HT for Women With Very Low Estradiol

BY ALISON PALKHIVALA
Contributing Writer

MONTREAL — Postmenopausal women with extremely low levels of bioavailable estradiol may benefit most from the bone-building effects of ultralow-dose hormone therapy, according to a study presented here at the annual meeting of the International Bone and Mineral Society.

It remains unclear, however, whether these women are also more vulnerable to the negative effects of hormone therapy. Although estrogen therapy has been shown to suppress bone turnover in postmenopausal women, the Women's Health Study also revealed in 2002 that it may increase cardiovascular risk. Experts are therefore exploring the possibility that a dose of estrogen exists, at least for some women, that is high enough to improve bone parameters but too low to affect cardiovascular risk.

Dr. Alison Huang, of the University of California, San Francisco, and colleagues explored whether an ultralow dose of estradiol—only 0.014 mg/day delivered transdermally—could be of benefit to postmenopausal women with very low or even undetectable estradiol levels. This group of patients was considered to have a high likelihood of benefiting because, as a group, they have a lower bone mineral density (BMD), increased bone turnover, and are at an increased risk for hip and vertebral fractures.

For the trial, 417 postmenopausal women were randomized to a 0.014-mg/day transdermal estradiol patch or to placebo for 24 months. Bioavailable estradiol levels in these women were calculated as the ratio of total estradiol to sex hormone–binding globulin.

The investigators measured the women's levels of serum osteocalcin and bone-specific alkaline phosphatase (BSAP), both markers of bone turnover, at 12 months. They also measured total hip and lumbar spine BMD at 24 months in women who adhered at least 80% to the study protocol.

Women in the lowest quintile of bioavailable estradiol had significantly greater reductions in osteocalcin and BSAP than women in the highest quintile of bioavailable estrogen in response to therapy. In women in the lowest quintile, there was also a trend toward greater improvement in total hip BMD, compared with women in the highest quintile. There was no evident impact of treatment on spine BMD.

On the basis of these results, the authors concluded that "measurement of bioavailable estradiol levels identifies women for whom the ultralow-dose 0.014-mg/day transdermal estrogen therapy may have significant reductions in bone turnover."

During a press conference, however, Dr. Huang warned that it is still not clear whether the very women who appear to have most to gain from estradiol therapy—those with very low baseline bioavailable estradiol levels—may also have most to lose. That is, these women may be most vulnerable to the effects of hormone therapy on cardiovascular health. ■

Flaxseed May Reduce Hot-Flash Frequency

BY FRAN LOWRY
Orlando Bureau

Preliminary data from a phase II pilot study suggest that flaxseed may be a useful alternative to estrogen in the management of hot flashes, according to Dr. Sandhya Pruthi of the Mayo Clinic, Rochester, Minn., and associates.

A 6-week regimen of crushed flaxseed, given at 40 g daily, decreased the number of hot flashes from a mean of 7.3 per day to 3.6 per day in women who did not wish to receive estrogen therapy, Dr. Pruthi and associates reported in the Journal of the Society for Integrative Oncology.

Estrogen therapy has been the effective hot-flash treatment most commonly used, but fears that it may cause breast cancer have made many postmenopausal women reluctant to take it for their menopausal symptoms. Their concerns have prompted a search for nonhormonal alternatives.

The authors tested the tolerability and effect of flaxseed therapy in 28 women who had at least 14 bothersome hot flashes per week for more than 1 month before study entry. Participants were instructed to sprinkle 2 tablespoons of crushed flaxseed on cereal, in juice, in yogurt, or on fruit twice daily for 6 weeks. Each tablespoon provided 10 g of flaxseed, and the women were instructed to drink at least 150 mL of liquid for each 10 g of flaxseed they consumed (J. Soc. Integr. Oncol. 2007;5:106-12).

In the last week of flaxseed therapy, the hot-flash score—a measure of hot-flash frequency and severity—decreased by a mean of 57%, with a median decrease of 62%. The mean decrease in the number of hot flashes per day (from 7.3 to 3.6) was significant. Participants also reported a statistically significant improvement in quality of life, with less anger, anxiety, and fatigue at the end of the trial than at the beginning.

Abdominal distention or bloating was experienced by half of the women at some time during the study, and six women failed to complete the full 6 weeks of flaxseed therapy because of abdominal toxicities, weight gain, or taste intolerance, the authors reported. "These issues need to be evaluated further in a placebo-controlled manner. It is possible that initiating flaxseed therapy at a lower dose—and titrating the dose upward—may decrease abdominal toxicities," Dr. Pruthi and associates wrote.

Flaxseed contains weak estrogenic properties that "seem to account for the most likely mechanism of its effectiveness in reducing hot-flash activity," according to the investigators. ■

Endometriosis, Parity Not Linked in Ca Risk

BY KATE JOHNSON
Montreal Bureau

LYON, FRANCE — The increased risk of cancer seen in patients with endometriosis is unrelated to parity, according to a large study—the first to examine this association.

"We found that contrary to what one might expect, endometriosis and nulliparity did not combine to give a higher cancer risk," said Dr. Anna-Sofia Mellin, who presented the results at the annual meeting of the European Society for Human Reproduction and Embryology. "We could not show a difference in risk between parous and nonparous women."

Her study identified 63,630 women, using the National Swedish Inpatient Register, who were discharged from hospital with a diagnosis of endometriosis between 1969 and 2002. From this cohort, 3,822 cancer cases were subsequently identified, using the National Swedish Cancer Register.

The study found no overall increased risk of cancer associated with endometriosis (standardized incidence ratio [SIR] 1.01); however, significantly elevated risks were found for specific cancers such as endocrine tumors (SIR 1.38), ovarian cancer (SIR 1.37), kidney cancer (SIR 1.36), thyroid cancer (SIR 1.33), brain tumors (SIR 1.27), melanoma (SIR 1.23), and breast cancer (SIR 1.08), said Dr. Mellin of the Karolinska Institute in Stockholm.

Endometriosis was associated with a reduced risk of cervical cancer (SIR 0.71).

When parity was considered, no significant differences were noted between parous and nonparous women, although a nonsignificant decrease in ovarian cancer was noted with parity (from SIR 1.48 in nonparous women to SIR 1.3 in parous women).

Most of the increased cancer risk was seen in women with ovarian endometriosis, with only a small but significant increase seen in those with peritoneal endometriosis and no increased risk associated with adenomyosis, she said.

Although the findings are cause for concern, Dr. Mellin said it is too early to recommend that all endometriosis patients receive cancer screening.

"We don't even have any screening for ovarian cancer, so we don't know how to follow these patients. We know that even if you get an ultrasound every year you still get ovarian cancer and it still may have grown too far," she said in an interview. ■