So Many Menopause Supplements, So Little Data

BY BRUCE JANCIN

COLORADO SPRINGS — Just how popular are natural herbs, vitamins, and supplements for the treatment of menopausal symptoms?

Here's a clue: 5 of the top 10 best-selling herbal dietary products in the United States for 2007 are used predominantly by women with menopausal symptoms, Dr. Walter L. Larimore said at the annual conference of the Colorado Academy of Family Physicians.

Those products are soy (No. 1), ginkgo biloba (No. 4), black cohosh (No. 7), ginseng (No. 9), and St. John's wort (No. 10). In addition, 4 other products used primarily for menopausal symptoms round out the list of the top 20 best-selling natural products in 2007, the most recent year for which data are available: evening primrose oil (No. 12), valerian (No. 13), grape seed (No. 16), and red clover (No. 18), noted Dr. Larimore, a Colorado Springs family physician.

It's worth noting, however, that the sales volume for most of these products has been on the decline since 2001.

"Our patients are beginning to understand that natural doesn't mean safe, that there are contamination problems, and natural certainly doesn't necessarily mean inexpensive," he said.

Natural medications are unregulated in the United States. As a result, the field of complementary and alternative medicine is "a Wild West arena," according to the family physician.

"You have no way of knowing if substances will be the same from bottle to bottle or lot to lot, whether the bottle actually contains what the label says, if there's contamination, or if the product is bioabsorbable," he continued.

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DR. LARIMORE

The evidence base for the use of natural medications for menopausal symptoms is generally paltry. The studies are typically small and short. Expert opinion as to which products have a reasonable likelihood of being safe and effective often changes quickly in response to new data.

To keep current in the face of a daily barrage of patient inquiries about alternatives to hormone therapy for menopausal symptoms, Dr. Larimore recommended the use of two subscription-based Web sites that provide trustworthy information: the Natural Medicines Comprehensive Database (www.naturaldatabase.com) and ConsumerLab (www.consumerlab.com).

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Two German extracts of black cohosh (shown above) are "possibly effective/possibly safe."

"I couldn't practice family medicine without them," he said.

The Natural Medicines Comprehensive Database (NMCD) provides access to 5,700 monographs, including systematic reviews, meta-analyses, and detailed descriptions of any interactions an agent may have with prescription drugs or disease states.

ConsumerLab is an independent quality testing laboratory. ConsumerLab staff buy products off the shelf in stores, test them for strength, labeling accuracy, the presence of lead and other contaminants, and bioabsorption, then report which ones pass or fail. Subscribers have access to roughly 1,200 monographs.

"Anytime you recommend something to a patient—say, a calcium supplement—you can look up the monograph and see a list of the specific products that pass their tests," Dr. Larimore said. "Print it out, hand it to your patient, and say, 'Buy the cheapest one.' "

Last fall, for example, ConsumerLab reported that three of five tested black cohosh products and two of three combined red clover/soy isoflavones products did not meet quality standards. And they named names.

Based on his synthesis of evidence from NMCD, the North American Menopause Society, the American College of Obstetricians and Gynecologists, and the Food and Drug Administration, Dr. Larimore created a list of recommended natural medications for menopausal symptoms. None of the natural products earned a "likely effective" rating. In the category of "possibly effective/likely safe," however, he listed soy foods, soy protein, lifestyle changes, flaxseed, vitamin E, and pycnogenol.

Under the heading "possibly effective/possibly safe," Dr. Larimore placed soy extracts and two German extracts of black cohosh sold in the United States under the brand names Remifemin and Klimadynon.

Because of insufficient evidence of safety and/or efficacy, no other natural medications that women are now taking for menopausal symptoms can reasonably be recommended, in his view. ■

Hormone Tx in All Forms Appears to Up Ovarian Ca Risk

BY MARY ANN MOON

All hormone therapy—regardless of the formulation, estrogen dose, progestin type, dose regimen, route of administration, or duration of use—appears to raise the risk of ovarian cancer, according to a report.

If the association between HT and ovarian cancer proves to be causal, it would mean that as many as 5% of such malignancies could be attributable to the treatment. "Even though this share seems low, ovarian cancer remains highly fatal, so accordingly this risk warrants consideration when deciding whether to use [HT]," said Lina Steinrud Mørch of Copenhagen University and her associates.

They assessed ovarian cancer using data from the Danish Sex Hormone Register Study, a national 10-year cohort study of nearly 1 million Danish women. Ms. Mørch and her colleagues restricted their analysis to the 909,946 women who were perimenopausal or postmenopausal at baseline in 1995.

This included 575,883 women who had never used HT and 334,063 who had. Among the current users of HT, nearly half had been taking the hormones for more than 7 years.

A total of 3,068 incident ovarian cancers developed in the study period, including 2,681 that were epithelial tumors.

Compared with women who had never taken HT, those who had showed a relative increase of 30%-58% in their risk of developing ovarian cancer, according to Ms. Mørch and her colleagues (JAMA 2009;302:298-305).

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DR. UTIAN

The risk did not differ significantly by duration of use, with women who took HT for up to 4 years showing similarly increased risk as those who took it for 5 years or more. Similarly, women who took estrogen alone had about the same risk as did those who took combined estrogen plus progestin.

Women who took cyclic HT had increased risk similar to that in women who took continuous HT. And ovarian cancer risk was elevated regardless of HT dosage and regardless of whether HT was delivered by oral tablet, patch, or gel.

"If the difference in risk between never users and current users is due to hormone therapy, these results imply that use of HT resulted in about 1 extra case of ovarian cancer for roughly every 8,300 women taking HT each year," the investigators wrote.

In commenting on the study, Dr. Wulf H. Utian, executive director of the North American Menopause Society, said, "The possibility of a very slight increase in ovarian cancer risk [with HT] should be added to the risk-benefit discussion" between physicians and patients. Women who have severe vasomotor symptoms negatively affecting their quality of life are likely to take the risk, he added.

Although Dr. Utian said the Scandinavian figures are probably "as reliable as you can get in a public health system," he said he had concerns about the study's methodology. In evaluating different HT regimens, the investigators included in the progestin category drugs that are not progestins such as cyproterone acetate, an antiandrogen, and raloxifene, a selective estrogen receptor modulator (SERM).

"What they've got here is fruit salad. They've got all different kinds of products lumped together, and they haven't adequately broken them out," he said. Of the progestins that were specified, norethisterone acetate, the one most widely used in the study, was significantly associated with an increased risk of ovarian cancer; however, medroxyprogesterone acetate and levonorgestrel were not associated with an increased risk of ovarian cancer.

In addition, the investigators did not specify the type of estrogen used in their study, he noted. This contrasts with the Women's Health Initiative, a randomized, controlled study that found that Premarin (conjugated estrogens) does not increase ovarian cancer risk. The conjugated estrogen formulation is not used in Denmark, he said, so it's unlikely that it was part of the current study.

Dr. Utian reported no conflicts of interest relevant to the European drugs used in the study, but said he has consulted for several pharmaceutical companies that make estrogen products, including transdermal estrogen and SERMs. He reported being an investigator in a study of a SERM manufactured by Wyeth Pharmaceuticals.

Ms. Mørch reported no conflicts of interest. Dr. Øjvind Lidegaard, an associate in the Danish study, reported receiving a grant from Schering AG, Berlin, to cover research expenses and has received fees for speeches from Schering Denmark and Novo Nordisk. This study was supported by a grant from the Danish Cancer Society. ■

Felicia Rosenblatt Black contributed to this report.