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The long-term management of patients with bleeding duodenal ulcers

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SUMMARY

Background: Gastrointestinal haemorrhage is a common complication of duodenal ulcers. Patients who bleed are at substantial risk of recurrent bleeding.
Aim: To determine whether appropriate therapeutic steps were taken to reduce the risk of recurrent haemorrhage in patients with a bleeding duodenal ulcer.
Methods: The management of patients surviving a duodenal ulcer bleed in the University Hospital, Nottingham, was assessed by case-note review before (1993) and after (1995–1996) institution of clinical guidelines. The following measures aimed at reducing the risk of recurrent haemorrhage were considered appropriate: stopping non-steroidal anti-inflammatory drugs (NSAIDs) when these were implicated in bleeding; successful eradication of *Helicobacter pylori* if present; and long-term maintenance acid-suppression therapy.
Results: In 1993, appropriate steps were taken to reduce the risk of recurrent haemorrhage in only 48% of cases. Following the institution of guidelines, management improved significantly in 1995–1996 (appropriate in 83% of cases, $P < 0.001$), was associated with increased referral to gastroenterologists ($P < 0.001$), improved patient compliance with follow-up ($P < 0.05$), and more rigorous attempts to identify ($P < 0.001$) and ensure clearance ($P < 0.001$) of *H. pylori*.
Conclusion: In this study, inadequate long-term management of patients with a bleeding duodenal ulcer was common. This was due to a failure to adopt strategies aimed at reducing the risk of ulcer relapse and rebleeding. The quality of care improved significantly following the institution of guidelines and encouragement to refer to gastroenterologists.

INTRODUCTION

Upper gastrointestinal haemorrhage, of which duodenal ulcer is the most common cause, accounts for 8% of acute medical admissions in the UK.[1] Despite a decline in the incidence of uncomplicated duodenal ulcer disease, the number of hospital admissions and operations for ulcer haemorrhage in the USA has remained relatively unchanged since the introduction of histamine H_2-receptor antagonists.[2, 3] Most ulcer deaths, of which there are over 4000 annually in the UK,[4] occur as a consequence of upper gastrointestinal bleeding, shown in a recent UK study to have a mortality rate of 14%.[5]

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Studies have shown that 20–40% of duodenal ulcer patients bleed within 20 years of diagnosis, and that the risk of further haemorrhage then increases to 50% or more.[4, 6] Although most were conducted prior to the widespread use of H_2-antagonists, it does not appear that intermittent acid suppression for symptom recurrence affects the natural history of the disease.[4, 6] Indeed, half of all patients with bleeding have no prior symptoms to indicate ulcer relapse.[2, 7] The management of these patients must, therefore, include strategies both to heal the ulcer and minimize the risk of recurrent bleeding.

The three main factors implicated in gastroduodenal injury which affect management are gastric acid, non-steroidal anti-inflammatory drug (NSAID) ingestion and *Helicobacter pylori* infection.[8] Long-term acid suppression with H_2-receptor antagonists has been shown to be

safe and effective in reducing rebleeding.[2, 9, 10] Whether NSAIDs cause duodenal ulcers is unclear, but they are associated with duodenal ulcer bleeding and ulcer death, and should be stopped if possible.[11] Successful eradication of *H. pylori* offers a potential cure of the ulcer diathesis, and there is emerging evidence that it effectively reduces rebleeding.[12–15] However, standard bismuth-based triple-therapy eradication regimes are complicated, cause side-effects in as many as 30% of cases, fail in 10–20% of cases and non-invasive means of determining the success of eradication are not widely available.[16]

There is currently, therefore, no simple, single, widely accepted strategy for the long-term management of patients who have had a bleeding duodenal ulcer. Rather, a rational treatment strategy must be devised for each patient depending on the risk factors involved, the ability of the patient to comply with and tolerate different treatment regimes, and the availablility of diagnostic resources. We have reviewed the management of patients who have survived a bleeding duodenal ulcer in order to determine whether they were appropriately investigated and treated to minimize the risk of recurrence. For the purpose of the study we have accepted three management strategies as appropriate: the use of maintenance acid-suppression therapy; stopping NSAIDs alone in patients without *H. pylori* infection; or successful eradication of *H. pylori*. As these patients are cared for by all physicians in this hospital, we compared the management by gastroenterologists with that by non-gastroenterologists. The audit was then repeated following the introduction of guidelines for the management of patients with bleeding duodenal ulcers.

METHODS

Patients with a bleeding duodenal ulcer in the University Hospital, Nottingham, in the year 1993 were identified through the ICD coding system, post-mortem reports and all available general medical and surgical discharge summaries. Data were collected from the case notes and further follow-up information obtained from general practitioners. The audit was repeated for all patients admitted from 1 June 1995 to 31 May 1996, following the introduction of management guidelines and encouragement to refer to gastroenterologists.

Statistics

Data were compiled and analysed using SPSS software. Statistical analysis was performed using the Chi-square test of association and Fisher's exact probability test.

RESULTS

Initial study (1993)

Seventy-one patients who had had 73 bleeding episodes during 1993 (44 males and 27 females; mean age 65 years) were identified. Eleven patients (15%) died during their hospital stay and 60 patients were eligible for study of the long-term management of their duodenal ulcer disease.

Clinical details

Of the 60 survivors, 16 (27%) were admitted under the care of a gastroenterologist, 38 (63%) under non-gastroenterologists and six (10%) were admitted directly to a surgical unit. Patients in each group did not differ with respect to mean age or mortality rate. A history of a previous duodenal ulcer was given by 23 patients (38%), of whom three had already suffered a complication (bleed or perforation). In all, 25 patients (42%) were taking NSAIDs on admission, the commonest of which was aspirin (10 patients). Endoscopic injection therapy was administered in 10 cases (17%) and five (8%) required surgery to achieve haemostasis.

Management of patients surviving their gastrointestinal bleed

Inadequate management was seen in 31 of the 60 survivors (52%). This was mainly due to failure either to test for *H. pylori* or to ensure its successful eradication without initiating long-term acid suppression therapy (Table 1). Fifty (83%) of the survivors had follow-up appointments arranged (for an out-patient clinic, endoscopy or a ^{14}C-urea breath test), of whom 10 (20%) failed to attend.

Management of patients taking NDAIDs

Non-steroidal anti-inflammatory drugs were stopped in 24 of the 25 survivors taking these drugs at the time of admission. In one case aspirin was continued as prophylaxis against myocardial infarction with

Table 1. Reasons for suboptimal care by gastroenterologists and non-gastroenteroligists in the initial audit. Values are numbers (percentages) of patients not treated with maintenance acid-supppression therapy

	Gastroenterologists	Non-gastroenterologists	Total
No. *H. pylori* investigation	2	12	14
H. pylori-positive; not eradicated	0	4	4
Attempted eradication; outcome unknown	2	7	9
H. pylori-negative; not on NSAIDs	2	2	4
Total	6	25	31
	(38)	(57)	(52)

omeprazole given long term, a course of action which we would deem appropriate. *Helicobacter pylori* status was determined in 17 (68%) of these patients, of whom nine (53%) were positive and seven received eradication therapy. Seven patients (28%) remained with a positive or unknown *H. pylori* status without being treated with maintenance acid-suppression therapy. Those taking NSAIDs were no more likely to be investigated ($P = 0.6$) or less likely to be treated ($P = 0.7$) for *H. pylori* infection than those on no medication on admission.

Management of patients not taking NSAIDs

In all, 25 patients (71%) in whom bleeding was not related to NSAIDs received either treatment aimed at eradicating *H. pylori* or maintenance acid-suppression therapy. Non-steroidal anti-inflammatory drugs were implicated in all but five (38%) of *H. pylori*-negative patients, of whom only one was treated with long-term maintenance acid-suppression therapy.

Management of H. pylori

Investigation of *H. pylori* infection was performed in 37 patients (62%), 23 of whom (62%) were found to be positive, 13 negative and one result was not recorded. This included 20 of the patients (57%) not taking NSAIDs on admission, of whom 14 (61%) were positive. The result of a rapid urease test (CLOtest; Delta West, Bentley, Australia) was recorded in only 23 of the 36 cases in which it was performed. Other diagnostic investigations performed included antral biopsies for histological examination (11 patients) and a urea breath test in one patient who had no biopsy test performed at initial endoscopy.

Twenty-six patients were given *H. pylori* eradication treatment, 19 of the 23 with positive *H. pylori* tests and eight patients treated empirically (five who were not investigated, two in whom a CLOtest had been negative and one whose test result was not recorded). Of patients not taking NSAIDs on admission, 12 (86%) of those who were *H. pylori*-positive received eradication therapy. Bismuth-based triple therapy was used in 16 patients, an omeprazole–amoxycillin combination in nine patients and a trial therapy in one patient. Later investigation to establish the success of eradication was arranged in 14 cases (52%) (although two patients failed to attend), which was done at a median of 9 weeks (range 4–69 weeks). This took the form of a ^{14}C-urea breath test in eight patients and repeat endoscopy (for CLOtests or histological examination of antral biopsies) in four.

Are gastroenterologists any better at long-term management?

Gastroenterologists investigated more survivors (75%; 12 patients) for evidence of *H. pylori* infection than did non-gastroenterologists (57%; 25 patients), but this difference did not reach statistical significance ($P = 0.3$). There were four patients (17%) known to be *H. pylori*-positive who were not treated: all were non-gastroenterology patients, two because the CLOtest was read too early (before a positive colour change) and not checked subsequently, one because advice was not taken up by the general practitioner and one who failed to attend a follow-up appointment. Non-gastroenterologists were no less likely to treat with eradication therapy than gastroenterologists ($P = 0.1$), but were given advice about who and how to treat in 30% of cases. This was usually provided on the written endoscopy report, but occasionally followed a ward or out-patient referral.

Gastroenterologists checked for eradication success in eight (80%) and non-gastroenterologists in four (25%) of their treated patients ($P < 0.01$). The two gastroenterology patients not checked for successful eradication

failed to attend follow-up appointments and remain on no therapy. Only three of the 12 remaining non-gastroenterology patients (five of whom were taking NSAIDs on admission) are on maintenance acid-suppressant therapy. Of those not taking NSAIDs on admission and who did not receive eradication therapy, nine non-gastroenterology patients and one gastroenterology patient (who did not attend out-patients) were left without long-term maintenance acid-suppression therapy ($P = 0.7$). When all causes of suboptimal care were considered (see Table 1), there was no significant difference between the two groups ($P = 0.3$).

Completion of the audit cycle

The audit was repeated for 98 patients who survived 99 bleeding episodes between 1 June 1995 and 31 May 1996. Of these, 71 (77.2%) were managed by gastroenterologists (compared to 27% in 1993; $P < 0.001$), and all were tested for *H. pylori* infection (compared to 62% in 1993; $P < 0.001$). Non-steroidal anti-inflammatory drug ingestion was associated with a similar proportion of ulcer bleeds in 1995–1996 (36%; 35 patients) as in 1993, was felt to be causal in 32 (all of whom tested negative for *H. pylori*) and was stopped in all but three cases. Sixty-six patients (72%) were infected with *H. pylori* (which included three patients taking NSAIDs). Eradication therapy was given to a proportionately smaller group of infected patients than in 1993 (62%; 41 patients), but this did not reach statistical significance. Follow-up appointments for a urea breath test were made for all patients, two of whom did not attend ($P < 0.001$ compared to 1993), and 10 (including the three *H. pylori*-infected patients taking NSAIDs) were treated with long-term acid suppressants. Thus, 17 patients (17%, $P < 0.001$ compared to 1993) received suboptimal long-term therapy following their duodenal ulcer bleed. This included the two patients who failed to attend follow-up appointments, 10 patients given *H. pylori* eradication therapy without being followed-up to ensure successful eradication, four patients given courses of proton pump inhibitors but no long-term therapy, and one patient who appeared to receive no treatment.

DISCUSSION

Survivors of duodenal ulcer bleeding received suboptimal care according to our defined management strategies in 52% of cases in 1993. Optimal care was compromised by poor patient compliance, practical problems in the diagnosis of *H. pylori* infection and inadequate medical management. Thus, a substantial proportion of patients remained potentially at risk of further duodenal ulcers and bleeding. Fewer than one third of the patients with bleeding duodenal ulcers were admitted under gastroenterologists, who tended to treat more patients for *H. pylori* infection and were more likely to reinvestigate to ensure success following attempted *H. pylori* eradication.

Poor patient compliance clearly prevented appropriate management in some cases, and may have affected others, as 20% failed to attend follow-up appointments. The need for follow-up for this potentially life-threatening condition should be carefully explained to patients, and the general practitioner should be made aware of the management plan.

More importantly, however, inadequate medical management was identified in the initial audit. Non-steroidal anti-inflammatory drugs were stopped whenever possible, but in only a third of presumed NSAID-related cases were these patients investigated and treated for *H. pylori* infection or given maintenance acid-suppression therapy to reduce the risk of ulcer recurrence. Patients in whom bleeding was not related to NSAID ingestion received *H. pylori* eradication or maintenance therapy in only 71% of cases. Evidence of *H. pylori* infection was sought overall in only 62% of patients. That concern over the side-effect profile of bismuth-based triple therapy led to under-investigation is not supported by our data showing that over a quarter of patients receiving eradication therapy were treated empirically. Of all those receiving eradication therapy, 50% had no further investigation to ensure its success, yet only three (23%) are taking maintenance acid-suppression therapy.

Incorrect or failed diagnosis occurred when the CLOtest was the sole means of diagnosis of *H. pylori* infection. Although most positive results are obtained within 1 h, some may take up to 24 h to induce a colour change.[17] Without facilities to store the tests or provide 24-h readings, tests were both read incorrectly and lost in this study.

Medical management significantly improved between the years 1993 and 1996 following institution of the guidelines. The majority of patients were cared for and followed up by gastroenterologists. Better communication about the need for, and the purpose of, follow-up is

likely to improve patient compliance. All patients were routinely investigated for evidence of *H. pylori* infection, reflecting a better appreciation of the importance of identifying risk factors for ulcers and ulcer bleeding. The majority of those testing positive received eradication therapy, all of whom were offered follow-up to ensure its success. There remained a small proportion of patients known to be infected with *H. pylori* who received neither eradication nor maintenance acid-suppressant therapy.

Management of patients presenting with duodenal ulcer bleeding in the long term should aim to minimize factors known to promote gastroduodenal injury. The three main therapeutic options are avoidance of gastrotoxic drugs, long-term maintenance acid suppression and *H. pylori* eradication. Non-steroidal anti-inflammatory drugs should be stopped if implicated in duodenal ulcer bleeding (Fig. 2). Where there are good indications to continue the treatment, however, ulcer healing occurs following treatment with H_2-receptor antagonists (albeit more slowly) or proton pump inhibitors (with no retardation of healing).[18] Furthermore, long-term H_2-antagonists or misoprostol therapy may prevent ulcer recurrence in patients taking NSAIDs.[18]

We aim to investigate all patients for evidence of *H. pylori* infection who are likely to comply with, and tolerate, eradication therapy (Figures 1 and 2). Our preferred treatment is omeprazole (20 mg), clarithromycin (250 mg) and metronidazole (400 mg), each given twice daily for 1 week, a regime recently shown in this unit to achieve 89% eradication, with only 1.6% of patients withdrawing from treatment owing to side-effects.[19] The presence of *H. pylori* does not obviously increase the risk of ulcer bleeding in patients who are taking NSAIDs, but, as their respective roles in causing ulcers and precipitating bleeding in a pre-existing ulcer are not fully elucidated, it is our policy to eradicate the organism if present. Should eradication therapy be unsuitable or fail, long-term acid suppression is an alternative strategy to reduce ulcer relapse and rebleeding.

Bleeding duodenal ulcer carries a high mortality rate and is liable to recur. The optimal treatment must aim to reduce the risk of recurrence and will depend on patient characteristics and the risk factors involved in each case. In this study we identified flaws in management arising from several sources and demonstrated a significant improvement following the institution of guidelines and encouragement to refer to gastroenterologists. The problems were partly due to poor patient compliance. It is clearly important to explain the need for follow-up appointments to patients and to inform the general practitioner of the long-term management plan in case of default. Problems arose in the diagnosis of *H. pylori* infection and this issue has been addressed by the establishment of a rapid urease test reading service. For follow-up and recruitment into clinical trials we encourage referral of patients by non-gastroenterologists.

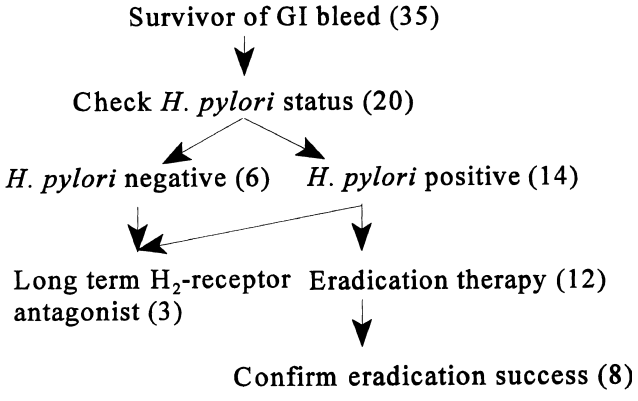

Figure 1. Acceptable long-term management of patients with bleeding duodenal ulcer not associated with non-steroidal anti-inflammatory drug ingestion. Numbers of patients in each subgroup in the initial audit are given in brackets. GI, gastrointestinal.

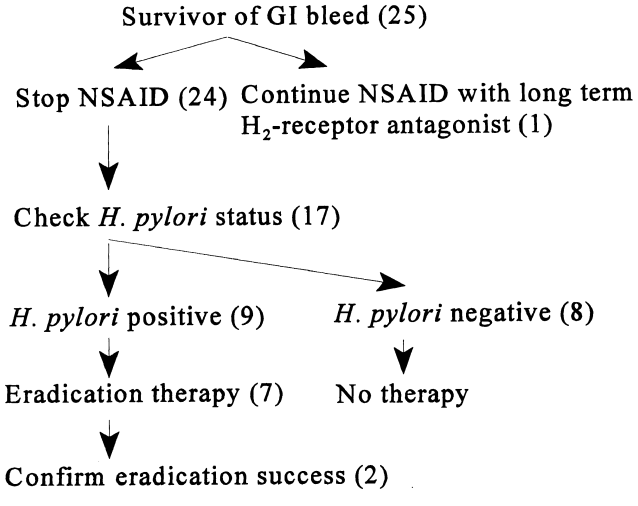

Figure 2. Acceptable management of patients surviving a bleeding duodenal ulcer associated with non-steroidal anti-inflammatory drug (NSAID) ingestion. Numbers of patients in each subgroup in the initial audit given in brackets. GI, gastrointestinal; NSAID, non-steroidal anti-inflammatory drug.

Finally, in order to promote effective and consistent management we have adopted the treatment protocol outlined (Figures 1 and 2) for patients with bleeding duodenal ulcers.

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