



Synopsis

Aspirin and colorectal cancer

In an effort to help reduce the incidence of colorectal or colon cancer, the South African Gastroenterology Society (SAGES), together with key pharmaceutical companies, is embarking on a consumer disease awareness and education campaign. The colon cancer campaign is the first of its kind in South Africa and the official Colorectal Cancer Prevention Day is set for Friday, 8 August 2003. Coincidentally, a number of articles on the topic of colorectal neoplasia appeared in a recent edition of the *New England Journal of Medicine*. They consider the place of aspirin in the prevention of colorectal cancer.

Sandler *et al.*¹ conducted a randomised double-blind trial to determine the effect of aspirin on the incidence of colorectal adenomas. They selected 635 patients with previous colorectal cancer and randomly assigned them to receive either 325 mg of aspirin per day, or placebo. They measured the number of patients with adenomas, the number of recurrent adenomas, and the time to the development of adenoma between randomisation and subsequent colonoscopy. A total of 517 of the subjects had at least one colonoscopy a median of 12.8 months after randomisation. One or more adenomas were found in 17% of the aspirin group and 27% of the placebo group. The mean number of adenomas was lower in the aspirin group than in the placebo group. The relative risk, adjusted for age, sex, cancer stage, number of colonoscopic examinations and time to a first colonoscopy, was lower in the aspirin group than the placebo group. The adjusted relative risk of any recurrent

adenoma in the aspirin group compared with the placebo group was 0.65 (95% confidence interval 0.46 - 0.91). The time to detection of a first adenoma was longer in the aspirin group than in the placebo group. The authors concluded that daily use of aspirin is associated with a significant reduction in the incidence of colorectal adenomas in patients with previous colorectal cancer.

In the second study² Baron and his colleagues performed a randomised double-blind trial of aspirin as a chemopreventive agent against colorectal adenomas. They assigned patients with recent histologically diagnosed adenomas to receive either placebo ($N = 372$), 81 mg of aspirin ($N = 377$) or 325 mg of aspirin ($N = 372$) daily. They compared the groups with regard to the risk of one or more neoplasms (adenomas or colorectal cancer) at least 1 year after randomisation. At 1-year follow-up colonoscopy in 1 084 patients (97% of enrollees) the incidence of one or more adenomas was 47% in the placebo group, 38% in the 81-mg aspirin group, and 45% in the group given 325 mg of aspirin. Unadjusted relative risks of any adenoma compared with the placebo group were 0.81 in the 81-mg group, and 0.96 in the 325-mg group. For advanced neoplasms (adenomas measuring at least 1 cm in diameter or with tubivillous or villous features, severe dysplasia or invasive cancer) the respective relative risks were 0.59 and 0.83. The authors concluded that low-dose aspirin has a moderate chemoprotective effect on adenomas in the large bowel.

In a commentary on these two studies³ Thomas F Imperiale writes: 'Aprotective effect of aspirin is

biologically plausible. Aspirin works in part through the inhibition of cyclooxygenase-2, an enzyme that is found in colorectal cancer tissue.' Epidemiological studies have consistently shown a 40 - 50% reduction in colorectal neoplasia with aspirin, and other agents such as sulindac and celecoxib have reduced the number and size of colorectal polyps. For a definitive study of the primary or secondary prevention of colorectal cancer by aspirin or non-steroidal anti-inflammatory agents, a very large sample size and long-term follow-up will be needed. Imperiale asks: 'Do the results of the two studies described above indicate that aspirin should now be recommended for secondary chemoprevention in persons with a history of colorectal neoplasia, or for primary prevention in the 90% of persons 50 years of age or older who are considered to be at risk for colorectal cancer?' To answer this question, one would need to consider the outcomes, the duration of treatment and the protective - or harmful - effects of aspirin. The cumulative clinical importance of episodes of bleeding probably exceeds the benefit of the neoplasm-related outcomes. Imperiale concludes: 'Although aspirin may be of some benefit in preventing colorectal cancer, it cannot yet be recommended for this indication and is not a substitute for screening and surveillance. The two trials described above, do nevertheless provide proof that aspirin moderately reduces the risk of recurrent colorectal neoplasia'.

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References

1. Sandler RS *et al.* *N Engl J Med* 2003; 348: 883-890.
2. Baron JA *et al.* *N Engl J Med* 2003; 348: 891-899.
3. Imperiale TF. *N Engl J Med* 2003; 348: 879-880.