Tamoxifen's Benefits, Risks Confirmed in Update

NSABP study follow-up proved the drug to be useful in cutting breast cancer and fracture risk in women.

BY MARY ANN MOON
Contributing Writer

Tamoxifen substantially cuts the risk of invasive and noninvasive breast cancer, researchers confirmed in an extended follow-up of the National Surgical Adjuvant Breast and Bowel Project that was initially reported in 1998.

This update of the NSABP study involved 13,207 women at high risk of developing breast cancer who had participated in the initial study in 1992-1997 and were followed for an additional 7 years. A total of 6,597 subjects composed the tamoxifen group and 6,610 formed the placebo group.

All the benefits and risks of tamoxifen therapy that had been reported in the initial study were borne out in this extended study, according to Bernard Fisher, M.D., scientific director of the NSABP and distinguished surgical professor at the University of Pittsburgh.

Tamoxifen was linked to a 43% reduction in the cumulative rate of invasive breast cancer. The rate was 24.8 cancers/1,000 women taking tamoxifen, compared with 42.5/1,000 women taking placebo.

Similarly, tamoxifen reduced the cumulative rate of noninvasive breast cancer by 37%. The rate was 10.2 cancers/1,000 women taking tamoxifen, compared with 15.8/1,000 women taking placebo.

The drug cut the risk of breast cancer in all subgroups of subjects categorized by age, history of lobular carcinoma in situ (LCIS), history of atypical hyperplasia, and level of predicted risk of breast cancer.

Among women who took tamoxifen, the incidence of breast cancer remained relatively constant throughout the 7 years of follow-up, remaining stable for at least 2 years after they finished a 5-year course of the drug (J. Natl. Cancer Inst. 2005; 97:1652-62).

As it did in the initial NSBAP study, tamoxifen also reduced the risk of osteoporotic fractures of the hip, spine, and radius in this extended study. Among women aged 50 and older—the group that sustained nearly 90% of such fractures—tamoxifen decreased the fracture rate by 29%.

However, this extended study also confirmed the adverse effects of the drug that had been reported in the 1998 study regarding endometrial cancer, thromboses, and cataracts.

Tamoxifen increased the rate of invasive endometrial cancer in women aged 50 or older. The cumulative rate was 15.6 such cancers/1,000 women, compared with 4.7/1,000 women in the placebo group. However, two related findings were encouraging. A total of 67 of the 70 cases of invasive endometrial cancer were stage I malignancies, and tamoxifen therapy did not alter the risk for cancer at sites other than the breast and endometrium, the investigators noted.

The drug also raised the rate of pulmonary embolism in women aged 50 or older. Tamoxifen also increased the rates of stroke and deep vein thrombosis, but not to a statistically significant degree.

Women who took tamoxifen also were at slightly higher risk of developing cataracts than were those who received placebo.

"Evaluation of the frequency of other adverse eye-related events from tamoxifen failed to demonstrate vision-threatening toxicity," the investigators said.

Mortality rates were similar among women who took tamoxifen and those who took placebo. This finding was not unexpected, given that it would require much longer follow-up—most likely 15-20 years—to detect a definitive reduction in mortality, Dr. Fisher and associates noted.

New trials on breast cancer prevention currently are underway in postmenopausal women "to evaluate other agents that could be more effective than tamoxifen in decreasing the risk of breast tumors and reducing the frequency of undesirable side effects noted with the drug. ... Until one of these trials demonstrates a greater net benefit from an alternative therapy, tamoxifen remains the only proven chemopreventive treatment for breast cancer risk reduction," they added. ■

Telephone Intervention Increases Cancer Screening Rates in Women

BY PATRICE WENDLING
Chicago Bureau

QUEBEC CITY — A series of telephone calls can significantly improve cancer screening rates among low-income women, a randomized controlled trial suggests.

Not all practices have the resources to implement such an intervention, Allen J. Dietrich, M.D., said at the annual meeting of the North American Primary Care Research Group. But the model is compatible with telephone support systems available in many health care groups.

He presented a study in which 1,390 women aged 50-69 years were recruited from 11 community and migrant health centers in New York City that are part of a practice-based research network. Most women were overdue for two or all three of the following cancer screenings: Pap, mammography, and colorectal.

Patients were randomized to usual care or to an intervention that included a series of telephone calls to assess patient barriers to screening, provide any needed education, and assist with access to services.

Many of the women were foreign born, and Spanish was the primary language for 445 (64%) of the 696 women in the intervention group. An average of four 15-minute telephone calls were made to the women by master's degree students, who followed a bilingual script. Education materials and clinician recommendation letters were mailed also.

An analysis showed that 37% of patients received education alone, 9% education plus an appointment reminder, 7% education plus access assistance, 2% access assistance alone, and 18% received a phone call but did not receive any of the three types of support.

Despite a large media campaign on colon cancer led by television anchor Katie Couric at the time of the study, the largest barriers were to colorectal screening, said Dr. Dietrich, associate director for population science at the Norris Cotton Cancer Center in Lebanon and Dartmouth Medical School, Hanover, both in N.H. Women had no information, disinformation, or had not received a clinical recommendation for this particular service.

When the subject of home fecal occult blood testing was broached, the response from many of the women was, "You want me to do what?" The response became so common that staff referred to it by initials alone.

Between baseline and follow-up at 18 months, all three screening services increased significantly more for the intervention group, compared with the usual care group.

Colorectal cancer screening increased the most, with more than a 60% increase observed for the intervention group.

There was a 17% increase in mammography and a 10% increase in Pap testing.

In the usual care group, mammography and Pap testing rates remained about the same as at baseline and colorectal screenings increase slightly.

The next step for the researchers is to replicate the findings in Medicare or managed care organizations in New York City. They plan to use billing data rather than chart records to identify women in need and perhaps to combine the telephone interventions with existing outreach efforts such as child immunization reminders.

"This is centralized telephone resources as an intervention, but clearly there are other things that are needed to address these health care disparities," Dr. Dietrich said. "This isn't the answer to everything anymore than office systems are the answer to everything. We need more intervention research that increases the options to address prevention care services and their disparities in primary care." ■

HT Use Increases Breast Cancer Risk for Women of All Races

Women of all ethnicities face the same increased risk for breast cancer related to postmenopausal hormone therapy, a study suggests.

The study also found that leaner women taking hormone therapy (HT) had a relatively greater increase in breast cancer risk than did heavier women.

The study, led by Sulggi Lee, M.D., of the Keck School of Medicine at the University of Southern California, Los Angeles, provides some of the first data comparing breast cancer risk among different ethnic groups in relation to HT use.

The cohort study was conducted among 55,371 African-American, Native Hawaiian, Japanese-American, Hispanic, and white postmenopausal women, aged 45-75 years, in the Hawaii–Los Angeles Multiethnic Cohort study.

A total of 1,615 incident invasive breast cancer cases were identified over an average of 7.3 years (Int. J. Cancer [Epub ahead of print] 2005;doi: 10.1002/ijc.21481 www.interscience.wiley.com).

Current estrogen-progestin therapy (EPT) use was associated with a 29% increased risk of breast cancer after 5 years of use. Current use of unopposed estrogen therapy (ET) was associated with a 10% increase in risk after 5 years. These results assume that women using hormones at baseline continued to do so.

The increase in risk with EPT use was clearly seen in all ethnic groups, whereas the increase with ET use was seen in all groups except African Americans.

Relative risks for current EPT and ET use were greater for women with a body mass index of less than 25 kg/m^2. But increases in risk were still evident in heavier women with a BMI of 30 kg/m^2 or more.

"Data on this aspect of the relationship between EPT use and risk are scarce, and it is too early to draw a firm conclusion," the authors wrote.

Current EPT use was significantly associated only with estrogen receptor–positive (ER+)/progesterone receptor–positive (PR+) tumors (relative risk 1.34), but risk also was increased for both ER+/progesterone receptor–negative (PR–) tumors (RR 1.15) and estrogen receptor–negative (ER–)/PR+ tumors (RR 1.18).

Estrogen therapy was associated with both ER+/PR+ and ER+/PR– tumors. These findings are generally consistent with earlier studies.

There was little difference in risk by stage of disease or histological subtype.

The authors noted the possibility that their results may have been influenced by the fact that HT users are more likely to be screened for breast cancer.

—Patrice Wendling