The use of proprietary medicines by patients presenting with peptic ulcer haemorrhage

J. F. MARRIOTT, P. A. ASQUITH & C. J. SHORROCK

Department of Medicine and Pharmacy Department, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5SS

- 1 Medication, social and symptom histories were compared in patients with severe haemorrhage from a peptic ulcer ($n = 71$) and matched control subjects. Self-medication with proprietary agents was catalogued in addition to therapy prescribed by general medical practitioners.
- 2 Prior to the bleed, only 4% of ulcer patients had been free of symptoms normally associated with peptic ulceration, whereas 76% of the control group had been asymptomatic.
- 3 Gastro-irritant proprietary medicines were used regularly by 23% of ulcer patients compared with only 4% of controls. However, proprietary antacids were used chronically by 46% of ulcer patients compared with only 7% of controls. Bicarbonate was the antacid of choice used by 13% of ulcer patients. The odds ratio for the association between development of bleeding peptic ulcer and the use of indigestion remedies was 11.5 (95% CI 1.1, 121).
- 4 Fifty-one percent of ulcer patients were prescribed agents known to cause gastrointestinal damage, whereas only 25% of the control group were prescribed similar agents. Only 7% of the control group were prescribed anti-ulcer therapy compared with 37% of those with bleeding ulcer.
- 5 A large proportion of patients with haemorrhage from a peptic ulcer had had symptoms sufficient to warrant recourse to self-medication with antacids without medical knowledge. Exacerbation of peptic ulcer by self-medication with proprietary products is likely to be of lesser significance.

Keywords proprietary medicines peptic ulcer haemorrhage

Introduction

Gastrointestinal bleeding can result from a number of conditions ranging from neoplastic change to mechanical damage, however, recent data indicate that almost three-quarters of cases can be attributed to upper gastrointestinal ulceration (Holman *et al.*, 1990). Although changes in the distribution and rates of peptic ulceration have been noted over the last three decades (Coggan *et al.*, 1981) mortality is still significant with recent studies providing estimates of about 5% in patients with peptic ulcer haemorrhage (Daneshmend *et al.*, 1992; Holman *et al.*, 1990; Katschinski *et al.*, 1989; Walt *et al.*, 1991). However, a relative increase in the incidence of gastrointestinal haemorrhage has also been demonstrated in the elderly (Bardhan *et al.*, 1989).

Anecdotal reports of perforation or haemorrhage being the first indicators of peptic ulcer are commonplace:

in an investigation of hospital admissions caused by bleeding peptic ulcer, Jorde & Burhol (1987) suggested that over one-third of patients had been previously asymptomatic. However, the validity of such findings must be questioned, since mild symptoms of dyspepsia might not be considered relevant by the critically ill patient. Furthermore, the treatment history is rarely found to be comprehensive (Herxheimer, 1989), a factor which must hinder the accurate evaluation of predisposing conditions.

Numerous factors have been implicated in ulcer generation (Bianchi Porro & Parente, 1991). Although the evidence supporting an ulcerogenic role for most of these is scant, cigarette smoking and the consumption of certain medicinal agents, notably non-steroidal anti-inflammatory drugs, do appear to be significant risk

factors (Bianchi Porro & Parente, 1991; Coggan *et al.*, 1981).

A wide range of compounds with the potential to modify ulcer progression are freely available through retail outlets in the United Kingdom. However, there have been no systematic studies of the use of proprietary medicines in patients presenting with bleeding peptic ulcer. The present case-control study was designed to investigate the use of 'over-the-counter' medicines and the prevalence and nature of gastrointestinal symptoms in patients presenting with peptic ulcer haemorrhage.

A preliminary report of the present study was presented to the British Pharmacological Society, Southampton, September 1991.

Methods

All patients presenting at East Birmingham hospital with haematemesis and/or melaena were considered for inclusion in this study, but only those patients with a primary endoscopic diagnosis of bleeding peptic ulcer were evaluated. Those patients with other primary causes of gastrointestinal bleeding were excluded. Control subjects were selected from visitors to the hospital and matched according to age (± 5 years), sex and residential area. No case or control refused to participate in this study.

The written clinical history of each patient was examined for gastrointestinal symptoms, medicine use and social history. Cases and matched controls were also interviewed in a non-judgemental manner (by JM) between May 1989 and December 1990 according to a structured framework similar to that suggested by Herxheimer (1989). Before each interview the general aims of the study were explained and consent obtained.

The interview covered general demographic information, the clinical course leading to admission, previous medical history and medicine use, diet, alcohol and tobacco use and also a review of ailments that might have precipitated recourse to proprietary medicines. The review did not solely concentrate upon the gastrointestinal tract.

In an attempt to limit misuse of their products, manufacturers of proprietary medicines recommend a maximum daily dose and a short treatment period of only a few days, unless medical advice is given to the contrary. Consequently, individuals were considered to be 'users' of those proprietary products only if taken at or above manufacturers' recommended doses for at least 7 consecutive days before admission or interview. Similarly, symptoms associated with peptic ulceration were considered relevant only if present for a period greater than 7 days before the bleeding episode or interview. These symptoms were pain in the lower abdomen and/or epigastrium, heartburn, nausea, vomiting, waterbrash and anorexia. No attempt was made to rank the severity of pain or symptoms experienced.

Estimates of the odds ratio and their associated 95% confidence intervals (CI) were calculated according to Rothman (1986) and Schlesselman (1982).

Results

The demographic data for cases and controls are shown in Table 1.

Five additional patients (7% of the final study population) died without being interviewed. Further data from these patients have not been included.

During the selection of the control group four patients (6% of the final control group) were encountered who

Table 1 Demographic data and summary of factors associated with bleeding peptic ulcer (PU) (gastric ulcer (GU): duodenal ulcer (DU)). Figures are numbers (percentages) of individuals unless otherwise stated

Variable	Cases (n = 71)	Controls (n = 71)	Odds Ratio	95% CI
Age (years) (♂:♀ 42:29)	62 $\pm$ 2	61 $\pm$ 2		
DU	45 (63)	—		
GU	32 (45)	—		
GU+DU	6 (8)	—		
Previous PU history	20 (28)	—		
<i>Social factors</i>				
Alcohol	32 (45)	25 (35)	1.5	0.3, 7.1
Cigarettes	31 (44)	18 (25)	2.3	0.4, 11.7
<i>Symptoms</i>				
Pain only	2 (3)	2 (3)		
Pain free GIT symptoms	13 (18)	6 (8)		
GIT symptoms + pain	53 (75)	9 (13)		
Symptom free	3 (4)	54 (76)		
<i>Prescribed medicines used</i>				
Gastro-irritant	36 (51)	18 (25)	3.0	0.6, 15.5
Anti-ulcer	26 (37)	5 (7)		
<i>Self-medication used</i>				
Gastro-irritant	16 (23)	3 (4)	6.6	0.3, 127
Antacids	33 (46)	5 (7)	11.5	1.1, 121

had previously suffered a gastrointestinal bleed. In three of these bleeding resulted from gastritis induced by non-steroidal anti-inflammatory drugs and in the other from an angiomatous malformation. These individuals were excluded from the control group.

Social factors

Numbers of cases and controls who smoked cigarettes or used significant quantities of alcohol, defined as greater than 21 units weekly for males and greater than 14 units weekly for females are shown in Table 1 together with the odds ratio estimates.

Pain and other gastrointestinal symptoms

The symptoms considered to be associated with peptic ulcer in the present study are given above. The number of cases and controls experiencing either pain and/or other gastrointestinal symptoms is shown in Table 1.

Of the three (4%) patients in the ulcer group previously pain and symptom free, one had been prescribed a non-steroidal anti-inflammatory agent and the remainder had taken proprietary analgesics.

Use of prescribed therapeutic agents

Of the patients with a bleeding ulcer, 36 (51%) were taking prescribed agents regularly with known potential to cause gastrointestinal damage as recorded in UK product data sheets. In this sub-group, 25 patients were using a non-aspirin non-steroidal anti-inflammatory drug. Of the other patients in this sub-group, seven were prescribed aspirin or salicylate derivatives, two received corticosteroids and one theophylline. Thirteen (18%) patients were prescribed concurrently two or more of the gastro-irritant agents described above.

In the control group 18 patients (25%) had been prescribed agents known to be gastro-irritant: 10 of these took non-aspirin non-steroidal anti-inflammatory drugs and 8 were prescribed salicylates or corticosteroids. The odds ratio estimates for development of bleeding peptic ulcer associated with prescribed medicines in the present study was 3.0 (95% CI 0.6, 15.5). Prescribed anti-ulcer therapy in the form of either antacids and/or antisecretory agents, was taken by 26 (37%) patients with bleeding ulcer. Anti-ulcer therapy was prescribed in combination with gastro-irritant agents in 12 patients: five received antacids, six histamine-receptor antagonists and one misoprostol. Of the control group, five individuals had been prescribed anti-ulcer therapy as defined above, although none had endoscopically proven peptic ulceration.

Self-medication

Of the patients with bleeding peptic ulcer, 16 (23%) had ingested regularly proprietary medicines likely to cause gastrointestinal damage. Of these, 15 had used aspirin based agents and one had taken proprietary ibuprofen before the bleed. In the control group only three individuals (4%) regularly used gastro-irritant proprietary products (two used aspirin, one ibuprofen). Although paracetamol was not considered to be gastro-irritant in

the present study, this analgesic was regularly taken by 17 (24%) of the ulcer patients. However, ingestion of paracetamol appeared to reduce pain associated with peptic ulceration in only four (6%). Proprietary antacid products likely to mask or allieviate symptoms of peptic ulcer were used by 33 (46%) of patients with bleeding ulcer. In each of these cases antacids were used for a period of months or years. Bicarbonate, chiefly in the form of sodium bicarbonate powder BP, was the primary antacid used by nine (13%) of these patients with a dose range of 100–1000 g each month. In the control group only five (7%) individuals used indigestion remedies regularly. The odds ratios for development of bleeding peptic ulcer associated with 'over-the-counter' agents are shown in Table 1.

Discussion

The present case-control study supports the previously reported association between peptic ulcer bleeding and ingestion of prescribed gastro-irritant medicines. In addition, this study provides an estimate of the risks associated with patient self-medication in peptic ulcer disease and suggests that the associated symptoms may be more prevalent than previously recognized. The patients examined in the present study appear to be representative of a wider population since the mortality associated with peptic ulcer haemorrhage was similar to that recently reported in a large district general hospital (Katschinski *et al.*, 1989). However, in the study conducted by Katschinski and co-workers (1989) the observed mortality of approximately 10% associated with peptic ulcer haemorrhage fell to about 5% when only death directly associated with bleeding was considered. Such considerations were not made in the present study. Gastric ulcer was observed more frequently than duodenal ulcer in the present study, contrary to the accepted distribution of these lesions in Britain (Coggan *et al.*, 1981), however, these findings might reflect an association of more serious symptoms with gastric ulceration.

Reports included in the review by Jorde & Burhol (1987) indicated that between 7 and 33% of patients presenting with bleeding peptic ulcer were previously asymptomatic. In these studies a high proportion of asymptomatic patients were found to be elderly or to have used non-steroidal anti-inflammatory drugs. Certain workers have suggested that these compounds mask ulcer symptoms (Shallcross & Heatley, 1990) in addition to exerting an ulcerogenic effect. However, in the present study few patients with gastrointestinal haemorrhage were asymptomatic even though over one-third took non-steroidal anti-inflammatory drugs regularly. These findings support suggestions that non-steroidal anti-inflammatory drugs present a real increase in bleeding risk in peptic ulceration (Chesner *et al.*, 1986).

In spite of suggestions that minor symptoms of peptic ulcer can be treated conservatively without significant risks of serious consequences (Brown & Rees, 1990), our findings indicate that in a proportion of ulcer patients this is clearly not the case. As a large proportion of ulcer

patients resorted to chronic self-medication without medical advice, the value of a comprehensive medical history is reinforced. The present study indicates that close examination of the lifestyle of an ulcer patient, particularly with regard to medicine ingestion, could prevent the spurious dismissal of minor ulcer symptoms, since heavy use of proprietary antacid preparations appears widespread amongst patients prior to a gastrointestinal bleed. Of particular concern is the chronic use of sodium bicarbonate powder as an antacid amongst this group of patients, in doses capable of masking serious symptoms.

It is also notable that the abuse of gastro-irritant proprietary products by patients with peptic ulcer is somewhat less common than the corresponding use of antacids. Of particular interest is the apparent lack of involvement of proprietary agents containing ibuprofen in precipitating a bleed from a peptic ulcer. These findings should however be treated with caution when considering the relative safety of 'over-the-counter'

ibuprofen, since gastrointestinal events arising from inflammatory conditions such as gastritis were not considered in the present investigation. About one-quarter of the ulcer patients used paracetamol regularly in the present study, which might reflect active avoidance of more gastro-irritant analgesics (Piper *et al.*, 1988), however, there was little evidence that their use of paracetamol masked ulcer symptoms.

This study shows that a large proportion of patients with bleeding peptic ulcer had had symptoms sufficient to warrant recourse to chronic, excessive self-medication with antacids without consulting a medical practitioner. It is unknown whether these actions delayed or prevented initiation of more appropriate therapy. It would also appear that gastrointestinal damage caused by self-medication is likely to be of lesser significance.

The authors should like to thank Glaxo plc and the West Midlands Regional Health Authority for their support.

References

- Bardhan, K. D., Cust, G., Hinchliffe, R. F. C., Williamson, F. M., Lyon, C. & Bose, K. (1989). Changing patterns of admissions and operations for duodenal ulcers. *Br. J. Surg.*, **76**, 230–236.
- Bianchi Porro, G. & Parente, F. (1991). Long term treatment of duodenal ulcer. A review of management options. *Drugs*, **41**, 38–51.
- Brown, C. & Rees, W. D. W. (1990). Dyspepsia in general practice. Try empirical treatment first and investigate patients who do not respond. *Br. med. J.*, **300**, 829–830.
- Chesner, I. M., Rhodes, L. E. & Montgomery, R. D. (1986). Occurrence of pain in peptic ulcer haemorrhage: relation to age and non-steroidal anti-inflammatory drugs. *Gut*, **27**, A1281–A1282.
- Coggan, D., Lambert, P. & Langman, M. J. S. (1981). 20 years of hospital admissions for peptic ulcers in England and Wales. *Lancet*, **i**, 1302–1304.
- Daneshmend, T. K., Hawkey, C. J., Langman, M. J. S., Logan, R. F. A., Long, R. G. & Walt, R. P. (1992). Omeprazole versus placebo for acute upper gastrointestinal bleeding: randomized double blind controlled trial. *Br. med. J.*, **304**, 143–147.
- Herxheimer, A. (1989). A framework for taking a treatment history. *J. Roy. Coll. Phys. (Lond.)*, **23**, 22–23.
- Holman, R. A. E., Davis, M., Gough, K. R., Gartell, P., Britton, D. C. & Smith, R. B. (1990). Value of a centralised approach in the management of haematemesis and melaena: experience in a district general hospital. *Gut*, **31**, 504–508.
- Jorde, R. & Burhol, P. G. (1987). Asymptomatic peptic ulcer disease. *Scand. J. Gastroenterol.*, **22**, 129–134.
- Katschinski, B. D., Logan, R. F. A., Davies, J. & Langman, M. J. S. (1989). Audit of mortality in upper gastrointestinal bleeding. *Postgrad. med. J.*, **65**, 913–917.
- Piper, D. W. & McIntosh, J. H. (1988). Paracetamol and peptic ulcer. *Lancet*, **ii**, 1192.
- Rothman, K. J. (1986). *Modern epidemiology*. Boston: Little Brown and Co.
- Schlesselman, J. J. (1982). *Case-control studies: design, conduct and analysis*. New York: Oxford University Press.
- Shallcross, T. M. & Heatley, R. V. (1990). Effect of non-steroidal anti-inflammatory drugs on dyspeptic symptoms. *Br. med. J.*, **300**, 368–369.
- Walt, R. P., Cottrell, J., Mann, S. G., Freemantle, N. & Langman, M. J. S. (1991). Randomised double blind controlled trial of intravenous famotidine infusion in 1005 patients with peptic ulcer bleeding. *Gut*, **32**, A571–A572.

(Received 21 April 1992,
accepted 12 November, 1992)