NEWS

More Evidence That Aspirin Lowers Cancer Risk

By Gunjan Sinha

Two studies at September’s American Association for Cancer Research meeting build on evidence suggesting that nonsteroidal anti-inflammatory drugs (NSAIDs) reduce the risk of developing several cancers and the risk that cancer will spread. But the evidence isn’t yet strong enough to persuade clinicians to recommend NSAIDs as a preventive.

In the first study, Adriana C. Vidal, Ph.D., assistant professor of surgery at Duke University School of Medicine in Durham, N.C., and colleagues studied data from a clinical trial that tested whether taking dutasteride could reduce risk of prostate cancer. The researchers wondered whether men taking NSAIDs concurrently for other conditions were less likely to develop prostate cancer, independent of dutasteride. The trial included 6,390 men, half of whom did not take NSAIDs. Among the other half, 21% took aspirin, 18% took other NSAIDs, and 11% took both. All men had prostate cancer–negative biopsy samples before the trial and received biopsies at 2- and 4-year intervals, regardless of prostate-specific antigen level.

Compared with participants not taking NSAIDs, men taking aspirin, other NSAIDs, or both cut their risk of prostate cancer by 13%. They also had a 17% reduced risk of high-grade prostate cancer. But researchers found no association between taking NSAIDs and risk of low-grade prostate cancer. Risk reductions held up regardless of whether patients were in the dutasteride or placebo arm or whether participants were from Europe or North America.

People commonly take aspirin to prevent heart attacks. At low doses, it inhibits the enzyme cyclooxygenase 1 (COX-1) in platelets, which then inhibits thromboxane A2. That keeps platelets from aggregating, so blood can’t clot. At high doses, NSAIDs inhibit COX-1 and COX-2 in other cell types. COX-2 regulates expression of prostaglandin E2 (PGE2). How inhibiting COX-2 affects cancer isn’t clear, but researchers think that it interrupts PGE2 in addition to other pathways that promote tumor growth. Many observational and retrospective studies suggest that NSAIDs reduce risk of several cancers. A meta-analysis of eight randomized clinical trials, for example, found that taking daily aspirin for 4 or more years reduced risk of death from cancer by about 20% (Lancet 2011;377:31–4).

The second study, however, suggests that low doses to minimize risks may yield the same benefits. Working with adenocarcinoma cells, scientists at Vanderbilt University in Nashville, Tenn., showed that aspirin inhibits COX-2–mediated PGE2 production in epithelial cells at doses up to 12 times lower than necessary to inhibit COX-1 in platelets. Fifty-four healthy people taking 81 mg of aspirin for 2 weeks had lower levels of PGE2 and prostacyclin—markers of inflammation—in urine samples by 45% and 37%, respectively. The study is the first to show that such a low dose of aspirin can inhibit nonplatelet COX enzymes. The study, however, has not yet been published.

If the findings hold up in vivo, “it’s a very important consideration,” said Raymond N. DuBois, M.D., Ph.D., director of the inflammation and cancer lab at the Bodesign Institute at Arizona State University, Tempe. DuBois was among the first researchers to show that inhibiting COX-2 disrupts cancer. “Aspirin is cheap and has been used by the population for over 100 years.”

At the same time, DuBois expressed skepticism. That aspirin inhibits COX-2 at such low doses is controversial, he said. The prevailing theory of how aspirin may prevent cancer posits that at doses lower than 325 mg, it inhibits primarily COX-1, DuBois said. Since this prevents platelets from aggregating, “platelet interaction with circulating tumor cells is disrupted, enabling the tumor cells to either be attacked by the immune system or undergo apoptosis.” The Vanderbilt team’s study suggests that antiplatelet and COX-2-inhibitory activities may act in concert to inhibit cancer. Dubois, however, has also studied aspirin’s effect on COX-2 at low doses in different cell culture models and has not seen the same effect.

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Raymond N. DuBois, M.D., Ph.D.
Regardless of the mechanism, together the studies suggesting NSAIDs can prevent cancer are thought provoking, said Gregory A. Masters, M.D., chair of the American Society of Clinical Oncology Communications Committee. But “you have to be cautious looking at retrospective analyses,” he added. “The individual studies are not convincing.” Until more data on the benefits and risks are available, “we aren’t ready for any broad recommendations,” he said.

“The risk of bleeding is not insignificant,” said Wendy Y. Chen, M.D., M.P.H., assistant professor of medicine at Harvard Medical School in Boston. “I would not feel comfortable telling my patients to take NSAIDs for cancer prevention alone.”

A prospective randomized trial looking at NSAIDs’ ability to prevent cancer or metastases would provide the necessary evidence. Such a study would require monitoring thousands of participants for 5–10 years. But according to one of the study’s authors, Pierre P. Massion, M.D., professor of medicine and cancer biology at Vanderbilt, such a study would not appeal to industry financially because NSAIDs are generic drugs.

Drugs that selectively inhibit COX-2 carry a lower risk of gastrointestinal side effects. But risk of cardiovascular side effects has vastly limited their use, making the pharmaceutical industry leery of studying them to prevent cancer, DuBois said. Also, industry may not see a huge market in cancer prevention, Chen added.

The UK and Singapore are planning clinical trials to study whether taking regular aspirin after treating early-stage cancer can prevent the cancer from returning. But these results are years away. Although taking aspirin to prevent cancer or metastases after diagnosis “is not yet ready for clinical implementation,” Massion said, at the very least, “there is going to be renewed interest in this.”

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Electronic Cigarettes Might Not Help Cancer Patients Quit Smoking
By Mike Fillon

One of the latest findings from the Office of the Surgeon General is clear: Even people diagnosed with cancer should benefit from quitting smoking.

According to the 2014 report The Health Consequences of Smoking—50 Years of Progress, enough evidence exists to infer “a causal relationship between cigarette smoking and adverse health outcomes” and that “quitting smoking improves the prognosis of cancer patients.” The question for cancer patients then becomes, “Fine, but how do I quit since I haven’t been able before?”

It’s no wonder, then, that electronic cigarettes (e-cigarettes) might appeal to cancer patients whose doctors have advised to quit smoking. The devices are marketed as a relatively benign alternative, although there is not yet adequate information to support this perception. They supply nicotine without the tar, carbon monoxide, and other harmful ingredients suggesting they may represent a stepping-stone to quitting. Plus, e-cigarettes produce only vapor, not smoke, thus eliminating the stigma. E-cigarettes also look like their tobacco-laden cousin and offer the same hand-to-mouth sensory experience.

Despite their allure, an observational study found that e-cigarettes are not an effective tool for cancer patients to quit smoking.

“Our study did not find evidence that there were benefits or differences in their quitting outcomes” from using e-cigarettes, said study coauthor Jamie S. Ostroff, Ph.D. She is chief of the Behavioral Sciences Service and director of the Tobacco Treatment Program at New York’s Memorial Sloan–Kettering Cancer Center. Ostroff added that they did not assess how people perceived the risk of using e-cigarettes. Even so, their findings suggested that although patients with cancer may perceive the devices to be less harmful than combustible cigarettes, that did not necessarily lead to quitting.

E-cigarettes were invented in China in 2003 and introduced in the U.S. in 2007. These battery-powered devices convert liquid nicotine into a vapor that the user inhales (known as “vaping”), similar to a regular cigarette. Propylene glycol, the primary ingredient in anti-freeze, and glycerin are the main ingredients of the liquid. The vapor delivers nicotine to the lungs. The user then exhales vapor that resembles a cloud of smoke. E-liquids come in flavors, adding to their appeal.

In Ostroff’s study (Cancer 2014;120:3527–35), 1,074 smoking cancer patients enrolled in a 2012–2013 tobacco treatment program at Memorial Sloan–Kettering. At enrollment, mean age was 56 years (range, 18–87 years); 607 (56.5%) were female and 467 (43.5%) were male. Of the participants, 968 (64.9%) had already tried quitting at least twice.

Between 6 and 12 months after enrollment, researchers collected data on attempts to quit. Approximately one-fourth (26.5%) reported having used within 30 days, and most e-cigarette users (92%) reported having also used traditional cigarettes. Between 2012 and 2013, the number of people using e-cigarettes during 30 days also increased from 10.6% to 38.5%. Meanwhile, e-cigarette users and nonusers had similar 7-day abstinence rates (44.4% and 43.1%, respectively).

Compared with nonusers, e-cigarette users had higher nicotine dependence, smoked more cigarettes per day, and were more likely to be diagnosed with either thoracic or head and neck cancer (even though both groups were demographically and clinically similar in many respects).

“These cancers are widely associated with cigarette smoking,” Ostroff said. E-cigarette users were also twice as likely to be chronic tobacco smokers, and fewer users of the product reported abstaining from cigarettes for 24 hours during the observation period.

“That may actually have averted or delayed quit attempts,” Ostroff said.

Although e-cigarettes may appeal to patients seeking to reduce smoking’s harms, Ostroff added, the findings do not support oncologists’ recommending them to cancer patients advised to quit smoking. Ostroff said that to the best of her knowledge, this study presents the first data on e-cigarette use among cancer patients.