Daily Aspirin and Prophylaxis Against Recurrent Colorectal Adenoma


Study Overview

Objective. To determine if daily aspirin intake reduces the risk of recurrent colon adenomatous polyps in patients with recent polypectomies.

Design. Randomized, double-blind, placebo-controlled trial with an intention-to-treat analysis.

Setting and participants. 49 gastroenterology centers in France. Eligibility criteria included age 19 to 75 years, recent adequate colonoscopy (little or no residual stool in the colon and cecum visualized), and adenomatous polyp visualized and removed during the examination. Patients were required to have either 3 polyps of any size or at least 1 polyp greater or equal to 6 mm in diameter. Patients with a personal history of colorectal cancer, familial adenomatous polyposis, inflammatory bowel disease, bowel resection, or debilitating or life-threatening disease were excluded. Patients were required to avoid the regular use of aspirin during the trial.

Intervention. Patients were randomized to either placebo or lysine acetylsalicylate (LAS) (160 mg/day or 300 mg/day).

Main outcome measures. The primary outcome was the number and size of new adenomatous polyps 1 year following colonoscopic clearance of pre-existing polyps. Adenomatous polyp burden was calculated as the sum of the diameters of all adenomas identified at 1-year colonoscopy.

Main results. 291 patients were initially considered eligible and entered into the 4-week run-in phase of the study. 19 patients were unable to complete the run-in phase, 272 patients were randomized, and 132 patients were assigned placebo. 140 patients were assigned to the LAS group; 73 patients were randomized to 160 mg/day and 67 patients to 300 mg/day. There were no significant differences between the groups in mean age, gender, body mass index, tobacco use, and personal history of adenoma or family history of colorectal cancer. A higher percentage of patients allocated to the LAS group had advanced adenomas (79.3% versus 68.2%; P = 0.04).

The rates of noncompletion of the 1-year follow-up colonoscopy was not statistically different between the 2 groups (10% in the LAS group and 15% in the placebo group), and colonoscopy data were available for 126 LAS patients and 112 placebo patients. 38 patients (30.2%) in the LAS group and 46 patients (41.1%) in the placebo group had 1 or more new adenomas diagnosed by colonoscopy at 1-year (crude relative risk [CRR] for recurrent adenoma in the LAS group, 0.73 [95% confidence interval [CI], 0.52–1.04]; P = 0.08). The LAS group had only 4 patients (3.2%) with 3 or more recurrent adenomas compared with 12 patients (10.7%) in the placebo group (CRR, 0.03 [95% CI, 0.10–0.89]; P = 0.03). Thirteen patients (10.3%) in the LAS group versus 26 (23.2%) in the placebo group had at least 1 adenoma greater than 5 mm found on colonoscopy (CRR, 0.44 [95% CI, 0.24–0.82]; P = 0.01). Mean number of recurrent adenomas was 0.45 in the LAS group compared with 0.86 in the placebo group (P = 0.01). Adjusted relative risk for recurrent adenoma for the 300-mg LAS group versus the 160-mg LAS group was 0.81 (95% CI, 0.53–1.18; P = 0.29).

Conclusion. Daily therapy with soluble aspirin reduces the risk of new adenomas in patients with personal history of adenoma after 1 year of therapy. Higher doses of LAS were associated with a greater protective effect, but this trend was not statistically significant.

Commentary

Several studies have been performed to determine if aspirin has a protective effect on colon cancer and recurrent adenomas [1–4]. While 1 study failed to demonstrate a protective effect of aspirin on recurrent adenomas [3], others have demonstrated a relative risk reduction of 0.81 for aspirin users (95% CI, 0.69–0.96) [4]. The current study contributes to the mounting evidence supporting prophylactic aspirin use for colorectal cancer while also testing out a different method of aspirin delivery. LAS is a water-soluble form of aspirin that is more bioavailable than standard aspirin and appears to be well tolerated. Benamouzig et al present preliminary data from the first year of a planned 4-year trial. Overall, the study had good follow-up and good compliance with colonoscopy at 1 year.
The authors’ results are promising, with a CRR of adenoma recurrence at 1-year colonoscopy of 0.73 (95% CI, 0.52–1.04). While this result was not statistically significant, the effect size is similar to prior data and supports the overall hypothesis that aspirin use is protective for recurrent adenomas. The study population did have a higher rate of recurrent polyps when compared with previously published estimates (35% adenoma recurrence rate in this study versus 15% to 33% in other studies) [2,5]. This elevated recurrence rate could have resulted from either an increased proportion of missed polyps on the intake exam or a patient population that was at higher risk for recurrence than prior studies. Another important question that remains unanswered is exactly what type of patient might derive the most benefit from prophylactic aspirin therapy. Undoubtedly, we will have more information to address these questions when the overall trial is complete. For now, the results are promising but not conclusive.

Applications for Clinical Practice
LAS therapy may reduce the risk of recurrent colorectal adenomas in patients 1 year after colonoscopic clearance of pre-existing polyps. Longer-term studies are ongoing that may better delineate which patients might derive the most benefit from aspirin prophylaxis.

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References