Long-term Use of Aspirin and Nonsteroidal Anti-inflammatory Drugs and Risk of Colorectal Cancer

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Context Randomized trials of short-term aspirin use for prevention of recurrent colorectal adenoma have provided compelling evidence of a causal relationship between aspirin and colorectal neoplasia. However, data on long-term risk of colorectal cancer according to dose, timing, or duration of therapy with aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) remain limited.

Objective To examine the influence of aspirin and NSAIDs in prevention of colorectal cancer.

Design, Setting, and Participants Prospective cohort study of 82 911 women enrolled in the Nurses' Health Study providing data on medication use biennially since 1980 and followed up through June 1, 2000.

Main Outcome Measure Incident colorectal cancer.

Results Over a 20-year period, we documented 962 cases of colorectal cancer. Among women who regularly used aspirin (2 standard [325-mg] tablets per week), the multivariate relative risk (RR) for colorectal cancer was 0.77 (95% confidence interval [CI], 0.67-0.88) compared with nonregular users. However, significant risk reduction was not observed until more than 10 years of use (P.001 for trend). The benefit appeared related to dose: compared with women who reported no use, the multivariate RRs for cancer were 1.10 (95% CI, 0.92-1.31) for women who used 0.5 to 1.5 standard aspirin tablets per week, 0.89 (95% CI, 0.73-1.10) for 2 to 5 aspirin per week, 0.78 (95% CI, 0.62-0.97) for 6 to 14 aspirin per week, and 0.68 (95% CI, 0.49-0.95) for more than 14 aspirin per week (P<.001 for trend). Notably, women who used more than 14 aspirin per week for longer than 10 years in the past had a multivariate RR for cancer of 0.47 (95% CI, 0.31-0.71). A similar dose-response relationship was found for nonaspirin NSAIDs (P = .007 for trend). The incidence of reported major gastrointestinal bleeding events per 1000 person-years also appeared to be dose-related: 0.77 among women who denied any aspirin use; 1.07 for 0.5 to 1.5 standard aspirin tablets per week; 1.07 for 2 to 5 aspirin per week; 1.40 for 6 to 14 aspirin per week; and 1.57 for more than 14 aspirin per week.

Conclusions Regular, long-term aspirin use reduces risk of colorectal cancer. Nonaspirin NSAIDs appear to have a similar effect. However, a significant benefit of aspirin is not apparent until more than a decade of use, with maximal risk reduction at doses greater than 14 tablets per week. These results suggest that optimal chemoprevention for colorectal cancer requires long-term use of aspirin doses substantially higher than those recommended for prevention of cardiovascular disease, but the dose-related risk of gastrointestinal bleeding must also be considered.

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