

## Upper Gastrointestinal Lesions in Elderly Patients Presenting for Endoscopy: Relevance of NSAID Usage

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The occurrence of upper gastrointestinal disease and the relevance of nonsteroidal antiinflammatory drug (NSAID) usage were documented in 511 consecutive patients (321 women, 190 men) over 70 yr old, referred for upper gastrointestinal endoscopy in a district general hospital. The findings were benign esophageal disease (43%), normal (15%), gastric ulcer (11.5%), and duodenal ulcer (11%). Gastric ulcers were more common in women taking NSAIDs (25%) than in NSAID abstainers (7%)  $p < 0.001$  and male NSAID users (8%)  $p < 0.001$ . Esophagitis and esophageal stricture were not influenced by NSAID usage, but gastric erosions were more common (10% vs. 3%)  $p < 0.01$ . Of 142 patients receiving NSAIDs, 41% presented with hemorrhage, compared with 20.5% of NSAID abstainers ( $p < 0.001$ ). Hemorrhage was as common in aspirin takers (15 of 33, 45%) as in standard-dose NANSNAID takers (43 of 109, 39%), even though 86% were taking 300 mg of aspirin per day or less. In elderly patients, esophageal disease is common. NSAID use, even low-dose aspirin, is associated with an increased risk of hemorrhage. In females, NSAID usage is associated with gastric ulcer.

### INTRODUCTION

Upper gastrointestinal endoscopy is a safe and valuable method of evaluating upper gastrointestinal symptoms; in the elderly, there is a higher diagnostic yield than in younger patients (1, 2). An association between NSAID usage and upper gastrointestinal disease has been reported, notably, in elderly females (3, 4). We have attempted to assess these problems as seen in a district gastrointestinal endoscopy service by a prospective evaluation in consecutive referred elderly patients.

### METHODS

#### *Patients*

Blackpool Victoria Hospital is a district general hospital serving a population of 320,000, of whom approximately 46,500 are more than 70 yr old (30,000 F,

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16,500 M). All patients over 70 yr of age referred for upper gastrointestinal endoscopy over an 8-month period were assessed prospectively.

#### *Procedures*

Details of drugs taken within the previous 3 months were obtained from the patients and from hospital records, and general practitioners were contacted for details of prescriptions issued in this period. In the description of patient's drug usage, patients taking nonsteroidal antiinflammatory drugs, including aspirin, were characterized as NSAID takers. Patients taking aspirin and its derivatives were categorized as ASA users, and patients taking nonsteroidal antiinflammatory drugs, but not aspirin or its derivatives, were categorized as NANSNAID users.

In assessment of peptic lesions, gastric and duodenal ulcer were diagnosed when there was a break in mucosal continuity greater than 3 mm in diameter, with crater formation. Gastric erosions were noted when mucosal continuity was broken, but with no depth to the inflammatory process. Gastritis was represented by redness, mucosal hypertrophy, and exudate. Duodenitis was not included in the endoscopic assessment.

Statistical analysis was performed by calculating  $\chi^2$ ;  $p < 0.05$  was considered significant.

### RESULTS

During an 8-month period, 2190 gastroscopies were performed in the Department. Of these, 589 examinations were carried out in 511 patients 70 yr old and over (321 F, 190 M); 290 (57%) were inpatients. Patients were referred by general physicians (57%), geriatricians (22%), general practitioners (5%), and other hospital consultants (16%).

Indications for referral and NSAID usage in these patients are shown in Table 1. NSAIDs had been prescribed for osteoarthritis (67%), cerebral transient ischemic attacks (TIA) (21%), musculoskeletal pain (10%), and rheumatoid arthritis (2%). Of 142 patients on NSAIDs, 58 (41%) presented with upper gastrointestinal hemorrhage, compared with 76 (20.5%) of the 369 NSAID abstainers ( $p < 0.001$ ). Of the 14 different

NSAIDs prescribed, aspirin was the most common (23%), followed by ibuprofen (16%), indomethacin (14%), and piroxicam (10%). There were insufficient numbers taking many of the NSAIDs to permit any conclusions to be drawn about the specific risk of hemorrhage. The duration of treatment with NSAIDs varied from 2 wk to 10 yr, an average of 16 months. Forty-five patients were on NSAIDs for more than 1 year, and 26 were taking them on an intermittent basis. The consumption of other supposedly gastro-toxic drugs (potassium, potassium-containing diuretics, oral corticosteroids, theophyllines, digoxin, allopurinol, and doxycycline) was comparable in NSAID takers (33%) and abstainers (28%). Aspirin had been prescribed for 33 patients (age range, 70–91 yr) in 30 of whom the indication was a supposed TIA. The mean dose was 336 mg/day with a duration to the time of presentation varying from 2 wk to 3 yr. Fifteen of 33 (45%) of the aspirin takers presented with gastrointestinal hemorrhage, compared with 43 of the 109 (39%) of the nonaspirin, nonsteroidal, antiinflammatory drug (NANSAID) takers.

Endoscopic findings are shown in Table 2. In the 511 patients, benign esophageal disease was most common (43%), followed by normal endoscopy (15%), gastric ulcer (11.5%) and duodenal ulcer (11%); other diseases were gastric carcinoma (6%), gastritis/erosions (5%), esophageal carcinoma (3%), gastric polyps (3%), varices (1.5%), and gastroduodenal angiodysplasia (1%). The prevalence of gastric ulcer was increased in women who were taking NSAIDs, compared with those who were NSAID abstainers ( $p < 0.001$ ), and in female NSAID takers compared with male NSAID takers ( $p < 0.001$ ). The prevalence of gastric ulcer in males did not appear to be influenced by NSAID usage. In both sexes, the prevalence of gastric erosions was significantly higher in NSAID takers (10% compared with 3%) ( $p < 0.01$ ). There was a tendency for duodenal ulceration to be commoner in NSAID takers, although this difference reached statistical significance only when figures for male and female takers were combined ( $<0.02$ ). The prevalence of esophagitis and stricture was not influenced by NSAID ingestion in either sex.

The prevalence of gastric ulcer was similar in aspirin takers and NANSAID takers (18% of 22%, respectively) (Table 3). In the NSAID takers presenting with hemorrhage, the prevalence of gastric ulcer in females was 24%, compared with 5% in the NSAID abstainers ( $p < 0.01$ ). Bleeding was as frequent in aspirin takers (16 out of 33, 45%) as in NANSAID takers (43 of 109, 34%). A high proportion (86%) of the aspirin takers were on a low dose (300 mg/day or less), whereas those in the NANSAID group were taking the equivalent of  $>1.2$  g of aspirin per day. In the NSAID group, there were seven patients (5 F, 2 M) who had both gastric and duodenal ulcers. Two of these patients presented with acute hemorrhage, but none of the NSAID abstainers had both types of ulcer. At the time of patient discharge from hospital, the overall mortality for those presenting with gastrointestinal hemorrhage was 8%, and for those presenting with bleeding peptic ulcer (54 patients), mortality was 20% (7 F, 4 M). There was no mortality due to gastrointestinal bleeding from causes other than peptic ulcer. No males underwent surgery, whereas six females had operations, three of whom died. Higher mortality (14% vs 4%) was observed in patients in the over-80 age group; on none of them were operations performed.

#### DISCUSSION

This study showed a high prevalence (85%) of abnormality in elderly patients referred for upper gastrointestinal endoscopy, and these elderly patients more frequently had serious disease. Endoscopy should be considered in any patient having significant upper gastrointestinal symptoms, and ready access to endoscopy in this group should be available (5, 6). In this study, elderly patients have shown a high prevalence of esophageal disease (43% of referred patients, 24% of bleeding lesions). The high prevalence of esophageal disease in the elderly may be related to deteriorating motor function (7). It was not related to NSAID usage. However, as observed previously (8), the situation with regard to gastric ulcer was different. Gastric ulcer has a high prevalence (20% of bleeding lesions) and is associated with NSAID usage. There also was a significant tend-

TABLE I  
Indications for Upper Gastrointestinal Endoscopy

	Total [n = 511 (190 M)]	On NSAIDs [n = 142 (36 M)]	Not on NSAIDs [n = 369 (154 M)]
GI bleed	134 (48 M)	58* (19 M)	76* (29 M)
Dyspepsia	157 (57 M)	36 (9 M)	121 (48 M)
Reflux	54 (22 M)	21 (3 M)	33 (19 M)
Dysphagia	76 (30 M)	9 (3 M)	67 (27 M)
Anemia	90 (33 M)	18 (2 M)	72 (31 M)

\*  $p < 0.001$ .

TABLE 2  
Endoscopic Lesions: NSAID Takers vs Abstainers

Endoscopic Findings	Men		Women		Total	
	NSAID takers (n = 36)	NSAID abstainers (n = 154)	NSAID takers (n = 106)	NSAID abstainers (n = 215)	NSAID takers (n = 142)	NSAID abstainers (n = 369)
Esophagitis/stricture	15 (42%)	63 (41%)	39 (37%)	105 (49%)	54 (38%)	168 (45%)
Gastritis/erosions	5 (14%)*	7 (5%)*	9 (8%)*	5 (2%)*	14 (10%)	12 (3%)
Gastric ulcer	3 (8%)†	13 (8%)	27 (25%)†‡	15 (7%)‡	30 (21%)	28 (8%)
Duodenal ulcer	5 (14%)	12 (8%)	19 (18%)	19 (9%)	24 (17%)§	31 (8%)§
Other diseases	4 (11%)	32 (21%)	2 (2%)	37 (17%)	6 (4%)	69 (19%)
Normal	4 (11%)	27 (18%)	10 (9%)	34 (16%)	14 (10%)	61 (16%)

\* Difference in occurrence of gastritis/erosions in men and women NSAID takers and abstainers,  $p < 0.01$ .

† Difference in occurrence of gastric ulcer between men and women NSAID takers,  $p < 0.001$ .

‡ Difference in occurrence of gastric ulcer in NSAID-taking and -abstaining women,  $p < 0.001$ .

§ Difference in occurrence of duodenal ulcer between total NSAID takers and abstainers,  $p < 0.02$ .

TABLE 3  
Endoscopic Lesions in Patients on NSAIDs: Aspirin and NANSAs Compared

Endoscopic Findings	Patients on NSAIDs (n = 142)		Patients on Aspirin (n = 33)		Patients on NANSAs (n = 109)	
	Total	GIH*	Total	GIH*	Total	GIH*
Esophagitis/stricture	54 (38%)	16	14 (42%)	6	40 (37%)	10
Erosions/gastritis	14 (10%)	8	3 (9%)	3	11 (10%)	5
Gastric ulcer	30 (21%)	15	6 (18%)	3	24 (22%)	12
Duodenal ulcer	24 (17%)	12	5 (15%)	2	19 (17%)	10
Others	6 (4%)	2	3 (9%)†	2	3 (3%)‡	
Normal	14 (10%)	6	2 (6%)		12 (11%)	6

\* Presenting with gastrointestinal hemorrhage (GIH).

† All three were ulcerated antral polyps.

‡ One gastric carcinoma, one esophageal carcinoma, one polyp. There were three patients, each with a single esophageal ulcer, who were on aspirin. These lesions were not seen on NANSAs takers.

ency for these gastric ulcers to be in females, as was observed also in Nottingham (8, 9) but not in the United States (10). In addition, when the numbers for males and females were combined, duodenal ulceration was commoner in patients taking NSAIDs. This was true also in one other study (11).

It has been noted in other studies that NSAIDs increase the risk of peptic ulceration by a factor of approximately 4, bleeding by a factor of approximately 2.5, and death by approximately 7.6 (3). This increased incidence is of particular relevance in elderly patients (12). Other studies have shown that elderly patients dying of peptic ulcer are three times more likely than controls to have been taking NSAIDs (13), and 60% of patients dying of peptic ulcer at any age would have been on NSAIDs (14).

Despite the widely held belief that low-dose aspirin is safe, in this study the risk of peptic ulcer appears as great for those on low-dose aspirin as for NANSAs takers. Acute gastrointestinal hemorrhage was a common feature of aspirin takers, compared with abstainers (42% vs 15%). Low-dose aspirin is gastro-toxic (15) and can produce more mucosal bleeding than warfarin (16). The UK TIA study group (17) found high-dose aspirin

more gastro-toxic than 300 mg/day, and in other similar aspirin trials (18, 19), the side effects vary from 9% to 10%. Low-dose aspirin has been a much-proposed therapy for vascular disease, but most studies relate to younger patients, and in the elderly this indication has not been validated. In addition, many of our patients had a diagnosis of TIA which was poorly substantiated, e.g., a single dizzy spell, or they were self-medicating, believing that aspirin would prevent vascular disease. The increased risk of bleeding suggests that more caution is needed in prescribing. Gastric ulceration in elderly patients is more likely to be painless (20) and, therefore, more likely to present with an unexpected complication. In another study (21), the frequency of gastric and duodenal lesions in patients on chronic aspirin and NANSAs therapy who had no upper gastrointestinal symptoms was 76% and 27%, respectively. For elderly patients needing an analgesic, paracetamol may be safer (9), but when the antiinflammatory effect of an NSAID is required, there is no agreement over whether some agents are less gastro-toxic than others for equivalent antiinflammatory effect (22).

In elderly patients incapacitated by musculoskeletal disease, NSAID usage is invaluable for relieving pain

and improving mobility. It is probable that only by prescribing NSAIDs less often will the considerable annual death rate of NSAID-attributable ulcers be reduced. New upper gastrointestinal symptoms in elderly patients merit early endoscopy, as they reflect a high incidence of pathology, much of which, particularly esophagitis, can be effectively treated. If they are on aspirin, irrespective of dose, or NANSAs, trivial symptoms should be investigated.

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