Tamoxifen's Breast Cancer Benefits Questioned

BY KATE JOHNSON
Montreal Bureau

Tamoxifen therapy may actually reduce life expectancy slightly in nonhysterectomized women at the low end of the high-risk range for breast cancer, according to an analysis based on hypothetical cohorts.

"The results of our analysis raise questions about the impact of tamoxifen for breast cancer risk reduction on short-term and longer-term mortality," wrote Dr. Joy Melnikow of the University of California-Davis, Sacramento, and her colleagues.

"Tamoxifen for breast cancer risk reduction is unlikely to have an important effect on overall mortality for women at a 5-year breast cancer risk of 1.67% … When the effect of the poorer prognosis of the [estrogen receptor–negative breast cancers that occur among women taking tamoxifen on their breast cancer mortality is accounted for, tamoxifen is projected to reduce life expectancy slightly until women reach a minimum 2.1% 5-year breast cancer risk," they wrote.

For women who have undergone a hysterectomy, tamoxifen becomes a more favorable approach, since the risks of endometrial cancer are eliminated in this group, they added. The study was published in the Sept. 1 issue of the journal Cancer.

Tamoxifen was approved by the Food and Drug Administration in 1998 for breast cancer prevention in women who have at least a 1.67% chance of developing the disease over the next 5 years.

The analysis used a state-transition Markov model to track tamoxifen use over a 5-year period in hypothetical cohorts of women aged 50 years or more whose 5-year breast cancer risk ranged from 1% to 5%. Health outcomes, life expectancy, and costs per life-year saved were estimated based on a 5-year risk of 1.67%, which is the threshold for risk reduction therapy used in the National Surgical Adjuvant Breast and Bowel Project (NSABP) P-1 trial.

Using outcomes described in the NSABP P-1 trial, the study examined tamoxifen's effect on reducing the risks of invasive breast cancer, ductal carcinoma in situ, and osteoporotic fractures, while increasing the risks of endometrial cancer, deep venous thrombosis, pulmonary embolism, and cataracts that require surgery.

The findings showed that tamoxifen therapy resulted in a negligible increase in life expectancy of 1.6 days for nonhysterectomized women—at high cost.

Cost-effectiveness analyses were performed separately for hysterectomized and nonhysterectomized women, because the former no longer face tamoxifen's increased risk of endometrial cancer.

Additionally, potential prognostic differences were estimated based on the presence of either ER-positive or ER-negative breast cancers—the latter carrying a worse prognosis. "To our knowledge, no previously published analysis has accounted for the difference in prognosis for women with ER-negative cancers," they wrote.

The findings showed that tamoxifen therapy resulted in a negligible increase in life expectancy of 1.6 days for nonhysterectomized women with a 5-year breast cancer risk of 1.67%—at an extremely high incremental cost per year of life saved ($1,335,690). At a 5% 5-year risk this cost decreased to $64,778 per life-year saved, with an improvement in mean life expectancy of 26.7 days.

For hysterectomized women the cost-effectiveness ratio was more favorable, showing a mean increase in life expectancy of 11.5 days at a cost of $177,116 per life-year saved in women with a 1.67% 5-year risk. Those with a 5% 5-year risk had a projected life expectancy improvement of 36.5 days at a cost of $46,954 per life-year saved.

The findings are highly sensitive to price of tamoxifen, which varies strikingly within the United States and between the United States and Canada, according to the authors.

The average wholesale price (AWP) in the United States is seven times higher than typical Canadian Internet pharmacy prices, they said.

Applying the Canadian drug cost to nonhysterectomized women with either a 1.67% 5-year risk reduced the incremental cost per life-year saved to $123,780 (from $1,335,690).

"For women at breast cancer risks of greater than or equal to 3%, tamoxifen at Canadian prices both may increase life expectancy and may reduce overall costs," wrote the authors.

"For health policy makers in the U.S., this illustrates the potential effect of negotiating pharmaceutical prices at a national level and the risk of using the AWP to define the negotiated price, which is done by most Medicaid plans." ■

Bacterial Vaginosis Prevalence In U.S. Tied to Race/Ethnicity

BY DAMIAN McNAMARA
Miami Bureau

JACKSONVILLE, FLA. — Prevalence of bacterial vaginosis varies significantly by race/ethnicity in the United States, according to a large, nationally representative study from researchers at the Centers for Disease Control and Prevention.

As in previous studies, douching behavior was also significantly associated with bacterial vaginosis (BV). Lower education level, poverty, smoking, higher body mass index, and a history of pregnancy were associated with BV, but not significantly, Dr. Emilia Koumans said at a conference on STD prevention sponsored by the CDC.

BV is the most common cause of vaginal complaints among reproductive-age women. The condition increases the risk of acquiring HIV and sexually transmitted diseases. In pregnant women, BV infection increases the risk of miscarriage, chorioamnionitis, preterm labor, and preterm delivery.

Most of the 1,999 participants in the study were asymptomatic. There are few data to support treatment of asymptomatic women to reduce associated risks, Dr. Koumans said in response to an attendee question.

"There are studies underway to assess if chronic treatment of BV reduces risk of STD acquisition. It is difficult … to convince asymptomatic women of the need to continue using medication," said Dr. Koumans, a medical officer in the division of STD prevention at the CDC.

Using 2001-2002 data from the National Health and Nutrition Examination Survey (NHANES), Dr. Koumans and her associates assessed self-collected vaginal swabs from 14- to 49-year-old females. The researchers determined pH, performed gram stains, and scored slides according to quantity of lactobacilli.

Overall prevalence of BV was 27%, and there were statistically significant differences according to race/ethnicity. "Non-Hispanic black women were disproportionately affected by BV," Dr. Koumans said. Prevalence was 22% among whites, 29% among Mexican Americans, and 50% among blacks. "With further research, we hope to understand the cause or causes of BV and reasons for racial disparities," she said.

BV prevalence did not vary by current pregnancy status, but women who had ever been pregnant and those who gave birth to a preterm baby showed a trend toward more BV, Dr. Koumans said.

Number of lifetime sex partners, age at first sex, and ever had sex with another woman were factors associated with increased prevalence of BV in univariate analyses. In a multivariate analysis, douching, income level, and ever having been pregnant were significant factors.

Another meeting attendee asked if BV is considered a sexually transmitted disease. "We would need more evidence," Dr. Koumans said. ■

Women With Hematuria Less Likely Than Men to Be Referred

BY FRAN LOWRY
Orlando Bureau

ATLANTA — Women with a new or a recurrent episode of hematuria are significantly less likely to be referred to a specialist for follow-up than are men with the same condition, researchers said at the annual meeting of the American Urological Association.

The gender disparity in referral was greatest in women over the age of 60.

DR. LEE

This delay in referral may be putting women at greater risk of death from bladder cancer, said Dr. Cheryl T. Lee, director of the Bladder Cancer Research Program at the University of Michigan in Ann Arbor.

Using insurance records from a nonprofit health plan, Dr. Lee and her colleagues performed a retrospective cohort study of 926 patients (60% men, 40% women) aged 18 years and older, who had new diagnosis codes for hematuria.

The investigators reported that 402 of 559 men (72%) were referred for urologic evaluation of hematuria, compared with 102 of 367 women (28%) over follow-up periods of 27 and 26 months, respectively. This gender disparity in referral was greatest in women over the age of 60, in whom bladder cancer is more common. "This unequal access to specialty evaluation of hematuria could potentially contribute to the delay in diagnosis of bladder cancer we so frequently see in women," she said.

Men were significantly more likely to be referred to a specialist upon first presentation to a general practitioner with hematuria, compared with women, who were not referred until their second or third episode. This bias was stronger as patients aged, with men being referred at higher rates than women in the 50- to 59-year-old age category and the over-60 age category.

Ultimately, an adjusted multivariate analysis showed that men were 65% more likely to undergo urologic evaluation of hematuria than were women, Dr. Lee said.

Blood in the urine from urinary tract infections occurs more commonly in women than in men but generally in women under the age of 40, she commented. "I would argue that women in their 50s are at risk for bladder cancer, but certainly there is no argument about the increasing risk for women over the age of 60. An alarm should really go off when you see these women in your practice," she said in an interview.

She conceded that the low prevalence of bladder cancer overall makes it difficult for the primary care physician to know when to refer. ■