Soy Fails to Cut Hot Flashes in Breast Ca Survivors

Some success in the first 4 weeks of the trial was attributed to discovery of triggers in online journals.

BY JANE SALODOF MACNEIL
Southwest Bureau

ATLANTA — High-dose isoflavone soy supplements failed to control the hot flashes of breast cancer survivors in a randomized controlled trial presented in a poster at the annual meeting of the American Society of Clinical Oncology.

Although the crossover trial was halted midway for failing to show benefit, 82% of participants reduced their hot flashes during the first 4 weeks of the study. The key to their success, Dr. William C. Dooley reported, apparently was an online Internet journal that all the women filled out each day.

"Most patients, whether they started on soy or placebo, came up with triggers for hot flashes that they could avoid and decrease the frequency," Dr. Dooley, chair of surgical breast oncology at the University of Oklahoma in Oklahoma City, said in an interview at the meeting.

"They were writing that in their journals and after the first month the hot flashes had dropped over 30% and the severity dropped dramatically just by avoidance of diet, emotion, or other triggers," he said. "There was no difference between the soy and placebo."

Dr. Dooley and his coinvestigators enrolled 168 breast cancer survivors for what was to be a 16-week crossover trial. All were suffering from hot flashes and had progressed at least 6 weeks beyond completion of surgery, chemotherapy, or radiation. Patients on tamoxifen or another adjuvant hormonal therapy were allowed.

The double-blind design called for all women to participate in a 4-hour-per-week exercise program and take two dietary supplements, one of which contained 130 mg of isoflavone soy. Dr. Dooley said the dose was comparable with the amount of soy in the Japanese diet and much higher than is usually studied in randomized trials.

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DR. DOOLEY

Of the original 168 enrollees, 51 dropped out either because they failed to complete the exercise requirement or because the physicians managing their care had objections. Another 13 participants stopped using the supplements. The usual reason was gas and/or gastrointestinal distress from the soy supplement or the casein placebo. This left 104 evaluable patients in the analysis.

Dr. Dooley said the journal component was added to the trial by breast cancer survivors who "wanted to share more information than multiple choice answers when it was over."

Patients recorded hot flash frequency, severity, and time of day as well as exercise time in Internet diaries, which they accessed by password on a server compliant with the Health Insurance Portability and Accountability Act.

This turned out to be the most interesting part of the study, according to Dr. Dooley. "There is some benefit of journaling, so they will learn to avoid hot flashes," he said.

Although the investigators did not find soy to provide any benefit in symptom control, Dr. Dooley said they have not ruled out other advantages.

"We did not look at cholesterol, bone density, or heart disease. … Those are some things we are going to look at in future," he said, adding that his group is assessing soy's impact on atypical hyperplasia in another ongoing trial. ■

No Breast Cancer Risk Reduction Seen With Calcium, Vitamin D

BY MELINDA TANZOLA
Contributing Writer

ATLANTA — Calcium plus vitamin D supplementation in postmenopausal women does not appear to reduce their risk of breast cancer, according to results from a Women's Health Initiative randomized trial presented at the annual meeting of the American Society of Clinical Oncology.

After a median of 7 years, women who received 1,000 mg of calcium carbonate plus 400 IU of vitamin D_3 were no less likely to develop breast cancer than were women who received placebo. In the study, Dr. Rowan T. Chlebowski and his colleagues randomized 36,282 women aged 50-79 years with no prior breast cancer who were already enrolled in the WHI diet or hormone trials to receive calcium plus vitamin D or placebo. Supplements were provided by GlaxoSmithKline.

In her discussion of the study, Dr. Carol Fabian suggested that several variables could have contributed to the lack of effect observed in the study. First, the mean calcium intake at baseline was 1,165 mg/day in both arms, already approaching the recommended optimal intake.

Second, women in either arm could, on their own, use supplements of up to 1,000 mg of calcium and 1,000 IU of vitamin D per day. During the fifth year of the trial, nonprotocol supplement use on average totaled 200 mg of calcium and 400 IU of vitamin D—an amount of vitamin D equivalent to the study dose, noted Dr. Chlebowski, a professor of medicine at the University of California, Los Angeles, in his presentation. This reduced the difference in vitamin D intake between the experimental and control arms.

Dr. Fabian, a professor of medicine at the University of Kansas Medical Center in Kansas City, said that recent studies indicate that the amount of vitamin D needed to see a benefit for breast cancer reduction may be quite high, about 3,000 IU per day. This is significantly higher than the study dose of 400 IU per day.

"I would like to suggest, although we don't know, that the intervention did not provide nearly enough vitamin D," Dr. Fabian said. She recommended that women strive to get 15-20 minutes of sun per day or take 1,000-2,000 IU vitamin D_3 per day. "If this sounds like a high level to you, I will point out … a number of vitamin D experts who think that the current recommendations that we see for vitamin D are way too low, and we must increase the levels to at least 1,000 units of vitamin D per day."

Whereas calcium intake at baseline was already high, women entering the study had fairly low vitamin D levels at baseline; 85% of women had a serum 25-hydroxyvitamin D level below 30 ng/mL, suggesting vitamin D insufficiency. Among the 19,115 women not using vitamin D supplements at baseline, those in the calcium plus vitamin D group had a significant 18% reduction in breast cancer risk. Dr. Fabian also said that by enrolling postmenopausal women, the trial could have started supplementation too late in the precancerous process.

The primary end point of the trial, the incidence of hip fracture, was not significantly different between arms (N. Engl. J. Med. 2006;354:669-83), nor was the incidence of colorectal cancer (N. Engl. J. Med. 2006;354:684-96). As previously reported, there was a significant 17% increased incidence of kidney stones with calcium plus vitamin D.

The current analysis found no relationship between baseline serum 25-hydroxyvitamin D levels and arthritis incidence. Moreover, after 2 years, calcium plus vitamin D had no effect on joint pain or swelling. Estrogen use did appear to significantly reduce joint pain. After 3 years, the incidence of joint pain in women taking estrogen was 70.6%, compared with 77.2% in those not taking estrogen. ■

Weight Gain in Adulthood Tied to Breast Cancer Risk

BY MARY ANN MOON
Contributing Writer

Women who gain weight either in early adulthood or after menopause are at increased risk for postmenopausal breast cancer, compared with women who maintain a stable weight, reported Dr. A. Heather Eliassen of Harvard Medical School and her associates in the Nurses' Health Study.

An estimated 15% of breast cancer cases may be attributable to weight gain of 2 kg or more since age 18.

Moreover, women who lose weight after menopause decrease their breast cancer risk (JAMA 2006;296:193-201).

The researchers based these conclusions on a prospective analysis of a subset of 49,514 women participating in the Nurses' Health Study, an ongoing survey of women nurses who were premenopausal when they enrolled in 1976 and have been followed since then. All the subjects for this analysis were postmenopausal. Weight change during two time periods—after age 18 and after menopause—was examined.

Compared with women who maintained a stable weight after age 18, those who gained at least 25 kg were at increased risk of developing breast cancer, with an adjusted relative risk of 1.45. Similarly, compared with women who maintained a stable weight after menopause, those who gained at least 10 kg were at increased risk of developing breast cancer, with an adjusted relative risk of 1.18.

Conversely, weight loss during either of those time periods was linked to a decreased risk of breast cancer. However, since relatively few women lost weight, particularly after menopause, "more follow-up is needed to confirm our findings [regarding weight loss] and characterize the benefits more precisely," Dr. Eliassen and her associates said.

The calculated incidence rate of breast cancer in women who gained at least 25 kg after age 18 was 429 cases per 100,000 person-years, compared with 296 cases in women with stable weight. The calculated incidence rate of breast cancer in women who gained at least 10 kg after menopause was 400 cases per 100,000 person-years, compared with 339 cases in women with stable weight.

"In addition, we estimated that 15% of postmenopausal breast cancer cases in our population may be attributable to weight gain of 2 kg or more since age 18 years, and 4.4% attributable to weight gain of 2 kg or more since menopause," the researchers said.

These calculations suggest that weight gain during either time period "contributes substantially" to breast cancer incidence, and that many cases of the disease could be avoided by maintaining weight throughout adulthood. ■