

Is cimetidine being prescribed indiscriminately? An analytic survey of patients who present with symptoms of peptic ulcer disease

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An analytic survey was done to determine the influence of previously documented peptic ulcer disease (PUD) on the frequency of prescribing cimetidine to patients who present at a family medicine centre with symptoms of PUD. It was found that of 293 patients who presented with such symptoms over 1 year cimetidine was prescribed to 57 (19%). From the 236 patients who did not receive cimetidine 57 patients were selected at random for comparison. Information on these two groups of patients was obtained by chart review. The patients who received cimetidine were found to be significantly more likely ($p < 0.001$) to have previously documented PUD than those who did not receive cimetidine. In patients in whom subsequent confirmation of PUD was not obtained, either because the results of investigations were negative or because the investigations were not ordered, cimetidine was prescribed to 63% of those who had previously documented PUD, compared with only 6% of those who did not. Of the patients who were investigated 73% of those with previously documented PUD had positive results, compared with 8% of those without previously documented PUD. The positive results were obtained by endoscopic examination in 88% of the patients with previously documented PUD, whereas upper gastrointestinal tract roentgenography was the definitive test in 73% of the patients without previously documented PUD. These findings suggest that previously documented PUD influences both the frequency of prescribing cimetidine and the investigations that are carried out.

Cette enquête analytique réalisée dans un centre de médecine familiale cherche à démontrer jusqu'à quel point la notion d'un diagnostic antérieur d'ulcère gastro-duodénal (UGD) confirmé porte à prescrire la cimétidine aux consultants qui accusent des symptômes d'UGD. Parmi les 293 de ceux-ci qui se sont présentés en l'espace de 1 an 57, soit 19%, ont été traités à la cimétidine. Des 236 restants, on a pris au hasard pour fins de comparaison un échantillon de 57 malades. La revue des dossiers de ces deux groupes montre que les sujets traités à la cimétidine ont un antécédent d'UGD confirmé dans une proportion plus grande que les non-traités; la différence est significative à $p < 0,001$. Parmi les malades chez qui l'UGD n'est pas confirmé par la suite, soit que l'exploration n'ait pas été faite, soit que les résultats se soient montrés négatifs, 63% de ceux qui ont un antécédent d'UGD confirmé sont mis à la cimétidine contre 6% de ceux qui n'en ont pas. Chez les malades explorés, 73% de ceux qui ont un tel antécédent, contre 8% de ceux qui n'en ont pas, ont des résultats positifs. L'épreuve concluante est l'endoscopie chez 88% des malades à antécédents, le repas baryté chez 73% des malades sans antécédents d'UGD confirmé. Ces trouvailles font croire que la notion d'un tel antécédent influe sur la prescription de la cimétidine et sur le choix du moyen d'exploration.

Is cimetidine being prescribed indiscriminately? This question is being asked more frequently because of the widespread use of cimetidine and the increased reporting of side effects.^{1,2} One of the concerns with cimetidine prescribing in hospital-based studies is its use in patients with unconfirmed peptic ulcer disease (PUD). In a family practice setting one would expect that an even higher proportion of patients would receive cimetidine for conditions diagnosed only on clinical grounds. When faced with a patient with symptoms thought to be related to acid-peptic disease family physicians have the option of prescribing cimetidine (or antacids) without investigating further; if they choose to investigate further they have to decide on the extent of the investigations and on how they will use the results. An important factor to consider is the patient's history of PUD.³ It is becoming more widely advocated to prescribe cimetidine without repeat investigation to patients with previously documented PUD who present with a recurrence of symptoms.⁴

We performed a study to determine the influence of

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previously documented PUD on the prescribing of cimetidine to patients who present with symptoms of PUD at a family medicine centre. One would expect that the patients who are subsequently found to have positive results of investigation for PUD would receive cimetidine regardless of whether they had the disease in the past. However, if cimetidine is prescribed selectively one would expect that the patients who are not investigated but who had previously documented PUD would be more likely to receive cimetidine than those without previously documented PUD.

Patients and methods

Patients

All the patients were from the family medicine centre at the Ottawa Civic Hospital. The centre, affiliated with the University of Ottawa, is a teaching practice where five principal physicians and 23 residents care for approximately 13 000 patients. The treating physician records the diagnosis, the prescribing data and other information about the patient on an encounter form after each visit. This form has been used since 1977 to generate health insurance cards for the Ontario and Quebec health insurance plans, as well as for research.⁵ Diagnostic information is coded according to the "International Classification of Health Problems in Primary Care" (ICHPPC).⁶ On Mar. 1, 1981 a revision was made to this form to improve the accuracy of the prescribing information. All prescriptions written in the family medicine centre are duplicated on chemically treated paper that imprints the prescription on the form. The prescription is torn off the form and given to the patient; the duplicate record is left on the form. The information on the form is then entered in a computer file along with other information about the visit.

A computer search was carried out using the diagnosis information from the patient encounter form to identify patients who presented with symptoms of PUD between March 1981 and March 1982. From a total of 27 610 patient visits recorded, 293 patients were identified as having the following ICHPPC-defined health problems:⁶ reflux esophagitis, duodenal ulcer, other PUD (e.g., gastric ulcer), indigestion, dyspepsia, gastritis, duodenitis or melena.

A second computer search, done with the prescribing information, identified 57 patients (19% of those with symptoms of PUD) for whom cimetidine was prescribed. All these patients were found to be a subset of the 293 patients who had been identified in the first search.

From the 236 patients who presented with symptoms of PUD but for whom cimetidine was not subsequently prescribed 57 were randomly selected using a table of random numbers⁷ (Fig. 1). The charts were reviewed and none of the patients were found to have been given a prescription for cimetidine in the family medicine centre. There were, however, four patients who had been referred to the gastroenterology consultation unit, where cimetidine had been prescribed and follow-up had been carried out. These patients were excluded from the study.

Data collection and analysis

For the two groups of 57 patients each, the charts were reviewed, and the following information was abstracted:

- Age and sex.
- Presenting symptom, initial diagnosis, treatment, and investigations performed during the study period, as well as any subsequent changes in management and diagnosis.
- History of PUD and previous use of cimetidine.

Previously documented PUD, as defined in this study, was confirmed by positive results of upper gastrointestinal-tract roentgenography or endoscopic studies, as recorded in the progress notes, the radiologic reports or the reports from gastroenterology consultation, and not merely by a clinical history of PUD.

The primary hypothesis of our study was tested by evaluating the differences in the frequency of previously documented PUD between the two groups of patients. We tested for statistical significance with the chi-square test (with Yates's correction for continuity). We also compared a number of other variables (e.g., age, sex and previous treatment for PUD) in the two groups.

Results

The frequency of previously documented PUD was significantly higher ($p < 0.001$) in the patients who received cimetidine than in those who did not (Table 1). Previous use of cimetidine and positive results of investigations for PUD were also significantly more frequent ($p < 0.001$) in this group. There were more men than women in this group, but the difference was of only borderline significance ($0.05 < p < 0.10$). There were no significant differences in age, in the frequency of other disorders or in the use of nonsteroidal anti-

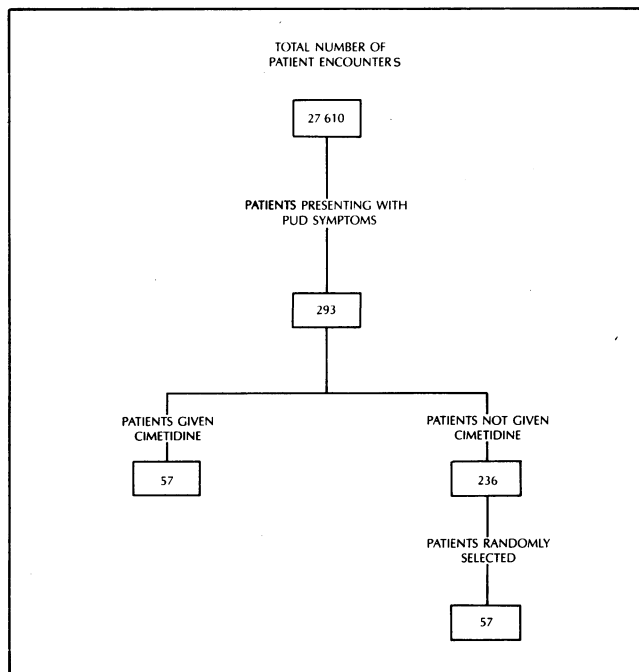


Fig. 1—Flow chart outlining patient selection. PUD = peptic ulcer disease.

inflammatory drugs (NSAIDs) within the 6 months before the encounter.

The main presenting symptoms are summarized in Table II. Epigastric pain, heartburn and dyspepsia accounted for 86% of the recorded presenting symptoms in the patients who received cimetidine and all of the symptoms in the patients who did not receive cimetidine.

Radiologic or endoscopic evidence of PUD was found in 38% of the patients who received cimetidine; the other 62% were given cimetidine on clinical grounds (Table III). Duodenal ulcer was the final diagnosis in 46% of the patients with positive results of the investigations; it plus gastric ulcer and gastroesophageal reflux accounted for 82% of the positive findings.

Since the patients who did not receive cimetidine were selected at random their data provided an unbiased estimate for the 236 patients from whom they were selected. Adjustment was made to maintain the overall frequency of cimetidine prescribing of 19% (e.g., the proportion of the 57 patients who did not receive cimetidine and who were investigated was multiplied by a factor of 236/57 to yield an estimate of the number of patients who would have been investigated if all 236 charts had been reviewed). After adjusting the data we designed a decision-making tree (Fig. 2).

Of the patients with previously documented PUD 22 (43%) were investigated and 16 (73%) were found to have positive results. In 87% of these patients the diagnosis was confirmed by endoscopic examination. In fact, 5 of the 16 patients had negative results of upper gastrointestinal tract roentgenography before being re-

ferred for further endoscopic assessment. Of the patients without previously documented PUD who were investigated (49%) only 8% had positive results of the investigations. In these patients nearly all of the diagnoses

Table II—Presenting symptoms

Symptom	No. of patients	
	Who received cimetidine	Who did not receive cimetidine
Epigastric pain	39	40
Heartburn	6	9
Dyspepsia	4	8
Melena	4	—
Abdominal pain	3	—
Anemia	1	—
Total	57	57

Table III—Indications for use of cimetidine

Diagnosis	No. of patients
Documented	22
Duodenal ulcer	10
Gastric ulcer	4
Gastroesophageal reflux	4
Gastritis/duodenitis	3
Esophageal ulcer	1
Clinical	35

Table I—Characteristics of patients with peptic ulcer disease (PUD) according to whether they received cimetidine

Variable	No. of patients or mean (and standard deviation)		p value*
	Who received cimetidine	Who did not receive cimetidine	
Sex			
Male	30	19	0.05 < p < 0.10
Female	27	38	
Age			
Male	46.8 (18.1)	50.6 (16.7)	NS
Female	51.9 (14.3)	53.1 (19.4)	
Age (yr)			
< 30	9	9	NS
30–49	16	18	
50–69	25	21	
> 69	7	9	
History of PUD			
Documented	34	4	p < 0.001
Clinical	13	15	
None	10	38	
Use of nonsteroidal anti-inflammatory drugs in the previous 6 months			
Yes	12	10	NS
No	45	47	
Previous treatment for PUD			
Cimetidine	35	2	p < 0.001
Other	22	55	
Present investigations			
Positive results	22	1	p < 0.001
Negative results	16	24	
No investigations	19	32	

*Statistical significance was determined by the chi-square test. NS = not significant.

were confirmed by upper gastrointestinal tract roentgenography; those with an initial negative result of this procedure were not referred for further assessment. The patients who had positive results of investigation received treatment (either with cimetidine or with surgery) regardless of whether they had previously documented PUD.

Of greater interest are the patients who had negative results of the investigations or were not investigated. Of those who had negative results all those with previously documented PUD, compared with only 9% of those without, received cimetidine; of those who were not investigated 55% and 3% respectively received cimetidine.

Discussion

We found that previously documented PUD influenced the physician's decision to prescribe cimetidine. The physician seemed more likely to base the diagnosis on clinical judgement without ordering investigations. The patients who were investigated were more likely to undergo consultation and endoscopy and to have a positive result of endoscopic examination. It appears that in this situation the physician had a strong suspicion of PUD since in 31% of the cases confirmed by endoscopy upper gastrointestinal tract roentgenography had already been done, with negative results. In comparison, of the patients without previously documented PUD not only was upper gastrointestinal tract roentgenography the most frequent investigation performed, but also no further assessment was done in the

109 patients who had negative results. However, all the patients with previously documented PUD who had negative results still received cimetidine. This finding also supports the impression that the physician was strongly influenced by the previously documented PUD despite the negative results of diagnostic tests. On the other hand, less than 10% of the 123 patients who had negative results but did not have previously documented PUD received cimetidine.

Although previous use of cimetidine was found to be significantly more frequent in the patients who received cimetidine than in those who did not, we believe that it was the previously documented PUD that influenced the physician's decision to prescribe cimetidine. Previous use of cimetidine may well be related to the physician's prescribing cimetidine again if the drug was found to be useful and well tolerated in the past. We can only assume that the patients' previous response to cimetidine was favourable. That more men than women received cimetidine most likely reflects the higher prevalence of PUD in men.^{4,8}

There are several methodologic issues relevant to retrospective studies that need to be addressed when interpreting these results. The major problem is that we must rely on the quality of information already recorded. There may be inaccuracies not only in recording the history of PUD but also in the current investigation and treatment information. Since the chart review was done in an unblinded fashion, the potential for an "exposure suspicion bias"⁹ exists; in other words, we might look more closely for a history of documented PUD in patients known to have received cimetidine. However,

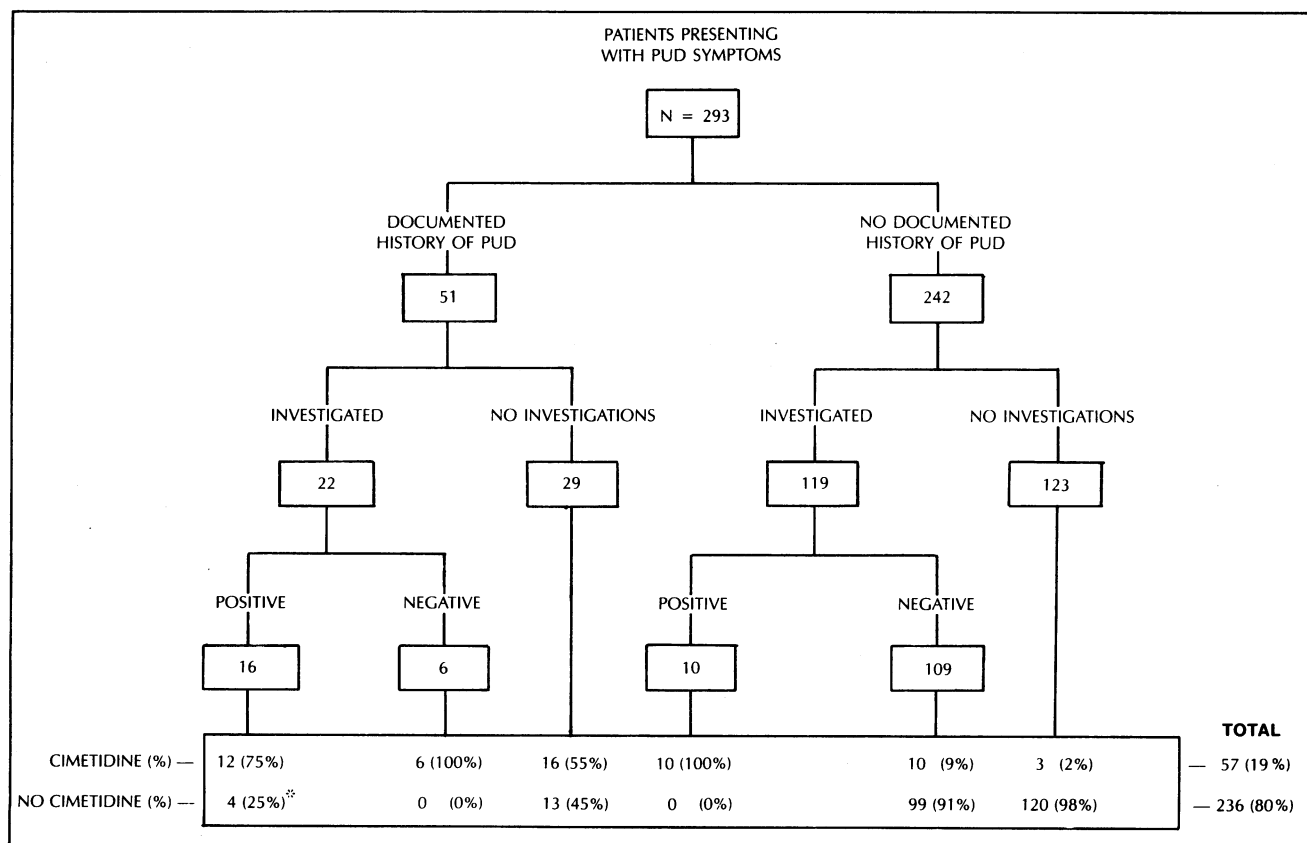


Fig. 2—Decision-making tree. Asterisk shows number (and %) of patients treated surgically.

since the forms used for the chart review were designed before the data were collected, and since a standard procedure for the review was followed, the potential for bias was minimized.

It is possible that there was an important unknown factor unrelated to previously documented PUD that was not equally distributed between the two groups of patients or that was responsible for both the previous PUD and the use of cimetidine. Therefore, one should look further at variables such as the severity of the presenting symptoms, which we did not measure in this study but which may be an important factor in differentiating the patients who receive cimetidine from those who do not.

The low rate of cimetidine prescribing in our study also provides evidence of the discriminating use of cimetidine. Our study was conducted in a teaching family medicine centre, which may account for the low prescribing rate and may influence the generalizability of the results.

Our study also provides general information on the use of cimetidine in a family practice. We found that the diagnosis of PUD was confirmed by objective investigation in 38% of the patients who received cimetidine. This proportion is similar to that reported in studies of patients in hospital.^{2,3,10,11} The main difference in our study was the condition that was diagnosed. Duodenal ulcer was the most common diagnosis; it plus gastric ulcer and gastroesophageal reflux represented over 80% of all the confirmed diagnoses. There was only one patient who was given cimetidine for prophylaxis. Hospital-based studies show that the most commonly reported diagnosis is upper gastrointestinal tract bleeding;¹² in other studies up to 50% of patients had been given cimetidine for prophylaxis.¹⁰ These differences reflect the differences in the severity of the conditions of the patients seen in each of these settings.

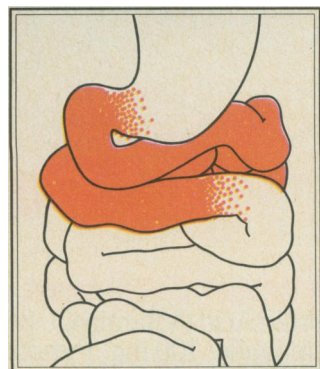
Conclusion

It appears from the results of our study that family physicians do not prescribe cimetidine indiscriminately. In the patients in whom positive findings of PUD were not obtained, either because the results of the investigations were negative or because investigations were not ordered, the rate of cimetidine prescribing was associated with previously documented PUD. This relation was also seen in the initial and subsequent investigations of the patients who presented with symptoms of PUD. With the high rate of recurrence of PUD, which has been estimated at 65% to 90%,¹³ the use of cimetidine in patients with previously documented PUD who present with recurring symptoms has been more widely promoted.⁴ However, caution must be taken in this approach. Twenty-seven percent of the patients in our study with previously documented PUD had negative results of the investigations. Also, we do not know how many of the patients who were not investigated would have had positive results. Further prospective studies on the natural history of patients with PUD must be done before we can confidently comment on the appropriateness of using the previous documentation of PUD as the basis for prescribing cimetidine.

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