Vitamin D From Diet or Sun Curbs Breast Ca Risk

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Women who get plenty of vitamin D, especially early in life, are less likely to develop breast cancer than women who get smaller amounts of the vitamin, according to data from two studies presented at the annual meeting of the American Association for Cancer Research.

Julia Knight, Ph.D., of Mount Sinai Hospital in Toronto, and her colleagues conducted a case-control, population-based study of women aged 20-59 years from a Canadian cancer registry and the surrounding community. They identified 971 cases of breast cancer and 1,135 controls and asked the women about lifetime sun exposure and dietary vitamin D.

Logistic regression analyses adjusted for variables including age, ethnicity, age at menarche, age at first pregnancy, duration of breast-feeding, and family history of breast cancer.

Overall, participating in any outdoor work at any point in life resulted in about a 40% reduction in breast cancer risk (odds ratio 0.60). Participation in at least six types of outdoor activities at ages 10-19 years and at least five types of outdoor activities at ages 20-29 years reduced the risk by about 35%. Outdoor activities did not have to involve physical activity, Dr. Knight noted. However, the risk reduction was not as robust in women who reported that they had kept their arms and legs covered outside.

In addition, drinking at least nine glasses of milk per week at ages 20-29 years was significantly associated with reductions in breast cancer risk, as was the regular consumption of cod liver oil for at least 10 years.

"In general, most women drank more milk when they were younger," Dr. Knight said. Vitamin D exposure during breast development or prior to pregnancy may be particularly important in preventing breast cancer later on, she added.

Women with 25-(OH)D levels less than 50 ng/mL were six times more likely to develop breast cancer than those with levels greater than 50 ng/mL.

The evidence for the protective role of vitamin D appeared to weaken with age. By ages 45-54 years, there was some evidence of reduced risk associated with outdoor activity, but it was no longer significant, although the risk was no longer affected by whether the arms and legs were covered.

When asked about the role of vitamin D supplements, Dr. Knight admitted that supplements of any sort complicate the picture. "The problem with supplements is that there tends to be a reduced risk in anyone who takes any kind of vitamin supplements, whether they include vitamin D or not," she said. People who take supplements tend to have other characteristics of a healthy lifestyle, she said.

"We did ask about sunscreen. We are still analyzing that because it is complicated, since sunblock use has only become common in the last 20 years," she said.

Increasing the levels of serum vitamin D in the body, regardless of age, may reduce the risk of breast cancer, according to a second study presented at the meeting by Cedric F. Garland, Dr.P.H., of the University of California, San Diego.

Dr. Garland and his associates reviewed data on a total of 1,760 women in two studies. In the first, a serum 25-hydroxyvitamin D (25[OH]D) level of 35 ng/mL was associated with a 20% drop in breast cancer risk (Cancer Epidemiol. Biomarkers Prev. 2005;14:1991-7).

A second study of 179 women with breast cancer and 179 controls showed that as vitamin D levels in the blood increased, the risk of breast cancer decreased. Women with 25-(OH)D levels less than 50 ng/mL were six times more likely to develop breast cancer than those with levels greater than 50 ng/mL (Eur. J. Cancer 2005;41:1164-9).

Dr. Garland chose these two studies because 25 (OH) D has been shown to vary with geography. Death rates from breast cancer could be as much as three times higher in the Northeast, compared with the Southwest, because of reduced vitamin D intake from sunlight, he noted.

Based on these studies, "if we can get women up to 20-22 ng/mL of serum vitamin D, we could expect a 20% reduction in breast cancer risk. We think this is a good aim," Dr. Garland said. Levels closer to 52 ng/mL—which are common among some women in sunny areas such as California—would be even better, he noted. Some women in the Northeast have vitamin D levels of about 15 ng/mL, and some women have levels so low that they are barely detectable, he added.

A vitamin D intake of 2,000 IU/day has been associated with vitamin D levels of 32 ng/mL. That intake is well above the average consumption of most American women, but below the upper limit of 2,400 IU that is currently recommended by the National Academy of Sciences. But even 1,000 IU/day may produce a vitamin D level of about 22 ng/mL.

"Levels above 2,400 IU are terra incognita," Dr. Garland said. The lowest level of vitamin D associated with toxicity is 3,800 IU, according to the National Academy of Sciences. Some scientists have proposed daily intakes of 4,000 IU. In any case, supplements and vitamin-fortified foods, such as cereals and grains, will be necessary for most people to maintain optimal levels of vitamin D, he noted. ■

Salpingo-Oophorectomy Cuts Cancer Risk in BRCA2 Carriers

BY MELINDA TANZOLA
Contributing Writer

ATLANTA — Salpingo-oophorectomy appears to significantly reduce the incidence of gynecologic cancers in all women with BRCA mutations and the incidence of breast cancer in women with BRCA2 mutations.

This conclusion is based on the results of a multicenter, prospective study presented at the annual meeting of the American Society of Clinical Oncology.

After about 3 years of follow-up, the 546 women who elected to receive risk-reducing salpingo-oophorectomy had a 90% reduction in gynecologic cancers and a 47% reduction in breast cancer incidence compared with the 325 women who chose not receive surgery. However, the risk reduction in breast cancer was limited to women with BRCA2 mutations.

"BRCA1 and BRCA2 cause related but distinct cancer susceptibility syndromes," explained Dr. Noah D. Kauff in his presentation. He therefore thought it was important to examine the benefit of risk-reducing salpingo-oophorectomy in each population.

In all, 597 women with breast tissue at risk at the start of follow-up were included in the breast cancer risk analysis. Among women carrying the BRCA1 mutation, 15 of 190 patients treated with risk-reducing salpingo-oophorectomy developed breast cancer, compared with 19 of 178 patients not treated with surgery, a 39% risk reduction that was not statistically significant.

Among BRCA2 carriers, the incidence with surgery vs. surveillance was 4 of 113 patients and 9 of 116 patients, respectively, resulting in a significant 72% reduction in cancer risk.

The study, led by Dr. Kauff, of the Memorial Sloan-Kettering Cancer Center in New York, evaluated two prospective cohorts of women carrying a BRCA mutation. Compared with women who chose not to receive risk-reducing salpingo-oophorectomy, those treated with surgery were significantly older (mean age, 47 vs. 43 years), were more likely to have had breast cancer in the past (59% vs. 46%), were more likely to have taken hormone therapy (11% vs. 7%), and were significantly more likely to have given birth (83% vs. 74%).

An exploratory analysis showed an overall 78% risk reduction in estrogen receptor–positive cancer, compared with no significant change in the incidence of ER-negative breast cancer.

"Since most breast cancers related to BRCA1 mutations are ER-negative, it could be postulated that hormonal manipulation—in this case, risk-reducing salpingo-oophorectomy—might not be effective in this population," said Dr. Banu Arun in her discussion of the study.

Dr. Arun, of the department of breast medical oncology at the University of Texas M.D. Anderson Cancer Center, Houston, suggested that future prospective studies should evaluate risk-reducing salpingo-oophorectomy plus a non-hormonal preventive agent, such as cyclooxygenase-2 inhibitors, retinoids, statins, or other agents, for women with BRCA1 mutations. ■

Transdermal Testosterone Fails to Boost Libido in Cancer Survivors

BY MELINDA TANZOLA
Contributing Writer

ATLANTA — Transdermal testosterone was no better than placebo for improving libido in female cancer survivors after 4 weeks, according to results of a randomized, blinded, crossover study presented at the annual meeting of the American Society of Clinical Oncology.

In the 131 women who completed the study, both testosterone and placebo provided similar significant improvements in libido.

The North Central Cancer Treatment Group's N02C3 study randomized 150 women to 10 mg/day transdermal testosterone in Vanicream (Pharmaceutical Specialties, Inc.) or placebo (vehicle alone) for 4 weeks, followed by a crossover to the opposite treatment arm for 4 weeks.

All women were postmenopausal with no active disease, and all had reported decreased sexual desire. The investigators excluded women with comorbidities that might confound results. Women were an average of 52 years old; 31% were receiving aromatase inhibitors during the study, and 47% were receiving tamoxifen. Most women (72%) had at least one intact ovary, 80% had received prior chemotherapy, and only 7% had received pelvic radiotherapy.

Efficacy was measured using the Changes in Sexual Functioning Questionnaire (CSFQ) after each 4-week period. The average CSFQ score was 5.5 with testosterone and 4.4 with placebo after the first period and 8.8 and 8.1 after the second period.

"These results might seem very surprising, given the plethora of evidence that shows that transdermal testosterone is effective," said study author Debra L. Barton, Ph.D., in her presentation. She suggested that the exclusion of women on supplemental estradiol in this trial and its relatively short duration might account for these differences. She also noted that previous studies had reported modest benefits with testosterone.

Low libido is a common issue in female cancer survivors. This clinical impression is validated by the speed with which the trial reached, and actually exceeded, its predicted accrual, according to Dr. Barton, of the Mayo Clinic College of Medicine, Rochester, Minn.

Testosterone treatment significantly increased the levels of free testosterone and bioavailable testosterone in the serum. A safety analysis of self-reported symptoms revealed no differences in side effects associated with virilization. ■

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