Gastro-duodenal injury associated with intake of 100–325 mg aspirin daily

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Summary: During the year 1991, 43 patients with upper gastrointestinal bleeding and one with severe epigastric pain associated with intake of non-steroidal anti-inflammatory drugs were admitted for emergency endoscopy to our unit. Fourteen patients (33%) had been treated with 100–325 mg aspirin daily, 11 of them for at least one year. The mean age of this group was 71. Only two patients had a previous history of peptic ulcer. Five patients used anticoagulants or antiplatelet drugs concomitantly with aspirin. The endoscopic diagnosis of the sources of bleeding was erosive gastritis in eight patients, gastric ulcer in four, duodenal ulcer in five and oesophageal ulcer in one. Our results support findings by other groups, showing that doses of aspirin as low as 75 mg daily should be used in the management of elderly patients with thrombo-embolic disease.

Introduction

The use of non-steroidal anti-inflammatory drugs (NSAIDs) is frequently associated with damage to the upper gastrointestinal (GI) mucosa, perforations and bleeding, especially in the elderly.^{1–4} Aspirin is considered a major offender.¹ Aspirin-induced mucosal damage may appear following brief or occasional treatment, or after continuous long-term intake.^{4–6} Generally, the severity of the damage is dose related^{4,7} and tends to decrease after the first months of treatment, due to gastro-duodenal adaptation.^{8,9} In order to overcome GI complications, several modalities, such as coating,^{10,11} buffering^{4,12,13} combining the aspirin with paracetamol¹⁴ or with synthetic prostaglandins,¹⁵ and applying in the form of suppositories^{16,17} have been adopted. Aspirin in daily low dosage is widely used in the treatment of cardiovascular disorders.^{7,13} It is believed that low dosage may avoid adverse gastroduodenal effects while maintaining the drug's beneficial, antiplatelet aggregation property.^{13,18,19}

However, Prichard *et al.*²⁰ clearly demonstrated that low-dose aspirin induced mucosal bleeding in healthy volunteers. In a recently published study,⁷ a significantly higher incidence of GI bleeding was found in patients using 325 mg of aspirin on alternate days as compared with those receiving

placebo. However, no endoscopic data regarding the source of bleeding or the severity of mucosal injury has been reported. The present work was initiated in order to examine the possible risk of a major upper GI damage associated with long-term aspirin treatment (100–325 mg daily) and to address the need for mucosal protection.

Patients and methods

In 1991, 189 patients with acute onset major upper GI bleeding were admitted to our hospital and underwent emergency endoscopy within 24 hours of the bleeding episode. Among these, 43 patients gave a history of NSAIDs intake. Bleeding in 14 (33%) of these patients was associated with daily consumption of 100–325 mg aspirin.

Age, sex, past medical and GI history were recorded from the patients' files and each of the subjects was prospectively interviewed in regard to use of medication, with particular stress on the consumption of NSAIDs (dosage and duration of use). Blood count on admission, number of blood units transfused, endoscopic diagnosis of the source of bleeding and therapeutic procedure, if performed, were also recorded.

Results

Fourteen patients with acute upper GI bleeding and one with epigastric pain associated with aspirin

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intake (236 ± 15 mg/day (mean $\pm$ s.e.), range 100–325 mg), were evaluated. The mean age was 71 ± 1.8 years (range 62–81) and the male to female ratio was 11:4. Twelve patients presented with melaena, one with melaena and haematemesis and one complained of coffee-ground vomiting. Of the 14 patients, 11 had used aspirin for at least 12 months, one for 8 months, one for one month and two for only 7 days. The major indications for aspirin were ischaemic heart disease (13 patients), peripheral vascular disease and transient ischaemic brain disease. The lowest haemoglobin on admission was 10.3 mg/dl ± 0.7 and the average number of blood units transfused was 1.4 ± 0.4 (mean $\pm$ s.e.). Five patients were also on dipyridamole, sulphapyrazone and coumarin derivatives. Steroid intake, the use of NSAIDs or alcohol were not reported by any of the patients. Only two patients had a previous history of duodenal ulcer. The source of the recent bleeding in one of them was active duodenal ulcer and the other, who had previously undergone vagotomy and pyloroplasty, bled due to erosive gastritis.

Endoscopic diagnosis of the source of bleeding

Erosive gastritis was found in eight patients, gastric ulcer in four and duodenal ulcer in five. Both erosive gastritis and duodenal ulcer were diagnosed in two patients, another patient had erosive gastritis together with oesophageal ulcer, and in the third, the coexistence of duodenal and gastric ulcers was found. In three patients, the bleeding called for haemostasis by BICAP electrocoagulation, and 10 patients required blood transfusions. No surgical intervention was necessary. All patients were treated with intravenous cimetidine and antacids during the peribleeding period.

Discussion

In the present study, we evaluated the association between daily intake of 100–325 mg aspirin and severe upper GI symptoms (mainly serious bleeding of more than 1,000 cc) in patients admitted for bleeding who had undergone emergency endoscopy in our unit in 1991. We found that among 43 patients in whom bleeding was

associated with the intake of various NSAIDs, 14 (33%) had received 100–325 mg aspirin daily. Concomitant antiplatelet or anticoagulant therapy which might have aggravated the bleeding was taken by five patients; no patient was treated with steroids. All bleeding patients were elderly and suffered from cardiovascular disorders, factors previously reported to increase the risk of bleeding and perforations in NSAIDs users.^{2,3}

Gastrointestinal lesions attributed to aspirin and other NSAID treatment are well documented in the literature, especially in the era of endoscopy.^{1,4,21–25} A significant proportion of rheumatic patients (20–30%) receiving prolonged NSAIDs treatment develop ulcers in the upper gastrointestinal tract.⁴ Lesion formation and bleeding is purportedly related to dose and duration of drug intake.^{1,4,6} Therefore, aspirin, commonly used in the treatment and prevention of cardiovascular diseases, was expected to be associated with significantly less upper GI injury. Prichard *et al.*²⁰ showed, however, that short-term administration of low-dose aspirin can induce gastric mucosal damage in healthy volunteers, and that long-term use of 325 mg on an alternate day basis for an average of 60 months was associated with a significantly increased risk of bleeding.⁷

The pathophysiology of aspirin-induced gastroduodenal injury, especially following long-term intake, has not been fully elucidated, although several mechanisms have been proposed.^{4,26,29}

Our retrospective study suggests that long-term daily intake of 100–325 mg aspirin in elderly patients with cardiovascular disorders, may be associated with significant gastroduodenal insult. Moreover, the actual risk of gastrointestinal damage eluding medical detection may be high. Reducing the daily aspirin dose to 60–80 mg may decrease the incidence of major gastrointestinal complications and yet inhibit the production of thromboxane A₂ almost completely.^{8,22,23} Thus, the anti-platelet activity of aspirin can be well preserved, while reducing the risk of gastrointestinal injury. Prospective studies are needed to elucidate the exact incidence of aspirin-induced gastroduodenal damage and the effectivity of co-treatment with 'protective' agents, such as sucralfate, bismuth chelate and synthetic prostaglandins in obviating damage.

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