Long term acid suppressing treatment in general practice

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Abstract

***Objective*—To determine the current practice in selected general practices for prescribing long term (>6 months) treatment to suppress gastric acid secretion.**

***Setting*—Seven general practices in the Harrow area that always or usually refer to Northwick Park Hospital.**

***Subjects*—60 148 patients on lists of the general practices.**

***Design*—Identification of patients receiving long term treatment through repeat prescribing data, followed by a manual and computer survey of patients' notes for indications and investigations. Patient compliance and views on treatment were sought by a postal questionnaire.**

***Main outcome measures*—Indications for treatment, treatment given, investigations undertaken before and during treatment.**

***Results*—492 patients (0·82% of the population) were taking long term acid suppressing treatment. The most common diagnosis was duodenal ulcer disease (183 (37%) of all patients); oesophageal disease (118 (24%)) was also common. 93 patients (19%) were treated for abdominal pain where no diagnosis had been reached or who had only a diagnosis of gastritis on endoscopy. Ranitidine was prescribed in 394 (80%) patients. 298 (74%) patients found treatment helpful, but 108 (27%) had a poor understanding of their diagnosis. 317 patients (78%) took their drug as prescribed. 37 patients were also taking prescribed non-steroidal anti-inflammatory drugs and an additional 43 patients took regular aspirin or ibuprofen without prescription.**

***Conclusions*—Long term acid suppressing treatment is common, and a substantial number of patients are taking these drugs long term without a diagnosis having been reached. It is hoped that protocols for investigation and treatment will improve these figures. Patients need to be better informed about their disease and the possible adverse effects of taking non-steroidal anti-inflammatory drugs in acid related upper gastrointestinal disease.**

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Introduction

The introduction of powerful acid suppressing drugs has revolutionised the management of acid related upper gastrointestinal disease. The H_2 receptor antagonists and proton pump inhibitors are highly effective in treating peptic ulcer and peptic oesophageal disease.[1,2]

Preparations for treating gastrointestinal conditions form the second most expensive group of drugs prescribed in the United Kingdom, with the H_2 antagonists forming the single largest budget item.[3] There were 1·2 million prescriptions for H_2 antagonists in 1990 at a total cost of over £90 million.[3] There has therefore been considerable interest in determining which patients require these drugs and for how long they should be treated.

There is currently much debate as to the optimal treatment for duodenal ulceration, with eradication of *Helicobacter pylori* becoming increasingly accepted as the best treatment for preventing relapse.[4] Difficulties exist, however, with eradication regimens, mainly due to the side effects of treatment[5] and a high incidence of metronidazole resistant organisms,[6,7] and the H_2 antagonists seem set to continue to play a major part in the treatment of duodenal ulcer disease.[8]

Most authorities suggest a six to eight week course of an H_2 antagonist as initial treatment for peptic ulcer disease.[9] There is, however, wide disagreement about the indications for and value of long term treatment of patients with peptic ulceration. Some authors have produced cost-benefit analyses to underpin lifelong maintenance treatment for a single episode of duodenal ulceration[10]; others would restrict the use of long term treatment to those with a complication of their peptic ulcer.[9,11]

While data are available to show the total number of prescriptions issued for acid suppressing drugs, little is currently available on their long term use. This is particularly true of their use in general practice, where most dyspeptic patients will be treated. Almost all published data rely on hospital studies, with their inherent bias in patient selection.[12,13]

The aims of this study were fourfold: to determine the number of patients taking long term acid suppressing therapy in seven practices in the Harrow area; to find from practice records what diagnosis had been established in these patients; to determine what investigations had been undertaken to arrive at that diagnosis; and to document whether patients take their drugs as directed and whether the drugs are of use to them.

Methods

Seven practices were studied. Four were multipartner practices (one had six partners; two, five partners; and one, 3·5 full time equivalents); two were two partner practices, and one a single handed practice. Five practices were computerised. The practices were chosen to provide a spectrum of types of general practice, from single handed to multipartner. Practices were approached after information was obtained from the local family health services authority as to practices that were likely to participate, with a range of prescribing costs in relation to prescribing for gastrointestinal disease. The information as to whether a practice was a high or low prescriber was not, of course, divulged to the audit group. Data from the family health services authority and practices showed that overall costs of prescribing gastrointestinal drugs among the seven practices were slightly below the national average. Three of the practices studied were teaching practices. Only a single practice (from the initial eight suggested) approached by the audit group was unwilling to participate. All practices chosen

usually refer gastroenterological patients to Northwick Park Hospital. The single exception was a group practice with a branch surgery considerably closer to another hospital—a proportion of the gastrointestinal workload was referred there.

Long term treatment was determined as continuous therapy for six months or more. This criterion was set for two reasons; a single episode of peptic ulcer disease with early relapse could amount to four months' treatment and would not be within the real group of interest of this study; also, by six months all patients would have been entered on the practice's repeat prescribing list.

The drugs studied were cimetidine, ranitidine, nizatidine, famotidine, omeprazole, and misoprostol (which, although not acid suppressing, is used for gastric cytoprotection).

IDENTIFICATION OF PATIENTS

Patients treated for longer than six months were identified from computerised repeat prescribing data where this was available or by noting the names of any patient requiring a repeat prescription for defined acid suppressing drugs over a three month period before the start of the study. This was carried out by the practice reception staff and the general practitioners involved, who were given a list of generic and brand named drugs. The list was then collected by the study group and patients' notes were examined; if patients fulfilled the criterion of six months' continuous treatment they were included in the study.

SURVEY OF PATIENTS' GENERAL PRACTICE NOTES

General practice notes of patients identified by this technique were then examined. The following information was extracted: name, age, and sex of patient; reason for long term prescribing of treatment; investigations of the upper gastrointestinal tract (barium meal and gastroscopy), with dates carried out; drug taken; date of starting treatment; any other medical condition present; whether or not the patient had been reviewed in hospital; who started the long term treatment (general practitioner or hospital consultant); presence of any complication of peptic disease (for example, gastrointestinal bleeding or oesophageal stricture); and other drug treatment, especially non-steroidal anti-inflammatory drugs.

PATIENT QUESTIONNAIRE

All patients were sent a simple questionnaire asking about family history of ulcer disease, smoking and alcohol consumption, how often they took their drugs, what they considered was the reason for taking the drugs, and whether the drugs helped their symptoms. They were also asked if they took other drugs, especially "over the counter" non-steroidal drugs such as aspirin and ibuprofen. They were also asked directly if they took antacids regularly or sporadically.

Results

NUMBERS OF PATIENTS

The total number of patients registered with the seven practices was 60 148. The practices studied had a similar age distribution to the general population, with 20·3% of patients in the study group being over 65 years of age (12 217/60 148; Harrow Family Health Services Authority, 1991/2 figures) compared with 17·9% of the United Kingdom population (9 820 130/54 888 884; 1991 census) (95% confidence interval for difference in proportion −0·0210 to 0·0274). A total of 492 patients identified were taking long term acid suppressing treatment (0·82% of the total population; 0·80% to 0·84%).

More men than women (275 *v* 217; 1·27:1) were taking long term treatment. The age range was 4 to 93 years with a mean of 63·9 years. Almost two thirds (65%) of patients receiving long term acid suppressing treatment were aged 60 or over; 25% were over 75.

Overall duration of treatment was difficult to establish from the practice notes in many cases. No definite date of starting continuous treatment was available and many patients seem to have had multiple short courses of treatment before long term therapy. It was always possible to establish a six month period during which treatment had become "long term" and continuous, allowing an approximate duration of treatment to be established. Three quarters of patients surveyed had been taking continuous treatment for more than five years at the time of survey.

DIAGNOSIS

The most common diagnosis leading to long term treatment was duodenal ulcer disease, accounting for 183 (duodenal ulcer, 168; duodenitis alone, 15), 37% of patients treated (table I). The second most common reason for treatment was oesophageal disease (78 (16%); oesophagitis, 61; oesophageal stricture, 17); when the 40 patients with hiatus hernia as the only positive finding and with a history suggestive of reflux were added to this group, oesophageal disease accounted for 24% of the total. Oesophageal motility disorders were the reason for long term treatment in six patients, four of whom had achalasia of the cardia and were receiving long term treatment after balloon dilatation.

Abdominal pain where no diagnosis had been reached (72 (15%) patients) was the third largest diagnostic grouping. In 21 (4%) patients an endoscopic diagnosis of gastritis was the only positive finding.

Gastric ulcer is a relatively uncommon reason for long term treatment (25 patients; 5%). The primary reason for prescribing antacid treatment was gastroprotection from the effects of non-steroidal anti-inflammatory drugs in 37 patients; a further eight were taking H_2 antagonists because corticosteroids had also been prescribed. Some patients (22; 4%) were receiving prophylaxis because they were receiving dialysis or had alcoholic liver disease and oesophageal varices.

UNDIAGNOSED ABDOMINAL PAIN

Of the 72 patients with undiagnosed abdominal pain, 34 had had no investigations, and in 38 at least one examination had negative results. In those who had been investigated, 10 had had both upper gastrointestinal endoscopy and barium studies; 21 had had only barium examinations, and the remaining seven had had gastroscopy alone.

The initiator of treatment in these cases was the general practitioner in 55 (76%), a gastroenterologist in one (2%), a physician in six (8%), and a surgeon in 10 (14%). Forty one of these patients had been seen in hospital at some point (usually soon after reporting

TABLE I—*Reasons for prescribing acid suppressing drugs or misoprostol in 492 patients receiving long term (over six months) treatment in general practice*

Diagnosis or indication	No of patients (n=492)
Duodenal ulcer	183
No diagnosis; abdominal pain or gastritis on endoscopy	93
Oesophagitis or stricture	78
Hiatus hernia	40
Prophylaxis with non-steroidal anti-inflammatory drug	37
Gastric ulcer	25
Prophylaxis for medical condition	22
Prophylaxis with steroids	8
Motility disorder	6

TABLE II—*Practice characteristics and rates of patients treated for abdominal pain, duodenal ulcer, and oesophageal disease*

Practice	No of partners	List size	Duodenal ulcer* (No (rate/1000))	Oesophageal disease (No (rate/1000))	Abdominal pain (No (rate/1000))
A	1	2030	5 (2·46)	10 (4·9)	0 (0)
B	2	4001	17 (4·2)	14 (3·5)	9 (2·2)
C	2	5501	7 (1·2)	9 (1·6)	10 (1·8)
D	3·5	9657	39 (4·0)	21 (2·2)	27 (2·8)
E	5	10599	23 (2·2)	11 (1·0)	5 (0·5)
F	6	15834	53 (3·3)	25 (1·6)	19 (1·2)
G	6	12526	38 (3·0)	28 (2·2)	23 (1·8)

*Includes patients with frank duodenal ulcers and duodenitis.

TABLE III—*Drugs prescribed for long term treatment of acid related upper gastrointestinal disorders in general practice*

Drug	No (%) of patients
Ranitidine	394 (80)
Cimetidine	60 (12)
Famotidine	4 (1)
Nizatidine	4 (1)
Misoprostol	2 (<1)
Omeprazole	28 (6)

TABLE IV—*Compliance with treatment as reported by patients in postal survey*

Frequency	No (%) of patients
Take as directed	317 (78)
Take 6/7 days	34 (8)
Take 4/7 days	27 (7)
Take once a week	16 (4)
Take once a month or less	11 (3)

TABLE V—*Regimens chosen for long term treatment with ranitidine of acid related upper gastrointestinal disease in general practice*

Ranitidine regimen	No completing form	No (%) taking regularly
Once daily:		
150 mg	126	103 (82)
300 mg	24	22 (92)
Twice daily:		
150 mg	100	83 (83)
300 mg	2	2 (100)

their symptoms) and 37 had been prescribed a short course of H_2 antagonists at this time. In the 15 patients whose treatment was started by a hospital doctor, no duration of intended treatment was stated in 11, and four were intended to have only a six week course.

The mean age of patients with undiagnosed abdominal pain did not differ significantly from that of the other patients receiving long term treatment (mean for abdominal pain 62·8 years, range 25 to 87 years; mean for other diagnoses 64·5 years, range 4-93 years; $P=0·64$, unpaired t test). In contrast with the patients with other diagnoses, there were more women than men (45 *v* 27; 1:1·6) with undiagnosed abdominal pain ($\chi^2=10·7$, df=1, $P=0·001$, Yates corrected χ^2).

There was a significant difference in the number of patients with undiagnosed abdominal pain per thousand on the list between practices, with rates varying between 2·8/1000 and 0/1000 (table II) ($\chi^2=24·3$, df=6, $P=0·0005$). Only one practice (a five partner group practice) had direct open access upper gastrointestinal endoscopy available; the number of patients with undiagnosed abdominal pain receiving long term treatment was significantly lower in this practice than in practices without an open access service (0·5/1000 *v* 1·5/1000 list patients; $\chi^2=8·78$, df=1, $P=0·003$, Yates corrected χ^2). The lowest rate of unexplained abdominal pain, however, was in a single handed practice with no open access service (no patients in this category, list size 2030). Numbers of patients with unexplained abdominal pain were not significantly correlated with age or qualifications of partners (scored as nil for basic qualifications; 1 for diplomas; 2 for MRCP, FRCS, or MRCGP; and 3 for FRCGP or FRCP; $P=0·48$, Spearman's rank correlation) or number of ancillary staff employed per patient ($P=0·6$).

PATIENTS WITH DUODENAL ULCERS

Duodenal ulcer was the most common reason for long term treatment. All patients in this group had had a definite diagnosis made (duodenal scar on barium meal with a suggestive history and response to treatment). Many patients, however, had had their diagnosis made many years ago, the median time between last positive test and the survey date being seven years. Forty six patients had last had positive results on investigation before 1980 and a further 16 before 1950. Most patients had been treated on the basis of similar symptoms to their previous documented ulcer. Perforation or bleeding from ulcers was almost totally confined to this group: 10 perforations (none with any other diagnosis) and 36 gastrointestinal bleeds (total for all patients 43) were documented (two patients had both). Cigarette smoking in this patient group was not significantly different from that in the other diagnostic groups (41 (22%) were smokers *v* 49 (16%) smokers in other groups; $\chi^2=1·9$, df=1, $P=0·17$, Yates corrected χ^2).

DRUG PRESCRIBING

Ranitidine was the drug most commonly prescribed (394 (80%) patients; table III). Prescribed dosage was 150 mg twice daily in 196/401 (49%), 300 mg once a day in 81 (20%), 150 mg once a day in 110 (27%), 300 mg twice daily in 12 (3%), and a higher dosage in 1 (<1%). Cimetidine was taken by 60 (12%) of the patients (43 at a dose of 400 mg twice daily, 22 at 400 mg at night). Nizatidine and famotidine were prescribed in four patients each (1% each of the survey sample). Omeprazole was used by 28 patients in this study, 15 with oesophageal disease (three strictures and 12 severe oesophagitis at endoscopy). Two patients with undiagnosed abdominal pain were treated with omeprazole, one for 15 months and one for 12 months. Despite a high usage of non-steroidal anti-inflammatory drugs in this group only two patients were taking long term misoprostol.

NSAIDs AND ACID SUPPRESSION

Of the 37 patients taking acid suppressing treatment as primary prophylaxis for concomitant treatment with non-steroidal anti-inflammatory drugs, 29 were started in hospital practice. Nine patients had rheumatoid disease, five had osteoarthrosis, and 15 were taking aspirin for angina or previous myocardial infarction. A further six patients were taking prescribed non-steroidal anti-inflammatory drugs but these drugs were not the primary reason for acid suppressing treatment —in five the non-steroidal anti-inflammatory drug was started after the long term H_2 antagonist. Forty three patients (identified by the patient questionnaire) took either aspirin or ibuprofen regularly (two patients took both) without prescription, giving a total of 82 patients (17% of the total) regularly taking non-steroidal anti-inflammatory drugs and H_2 antagonists or omeprazole.

PATIENTS' VIEWS

In all, 405 questionnaires were returned (82%). There was no difference between responders and non-responders in age ($P=0·4$), sex ($P=0·3$) or diagnosis ($P=0·5$; all χ^2). A total of 298 (74%) thought that the tablets they were prescribed helped their symptoms, but these symptoms were rather diverse. Overall, 202 patients knew or had a clear understanding of their diagnosis (duodenal ulcer 89, stomach ulcer 55, oesophagitis 17, hiatus hernia 31, indigestion caused by other drugs 10), and a further 95 patients took the tablets for abdominal pains of varying type; 108 patients did not know (n=9), had unusual symptoms (headache, pain in the knees), or were merely following medical advice ("prescribed them after my gallbladder operation"; "prescribed after tests").

Compliance with treatment was generally reported as good, with 317 patients (78%) taking the treatment as prescribed. Eleven patients (3%), however, took the tablets once a month or less despite regular repeat prescriptions being issued (table IV). Compliance did not seem to vary greatly with dose or frequency of dose (table V).

Discussion

Less than 1%—0·8%—of this general practice population was taking long term acid suppressing treatment. There are few other data on long term prescribing of these drugs in general practice, and the total number of prescriptions for acid suppression gives little information on this grouping as most dyspeptic patients would be treated with a short course of treatment. It is, however, not surprising that such a large number of patients is being treated long term if the huge number of prescriptions is considered. The only other study looking specifically at a general practice setting showed that 2% of the practice population had received at least one prescription for these drugs in the 12 months before the survey.[14] The clinical and financial implications of this treatment are therefore

considerable. The cost of a month's treatment with an H_2 antagonist is £20-30; thus, treating the 492 patients identified here for a year will cost these practices about £150 000. There is therefore considerable financial as well as clinical benefit to be gained by appropriate prescribing of these drugs.

Duodenal ulcer disease accounted for the majority of patients requiring long term treatment. Recent advances in the treatment of these patients suggests that they may have a better chance of remaining free of symptoms and ulcers over a long period if they are treated by eradication therapy rather than long term H_2 antagonists[15]—this may provide better and more cost effective treatment in the future. At present, however, it is clear that patients with bleeding or perforated ulcers require long term therapy, although this patient grouping accounted for only 23% of all patients receiving long term treatment for duodenal ulcer disease. Most patients are therefore taking long term treatment for multiple clinical relapses of their duodenal ulcer disease or because the physician initiated long term therapy after a single episode.

The length of treatment in patients with multiple relapses is also a point of some dispute: some studies have shown a tendency for peptic ulcer disease to "burn out" after 12 to 15 years,[16] although others maintain that this is a lifelong condition.[17] A consensus seems to be that one or two years' treatment is required to realise the benefits of long term therapy in this group.[18] Our data suggest that long term, for most patients given more than six months' treatment, is at least five years.

This study has highlighted a large number of patients with symptoms suggesting duodenal ulcer disease who have not been investigated for many years. In this group it would seem to be good clinical practice to reinvestigate before starting further treatment, especially in elderly patients. In this study six patients had a total of at least 85 patient years of continuous treatment on the basis of the findings of single contrast barium studies undertaken in the 1940s and 1950s. The possible economic benefits of this are less clear cut: endoscopy or barium studies cost the equivalent of three or four months' treatment.

The group with undiagnosed abdominal pain represents a large financial burden and shows a poor clinical management strategy. Some of these patients will have gastrointestinal disease, but it cannot be good practice to treat these (predominantly elderly) patients with no diagnosis established. H_2 antagonists have been widely prescribed for non-ulcer dyspepsia (this is an indication in their licensing agreements). There is little or no evidence that these drugs are of great benefit,[19,20] although it is possible that certain subgroups may exist with "H_2 blocker responsive" non-ulcer dyspepsia.[21,22] It is hoped that the introduction of treatment protocols for the management of dyspeptic patients can reduce the size of this patient group.

This study emphasises the importance of prescribing non-steroidal anti-inflammatory drugs in the general practice population. Almost a fifth of the patients in this study took non-steroidal anti-inflammatory drugs as well as anti-ulcer drugs. It seems likely that this group will continue to grow as the use of non-steroidal anti-inflammatory drugs in an increasingly elderly population continues to increase.[23] Aspirin has proved a major advance in the treatment of ischaemic heart disease, and non-steroidal anti-inflammatory drugs are now available over the counter. This study underlines the point that non-prescription aspirin and ibuprofen are taken by considerable numbers of patients who are clearly known to have peptic ulcer disease. It is unlikely that the general practitioner would be aware of this unless specific questions are asked at the time of renewal of the prescription for ulcer treatment. It is interesting to note that despite wide publicity and proved effectiveness in preventing gastric ulceration in patients taking non-steroidal anti-inflammatory drugs[24,25] only two patients in this study were taking misoprostol for gastric protection.

Guidelines have been implemented after analysis of these results, and the impact of this intervention on prescribing practice will be monitored.

Practice implications

- The indications for and value of long term treatment with acid suppressing drugs are controversial
- In this study of seven general practices 492 patients were taking such drugs long term, three quarters of them for duodenal ulcer or oesophageal disease
- A fifth of patients, however, were taking the drugs for abdominal pain of unknown cause or for gastritis (the sole diagnosis on endoscopy)
- Three quarters of the patients found their treatment helpful, but a tenth were additionally taking non-prescribed aspirin or ibuprofen
- Patients need to be better informed about their disease and the side effects of non-steroidal anti-inflammatory drugs

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