Low dose aspirin, *H. pylori* infection, and the risk of upper gastrointestinal bleeding

Carlos Sostres1, Angel Lanas2

Defining patients at high risk and eradicating infection may reduce bleeding risk, but further pharmacoeconomic analysis is required

Helicobacter pylori infections and low dose aspirin (75–325 mg daily) are the two most important, independently modifiable risk factors in the pathogenesis of peptic ulcers and peptic ulcer complications.1 Low dose aspirin use has increased over the past decade because of its benefits for preventing cardiovascular events and even colon cancer. Despite assertions that *H. pylori* infections increase the risk of aspirin-related gastrointestinal bleeding, the influence of this interaction is complex, poorly defined, and contentious. *H. pylori* infection is common among patients taking low dose aspirin,2 and the consequences of interactions between the two factors would therefore have important implications. A 2010 systematic review3 explored the impact of *H. pylori* on upper gastrointestinal bleeding risk in low dose aspirin users, but the available evidence was insufficient for strong conclusions. Of the 13 studies included in the analysis, ten were cohort studies with heterogeneous inclusion criteria, types of *H. pylori*, and upper gastrointestinal bleeding diagnoses, and the dosage and duration of aspirin use were also diverse; two randomised controlled trials had short follow-up periods and relatively small sample sizes.3

International consensus groups have recently attempted to define a standardised treatment approach for managing *H. pylori* infection in low dose aspirin users,4,5 but the narrow evidence base means that firm recommendations have not been possible. The increasing frequency of this clinical scenario and the need for more specific, evidence-based guidance for general physicians therefore necessitate further investigation of the question.6

The systematic review and meta-analysis article published in this issue of the *MJA*7 includes evidence from several new studies involving a total of 1172 patients from Europe and Japan with upper gastrointestinal bleeding, including seven case–control studies. Ng and Yeomans conclude that *H. pylori* infection (detected with the urea breath test or serology) increased the odds of gastrointestinal bleeding in low dose aspirin users by a factor of 2.32 (95% CI, 1.25–4.33). However, it is doubtful whether this increase is sufficient to support a test-and-treat strategy for all low dose aspirin users; based on all the available evidence, the current answer is probably: no.

Low dose aspirin is one of the most frequently prescribed drugs worldwide; more than 30 million primary care prescriptions were issued in England in 2007, and the number increases each year.8 The test-and-treat strategy would thus target a huge population, with important clinical and financial implications, particularly in countries where the prevalence of *H. pylori* infection is high. Further, Ng and Yeomans estimated that at least 100 patients would need to be treated to prevent one bleeding event, but perhaps more than 1000, underlining the need for further approaches to this clinical problem. An alternative to the test-and-treat strategy would be to include only the patients at greatest risk of gastrointestinal bleeding, with the aim of reducing (not eliminating) the risk.

*H. pylori* eradication as a primary strategy for preventing peptic ulcer disease or complications in low dose aspirin users at low to medium risk of bleeding has not been evaluated in large studies. The Helicobacter Eradication Aspirin Trial (HEAT) aims to provide quality evidence about the effect of *H. pylori* eradication on the incidence of bleeding peptic ulcers in low dose aspirin users.9 The only study that included a separate group of patients at average risk of bleeding (low dose aspirin users with no history of bleeding ulcer) found that the incidence of bleeding peptic ulcers in this group (0.66 events/100 patient-years; 95% CI, 0.38–0.99) was similar to that for patients with a history of gastrointestinal bleeding in whom *H. pylori* had been eradicated (0.97 events/100 patient-years; 95% CI, 0.53–1.80; incidence rate ratio, 1.47; 95% CI, 0.75–3.38). Moreover, the concomitant use of drugs associated with gastric damage significantly increased the predicted risk of a bleeding ulcer.10

1Instituto de Investigación Sanitaria Aragón, Zaragoza, Spain. 2Centro de Investigación Biomédica en Red (CIBER), University of Zaragoza, Zaragoza, Spain. alanas@unizar.es • doi: 10.5694/mja18.00742 • See Meta-analysis, p. 306
An interesting strategy would therefore be to divide low dose aspirin users into low and high gastrointestinal bleeding risk groups, stratified by risk factors such as age and use of concomitant non-steroidal anti-inflammatory drugs (NSAIDs), anticoagulants, non-aspirin anti-platelet medications, and corticosteroids. This strategy would reduce the target population to the subgroup of patients who could theoretically benefit most from successful H. pylori eradication, including those with a history of gastroduodenal peptic ulcer, in whom H. pylori eradication is always indicated if infection is present.

The growing population with indications for H. pylori eradication will increase health care costs, the health care burden for primary care physicians and gastroenterologists, and rates of H. pylori resistance. H. pylori testing and eradication should be offered to low dose aspirin users with a history of peptic ulcer or with other risk factors for gastrointestinal bleeding, including being aged 70 years or more, and concomitantly using of anticoagulants, NSAIDs, or non-aspirin antiplatelet drugs. Further pharmaco-economic research focused specifically on the benefits and risks of H. pylori eradication in low dose aspirin users stratified by gastrointestinal bleeding risk may provide a stronger basis for new recommendations and guidelines.

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