Aspirin’s Chemopreventive Effects Seen 10 Years After Tx Initiation

BY JONATHAN GARDNER
London Bureau

Taking 300 mg of aspirin daily for at least 5 years was shown to prevent colorectal cancer in an analysis of two large randomized trials. The effect was seen beginning 10 years after treatment was initiated.

Although this strategy might be effective in certain high-risk groups, further research is needed to elucidate the risks and benefits of aspirin chemoprevention in various clinical settings, the researchers wrote. The effectiveness of colonoscopy screening and the risk of bleeding complications with long-term aspirin use also should be considered, they noted.

Dr. Andrew Chan of the gastrointestinal unit at Massachusetts General Hospital, Boston, agreed in an accompanying commentary. “These findings are not sufficient to warrant a recommendation for the general population to use aspirin for cancer prevention,” he wrote (Lancet 2007;369:1577-8).

Previous observational studies had reported a decreased incidence of colorectal cancers in regular users of aspirin, but two large trials did not demonstrate a decreased risk. Long-term follow-up. Longer follow-up is needed, given that the delay is 10-15 years between initiation of development of an adenoma and colorectal cancer, wrote Dr. Peter Rothwell, professor of clinical neurology at the University of Oxford (England), and associates (Lancet 2007;369:1603-13).

Their analysis focused on the British Doctors Aspirin Trial and the UK Transient Ischaemic Attack Aspirin Trial; there was a median follow-up of 23 years in both trials. During that follow-up period, subjects who took at least 300 mg of aspirin a day for at least 5 years were significantly less likely to develop colorectal cancer than were controls (hazard ratio [HR] 0.65), according to a pooled analysis of the two trials.

The researchers found no significant effect on any other type of cancer.

The preventive effect was strongest in years 10-19, when the HR for aspirin users was 0.60, but a significantly reduced HR of 0.74 was seen in years 20 and later for the subjects who took aspirin. No significant preventive effect was seen at 0.9-9 years (HR 0.92).

The British Doctors Aspirin Trial randomized doctors in 1978 and 1979 into a group of 3,429 taking a daily dose of 500 mg of aspirin and a control group of 1,710 who took nothing. Treatment continued for 5-6 years.

The UK Transient Ischaemic Attack Aspirin Trial randomized 2,449 patients over age 40 who had already had a transient ischaemic attack or mild ischaemic stroke to receive daily doses of either 1,200 mg or 300 mg to come back for surveillance place between 1978 and 1985, with the trial ending in 1986. The researchers performed a subgroup analysis of only those patients who used aspirin for at least 5 years.

Aspirin May Reduce Risk of Certain Colorectal Cancers

BY LEANNE SULLIVAN
Associate Editor

Regular aspirin use for at least 10 years appears to reduce the risk of colorectal cancers that overexpress cyclooxygenase-2, Dr. Andrew T. Chan, of Massachusetts General Hospital and Harvard Medical School, Boston, and his associates reported.

The researchers mailed questionnaires every 2 years to 121,701 women in the Nurses’ Health Study and 51,529 men in the Health Professionals Follow-Up Study to determine aspirin use and incidence of colorectal cancer. The women (age range at entry, 30-55 years) received the survey starting in 1976, and the men (age range at entry, 40-75 years) received it starting in 1986.

More detailed questions on aspirin use, including frequency and amount, were added in 1980 for the women and in 1992 for the men. For women, regular aspirin use was defined as taking two or more 325 mg aspirin tablets per week; for men, it was defined as using aspirin at least twice a week (N. Engl. J. Med. 2007;356:2131-42).

Medical and pathology reports were obtained for participants who reported colorectal cancers, said Dr. Chan of Massachusetts General Hospital and Harvard Medical School, Boston, and his associates.

During follow-up, 636 specimens sufficient for immunohistochemical analysis were obtained from patients with confirmed colorectal cancer. Of the 636 tumors, 423 (67%) were COX-2 positive, or had moderate or strong expression of the enzyme.

The researchers analyzed the association between the expression of COX-2 in the tumors and the patients’ use of aspirin, and calculated multivariable relative risk after adjustment for factors including age, gender, smoking, BMI, exercise, family history of colorectal cancer, history of polyps, and meat and alcohol consumption.

The multivariate relative risk of colorectal cancer for aspirin users versus non-regular users was a significant 0.64 for COX-2–positive cancers and a non-significant 0.96 for COX-2–negative tumors. Thus, aspirin use was of benefit only in tumors in which COX-2 was overexpressed. However, this benefit was not seen until aspirin had been used for more than 10 years.

A greater amount of aspirin use also was associated with lower incidence of COX-2–positive disease, with more than five tablets per week associated with significantly fewer such cancers; the association was not significant for COX-2–negative disease. This “is consistent with the results of studies in which higher doses of aspirin were required to inhibit COX-2 than to inhibit COX-1,” the investigators noted.

The results of this observational study “suggest that the antioxidant benefit of aspirin is mediated, at least in part, by inhibition of COX-2,” Dr. Chan and his associates concluded.

In an accompanying editorial, Dr. Sanford D. Markowitz of Case Western Reserve University, Cleveland, pointed out that aspirin use has its own risk of adverse effects (N. Engl. J. Med. 2007;356:2195-8).

Researchers “need to ask whether there are alternative strategies for targeting the COX pathway that have better efficacy and fewer untoward effects,” Dr. Markowitz said. Inhibitors of the COX-2–generated prostaglandin PGE2, receptors or syn- thases “might provide better specificity for the prevention of colon cancer and, hence, reduced adverse effects,” he suggested.