IgG and 0.13 for IgM—a statistically significant difference in both cases.

The investigators also tested another group of 98 patients for IgE antibodies against both progesterone and estrogen,

Supplement Raises Venous Thrombosis Risk

Conjugated equine estrogen raises the risk of venous thrombosis in postmenopausal women who have undergone hysterectomy, particularly within the first 2 years of starting the therapy, according to Dr. J. David Curb and his associates in the Women's Health Initiative study.

The portion of the WHI trial that was designed to determine the incidence of cardiovascular events associated with conjugated equine estrogen (CEE) therapy was terminated early because interim analysis showed that risks, particularly stroke risk, outweighed benefit. The final adjudicated data on venous thrombosis from this portion of the WHI trial has now been reported by Dr. Curb, of the University of Hawaii and the Pacific Health Research Institute, Honolulu, and his WHI associates.

In this portion of the WHI trial, 10,739 women aged 50-79 years who had undergone hysterectomy were randomly assigned to receive either 0.625 mg of CEE (Premarin) or placebo. They were followed every 6 months for a mean of 7 years.

During that time, venous thromboembolism occurred in 111 women (0.30% per year) in the CEE group and 86 women (0.22% per year) in the placebo group, with a hazard ratio (HR) of 1.32.

Deep vein thrombosis occurred in 85 women (0.23% per year) in the CEE group and 59 women (0.15% per year); the HR was 1.47. Pulmonary embolism was reported in 52 women (0.14% per year) in the CEE group and 39 women (0.10% per year) in the placebo group, for an HR of 1.37. The increased risk was highest during the first 2 years of estrogen therapy (Arch. Intern. Med. 2006;166:772-80).

"Our data suggest that although the absolute incidence is relatively low, the use of CEE increases the relative risk of venous thrombosis in postmenopausal women without a uterus. Women with appropriate indications, such as short-term treatment of severe menopausal symptoms, should use CEE only after careful consideration of the relative risks and benefits, especially if the women have other risk factors for venous thrombosis, including previous venous thrombosis, older age, obesity, and perhaps factor V Leiden," the researchers said.

—Mary Ann Moon

using a control group of 320 patients (the same 288 from a commercial laboratory plus 32 from their clinic with possible hormone allergy).

For progesterone, test patients had a mean optical density of 0.42, compared with a mean optical density of 0.11 in the lab-based control group and 0.23 in the clinic-based control group—a highly significant increase, the investigators noted.

For estrogen, the test group's mean optical density was 0.69, compared with 0.15 for the lab-based controls and 0.24 for the local controls—also a highly significant difference. ■

Estrogen Alone Didn't Raise Breast Ca Risk

BY MARY ANN MOON
Contributing Writer

Unopposed estrogen therapy in postmenopausal women who have undergone hysterectomy does not appear to raise the risk of breast cancer, in clear contrast to the significant rise in breast cancers among postmenopausal women with intact uteri who take estrogen plus medroxyprogesterone.

However, conjugated equine estrogen (CEE) therapy alone does increase the number of abnormal mammograms requiring follow-up, which includes aspiration and biopsy as well as the attendant emotional and economic costs of each, according to Marcia L. Stefanick, Ph.D., and her associates in the Women's Health Initiative (WHI) study.

The decision to use CEE in postmenopausal women without a uterus, therefore, "should continue to be based on careful consideration of potential risks and benefits for a given individual," said Dr. Stefanick, a professor of medicine in the prevention research center at Stanford (Calif.) University, and her WHI associates.

The portion of the WHI study that addressed estrogen-only therapy involved 10,739 postmenopausal women aged 50-79 years who had undergone prior hysterectomy and were treated at 40 clinical centers across the United States between 1993 and 1998. The women were randomly assigned to receive either 0.625 mg of CEE (Premarin) or a placebo and were assessed at 6-month intervals.

The study was terminated early in 2004 because interim analysis showed that CEE raised stroke risk without reducing the risk of coronary heart disease. But preliminary analysis of the results up to that date also showed that compared with women taking placebo, those taking CEE had fewer breast cancers. This finding of a possible protective effect prompted an updated analysis, and the WHI investigators now report the results on 237 invasive and 55 in situ breast cancers that developed by the date that subjects were instructed to stop taking their study pills (JAMA 2006;295:1647-57).

After 1 year, 9.2% of the women on estrogen and 5.5% in the placebo group had abnormal mammograms.

DR. STEFANICK

In an intention-to-treat analysis, there were nonsignificant reductions in invasive breast cancers and total breast cancers among women taking CEE only, compared with those taking placebo. There was no effect on in situ disease. Further analysis showed that the number of advanced cancers was comparable between the two groups of patients, but there were fewer cases of localized disease in the CEE group.

"In the completed trial database, the invasive breast cancer incidence did not differ significantly between the CEE group and the placebo group," investigators said.

After 1 year of therapy, the percentage of abnormal mammograms was "substantially higher" in the CEE group (9.2%) than in the placebo group (5.5%). This pattern held constant for each year thereafter, for a cumulative rate of 36.2% in the CEE group and 28.1% in the placebo group.

By the end of the study, women in the CEE group had undergone 198 biopsies or aspirations that yielded negative findings, Dr. Stefanick and her associates noted.

The percentage of mammograms showing "suspicious" rather than simply abnormal findings was similar for both groups, as was the percentage of mammograms that were highly suggestive of malignancy. In contrast to these findings, the results of the CEE plus progesterone portion of the WHI trial showed a definite increase in invasive breast cancers with combined therapy, as well as a definite increase in mammograms deemed "suspicious" or "highly suggestive of malignancy," they noted. ■