

Nonsteroidal Anti-inflammatory Drugs (NSAIDs) and Chemoprevention of Breast Cancer

Randall Harris,^[1] of Ohio State University, Columbus, Ohio, and colleagues presented very interesting results from a prospective study on the effects of anti-inflammatory agents in the chemoprevention of breast cancer in women enrolled in the Women's Health Initiative observational study. A total of 80,741 postmenopausal women (50-79 years of age) with no previous history of cancer (other than nonmelanoma skin cancer) were included, 1392 of whom developed breast cancer during the study as documented by pathologic exam. Average follow-up was 43 months. Use of anti-inflammatory agents and general medical histories were recorded at baseline and throughout the study.

Regular intake of 2 or more tablets per week of over-the-counter anti-inflammatory drugs (aspirin, ibuprofen, or other compounds) at standard doses (aspirin, 325 mg/dose; ibuprofen, 200 mg/dose) for 5-9 years was found to have a protective effect against the development of breast cancer, with an overall reduction in cancer risk of 21% (relative risk [RR] 0.79; confidence interval [CI], 0.60-1.04). Protection was greater with longer use of the anti-inflammatory agent (28% risk reduction with a > 10-year use) and when ibuprofen was used instead of aspirin (ibuprofen: RR, 0.51; $P < .04$; aspirin: RR, 0.79; $P < .06$).

Concomitant evaluation of other factors, including age, body mass, estrogen use, family history, parity and exercise, did not seem to modify the protective effect attributed to the anti-inflammatory agents. Of note, low-dose aspirin and the pain reliever acetaminophen were not effective in modifying breast cancer incidence.^[1]

These new results seem to confirm previous data obtained in smaller trials by the same group,^[2] who previously found a significant reduction in risk of breast cancer (RR, 0.66; CI, 0.52-0.83) in a case-controlled study of 511 breast cancer patients who used anti-inflammatory agents at least 3 times weekly for more than 1 year. Similarly, a 5-year follow-up of a cohort of 32,505 women in central Ohio had shown that incidence of breast cancer was inversely related to use of NSAIDs. Breast cancer rates were 50% lower in women using NSAIDs and 40% lower with regular doses of aspirin ($P < .05$).^[3]

These are very intriguing results that might change the way we look at and implement chemoprevention of breast cancer. Are a couple of pills of ibuprofen or aspirin per week indeed good and enough for all? As noted by the authors of these studies, further analysis of the data and confirmatory trials are needed before any formal recommendation can be made for the general public. Although not frequently linked with high toxicities, daily or weekly use of NSAIDs may be associated with toxic effects.^[4]

A careful assessment of the balance between individual breast cancer risk, chemoprotective effects, concomitant morbidities, and acute/chronic toxicities will help to define whether and which women should indeed receive this form of chemoprophylaxis, as well as the optimal schedule or agent to be used. Previous studies of chemically induced breast cancer in rats have shown that the cyclooxygenase (COX)-2-blocker celecoxib seemed more effective than ibuprofen in reducing incidence, multiplicity, and volume of anthracene-induced breast tumors in rats.^[5] It remains to be seen whether these findings apply also to human breast malignancies. COX-2 inhibitors show a high selectivity for this enzyme and a lower gastrointestinal toxicity when compared with conventional NSAIDs such as aspirin or ibuprofen. They are, however, not completely devoid of toxicity, as inhibition of the COX-2 enzyme may delay wound healing, negatively affect ovulation, and induce a prothrombotic diathesis.^[4,6,7]