



How Do Primary Care Physicians Use Long-Term Acid Suppressant Drugs?

A Population-Based Analysis of Dutch General Practices

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■ **OBJECTIVES** A considerable proportion of the medication budget of Dutch general practitioners is spent on prescribed long-term acid suppressant drugs. We investigated the magnitude of long-term prescription of acid suppressant drugs in general practice and the frequency and means of confirming the primary working diagnosis.

■ **STUDY DESIGN** We used a retrospective descriptive study of 24 general practices in the Amsterdam region.

■ **POPULATION** We identified those receiving long-term acid suppressant therapy (12 or more weeks/year) from a total of 46,813 patients by extracting data from pharmacy databases.

■ **OUTCOMES MEASURED** We measured the amount and duration of prescriptions for each medication, indications for prescription, and investigations performed by general practitioners.

■ **RESULTS** Of the 46,813 patients, 922 (2%) received long-term acid suppressant therapy. The duration of prescription varied from 12 weeks in 8% of patients to > 52 weeks in 23% of patients (mean = 33 weeks). In 25% of patients, no investigations were performed; 75% of patients underwent endoscopy or ingested a barium meal. The predominant diagnoses in investigated patients were ulcer disease (39%), gastroesophageal reflux disease (49%), and functional dyspepsia (gastritis, normal aspect; 18%). *Helicobacter pylori* status was available in 29% of patients with ulcer disease. Eradication therapy was reported in 44% of these patients.

■ **CONCLUSIONS** Among patients of physicians in general practice in the Amsterdam region, 2% used long-term acid suppressants. Patients with ulcer disease may stop taking acid suppressants after apparent successful *H pylori* eradication. Tapering strategies must be developed for patients with mild reflux disease or functional dyspepsia.

■ **KEY WORDS** Dyspepsia; primary health care; acid suppressant drugs [non-MeSH]; peptic ulcer; *Helicobacter pylori*. (*J Fam Pract* 2002; 51:241-245)

KEY POINTS FOR CLINICIANS

- In Dutch general practice, 2% of patients take long-term acid suppressant drugs.
- One third of patients taking long-term acid suppressant drugs have peptic ulcer disease and may not need medication as soon as *Helicobacter pylori* has been eradicated.
- One fourth of patients taking long-term acid suppressant drugs have never undergone endoscopy or barium study.
- Because patients often do not tolerate sudden cessation of chronic acid suppressant drug use, tapering strategies must be developed.

The average Dutch general practice includes approximately 2350 patients. Of these, 2 to 3 per week, on average, visit their general practitioner (GP) with a complaint of dyspepsia.¹ According to the guidelines of the Dutch College of General Practitioners, the treatment of dyspepsia is directed toward symptom relief, usually on an empirical basis, except for patients with symptoms such as sudden weight loss or hematemesis that suggest cancer; these are referred for endoscopy.² Medication is prescribed in a stepwise fashion from less potent antacids and prokinetics to the more potent H₂-blockers and proton pump inhibitors. During our study, long-term treatment with acid suppressant drugs (ASDs) was indicated only for relapsing ulcers

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TABLE 1
CHARACTERISTICS AND PRESCRIPTIONS IN 922 PATIENTS (%) WITH
LONG-TERM ACID SUPPRESSANT DRUG PRESCRIPTION
IN 24 GENERAL PRACTICES IN THE REGION OF AMSTERDAM, THE NETHERLANDS

Characteristics	DIAGNOSIS AFTER INVESTIGATION				NI: Stomach Complaints Without Investigation (n = 230)
	Total (N = 922)	I-ULCER (n = 271)	I-GERD (n = 294)	I-FUNCTIONAL (n = 127)	
Patients					
Female	511 (55)	41%	57%	72%	62%
15-44 years	169 (18)	11%	17%	25%	25%
Mean age, years	61	63	63	57	59
Medication, No.					
Ranitidine	442 (48)	141 (52)	115 (39)	70 (55)	116 (50)
Cimetidine	236 (26)	82 (30)	48 (16)	39 (31)	67 (29)
Omeprazole	241 (26)	63 (23)	130 (44)	22 (17)	26 (11)
Famotidine	43 (5)	16 (6)	15 (5)	4 (3)	8 (3)
Lansoprazole	13 (1)	3 (1)	5 (2)	5 (4)	0 (0)
Prescription Time					
12-19 weeks	231 (25)	67 (25)	44 (15)	44 (35)	76 (33)
20-29 weeks	184 (20)	56 (21)	46 (16)	27 (21)	55 (24)
30-39 weeks	148 (16)	40 (15)	50 (17)	22 (17)	36 (16)
40-51 weeks	143 (16)	44 (16)	60 (20)	15 (12)	24 (10)
> 52 weeks	216 (23)	64 (24)	94 (32)	19 (15)	39 (17)
Mean, weeks	33	34	38	29	29
No. of Episodes of Prescription					
1	485 (53)	144 (53)	179 (61)	51 (40)	111 (48)
2	271 (29)	78 (29)	81 (28)	48 (38)	64 (28)
> 2	166 (18)	49 (18)	34 (12)	28 (22)	55 (24)

Group I-ULCER includes all patients with a duodenal, -gastric, or nonspecified ulcer; group I-GERD includes all patients with symptomatic or erosive gastroesophageal reflux disease; group I-FUNCTIONAL includes patients with gastritis or with normal aspect on endoscopy or barium meal.
 *Total equals more than 100% because of different types of medication per patient; rarely prescribed medications are not mentioned.

Patients were identified from a medication database obtained from all cooperating pharmacists that included patient demographics; type, dose, and duration of medications; and use of possible risk-bearing comedications (aspirin, nonsteroidal anti-inflammatory drugs, or prednisone for more than 6 weeks during the study year). In this way we were able to identify almost all patients from the participating general practices who received long-term treatment with ASDs.

Confirmation of Gastrointestinal Diagnosis

In the Netherlands, a GP receives all available medical information on his patients (ie, letters from specialists, results from any examinations performed) and stores this information in the patient's medical history file. When a patient

or ulcerlike complaints, relapsing esophagitis, and relapsing gastroesophageal refluxlike symptoms.²

ASDs are responsible for a disproportionate share of the medication budget of Dutch GPs because of their high cost, their high frequency of prescription, and their use on a long-term basis.³ We therefore wondered whether the indication for prescribing an ASD was always appropriate. The aim of our study was to describe how commonly ASDs are prescribed and to describe the initial working diagnosis, the diagnostic tests performed to confirm the working hypothesis, and the final diagnosis for each patient.

METHODS

Patients

We retrospectively collected data from 24 general practices in Amsterdam from September 1994 to August 1995 on patients taking long-term ASDs (12 or more weeks during the previous year). ASDs included antacids, mucosa-protective agents, prokinetics, H₂-blockers, and proton pump inhibitors.⁴

switches to another GP, the entire medical history is sent to this new physician. Our principal investigator used these medical history files to determine the diagnosis and reason for the ASD prescription and the diagnostic tests (including *Helicobacter pylori* investigations) that were ordered to confirm the working diagnosis. Gastroscopy or barium meal radiography at any time during a patient's life was considered the investigation for confirmation of the diagnosis. If the prescription started after this investigation or as a consequence of it, the investigation was considered the reason for initiating the current long-term treatment. Verification and completion of the obtained data took place in a face-to-face evaluation between the principal investigator and the GP, ensuring the completeness and reliability of the data.

Analysis and Statistics

Patients were categorized into group I (investigations to confirm a working diagnosis were performed) and group NI (no investigations were performed).

TABLE 2
INDICATIONS FOR LONG-TERM (≥ 12 WEEKS) PRESCRIPTION
OF LONG-TERM ACID SUPPRESSANT DRUGS

	No. (%)
Final Diagnosis	692 (75)
I-ULCER*	271 (29)
Duodenal ulcer	196 (21)
Duodenal and gastric ulcer	17 (2)
Gastric ulcer	43 (5)
Nonspecified ulcer	15 (2)
I-GERD	342 (37)
Esophagitis and ulcer*	48 (5)
Esophagitis	116 (13)
Esophagitis and hiatal hernia	101 (11)
Symptomatic (hiatal hernia)	77 (8)
I-FUNCTIONAL	127 (14)
NI: Stomach Complaints	
Not Investigated	230 (25)
Preventive	45 (5)
Nonspecific stomach complaints	146 (16)
Refluxlike complaints	27 (3)
Ulcerlike complaints	6 (1)
Motilitylike complaints	6 (1)

Group I-ULCER includes all patients with a duodenal, gastric, or nonspecified ulcer; group I-GERD includes all patients with symptomatic or erosive gastroesophageal reflux disease; group I-FUNCTIONAL includes patients with only gastritis or with no imaging abnormalities. No investigations were performed on patients in group NI.
 *Total equals more than 100% because 48 patients with esophagitis and ulcer disease are included in both I-ULCER and I-GERD.

Three subgroups were identified within group I. We included all patients with a duodenal, gastric, or unspecified ulcer in group I-ULCER; group I-GERD included all patients with symptomatic or erosive gastroesophageal reflux disease (GERD); and group I-FUNCTIONAL included patients with only gastritis or with no imaging abnormalities. Patients with an ulcer and esophagitis were placed in group I-ULCER for their patient characteristics and medication prescription and in both groups I-ULCER and I-GERD for their medication indication, diagnostic tests, and eradication of *H pylori*.

Data were analyzed with the use of Statistical Package for the Social Sciences software (version 7.5.3). The chi-square test was used for comparison of proportions. Significance was set at $\alpha = .05$ (two sided).

RESULTS

General Characteristics and Medication Prescription

Of 46,813 patients listed with the 24 general practices, 988 (2.1%) were identified as long-term users of

ASDs. Of these 988 patients, 66 were excluded because of ASD use for gastric or esophageal cancer, nongastric-related indications such as renal failure, or discontinuation of visits to the GP (patient moved or was a temporary visitor). The demographic and prescription characteristics of the remaining 922 patients are presented in Table 1. All patients had used H₂-blockers and proton pump inhibitors for 12 weeks or more during the previous year.

Group I-ULCER consisted of 271 ulcer patients; group I-GERD, of 294 patients with reflux disease; and group I-FUNCTIONAL, of 127 patients with functional dyspepsia. Group NI consisted of 230 patients who did not undergo any confirmatory diagnostic testing (no endoscopy or barium study). Among the long-term users, treatment was more frequently prescribed for women than men (55% vs 45%, respectively; $P < .05$). Women were more likely not to undergo any diagnostic investigation (28% vs 21%, $P < .05$). If investigated, however, women were less likely than men have an ulcer (30% vs 50%, $P < .05$) and more likely to have functional dyspepsia (25% vs 11%, $P < .05$).

Overall, ranitidine was the drug most commonly prescribed. The mean duration of prescription was 33 weeks in the year of study, with a high of 38 weeks in group I-GERD. Almost one fourth of all patients (23%) had been using these drugs for more than 1 year. In more than half of all patients (53%), the medication was prescribed for 1 episode; in the other 47%, medication was prescribed for 2 or more episodes (ie, intermittent prescription). During the study period, 154 patients (17%) had used potential risk-bearing comedication for more than 6 weeks, including 48 with ulcer.

Confirmation of Working Diagnosis

In 692 of the 922 (75%) patients a diagnostic test was performed to confirm the primary working diagnosis. In 519 (75%), a gastroscopy was performed and in 138 (20%) a barium meal radiograph was taken. In 35 patients, the specific form of investigation was unclear.

The specific diagnoses of the subgroups are shown in Table 2. In patients with ulcer, use of NSAIDs or prednisone was mentioned as the cause of the ulcer in 26 of 271 (9.6%) patients. Barrett's esophagus was diagnosed in 29 of 342 (8.4%) patients in group I-GERD. In approximately 50% of the total number of patients, the investigation had been performed more than 5 years previously. Each patient had been treated accordingly during the subsequent years.

H pylori status was evaluated in 147 of the

TABLE 3
H PYLORI DIAGNOSTICS AND ERADICATION THERAPY
PRESCRIPTIONS IN 692 INVESTIGATED PATIENTS*

Final Diagnoses After Investigation†	<i>H pylori</i> Diagnostics Ordered, No. (%)	<i>H pylori</i> Eradication Therapy Prescribed, No. (%)
I-ULCER (n = 271)	78 (29)	34 (13)
I-GERD (n = 342)	34 (10)	7 (2)
I-FUNCTIONAL (n = 127)	35 (28)	7 (6)

*The current *H pylori* status, prescription, and success of eradication therapy often remained unknown. Group I-ULCER includes all patients with a duodenal, gastric, or nonspecified ulcer; group I-GERD includes all patients with symptomatic or erosive gastroesophageal reflux disease; group I-FUNCTIONAL includes patients with only gastritis or with no imaging abnormalities.
 †Forty-eight patients with gastroesophageal reflux disease and ulcer disease were included in both I-ULCER and I-GERD.

692 patients (21%). In most of these cases the correspondence between the hospital staff and the GP did not mention current *H pylori* status. In addition, it remained unknown whether eradication therapy was administered with or without successful eradication of the microorganism (Table 3).

No investigations were performed in 230 of the 922 patients (25%). "Nonspecific stomach complaints" was the most common indication for ASDs in this group (Table 2).

DISCUSSION

During our 1-year study, 2% of patients used an ASD for more than 3 months, and 0.8% for more than 6 months. Data from other studies, although not entirely comparable with ours, give an impression of the magnitude of long-term ASD prescription in other countries. In London, 0.8% of the general practice population used an ASD for more than 6 months continuously, a situation comparable with our results.⁵ One third of these patients had a history of ulcer disease. In Dundee, 4.4% of patients in 6 general practices were authorized to receive maintenance therapy.⁶ Many had a history of confirmed ulcer disease (27%), esophagitis (23%), or both (6%). Investigations in 23% of all patients revealed gastritis, duodenitis, hiatal hernia, or no pathology.

ASDs were used continuously for more than 1 year by almost one fourth of patients for whom they were prescribed; prolongation of the prescription was usually based on diagnostic tests performed years before. According to the guidelines that were in use during the course of this study, the indication for maintenance ASD was justified for most patients.²

Almost one third of all patients had a history of ulcer and continued to take an ASD (only 48 had concomitant GERD). For most of them, the ASD was probably prescribed as a preventive treatment.

H pylori diagnostics were performed in a minority of patients. The major change in the most recent version of the guidelines of the Dutch College of General Practitioners (1996) is the role of *H pylori* infection. Patients with duodenal ulcer (active or inactive) not caused by NSAID use should be treated with *H pylori* eradication therapy.⁷ In principle, long-term ASD use is not necessary after successful eradication of *H pylori*, since the ulcer is not likely to relapse.^{8,9} However, a few patients with severe concomitant symptoms of functional dyspepsia or reflux disease may require therapy despite successful *H pylori* eradication.^{9,10} It is the GP's task to identify patients with a history of ulcer disease and to eradicate *H pylori*. The clinician can easily identify patients with a history of ulcer disease with the help of computerized prescription data and the patient's history file. However, implementation of these systems remains an important issue. Many such patients are invisible to the GP because they are treated with repeated prescriptions and without further consultation and therefore are not treated for *H pylori*.

The current Dutch guidelines do not advise testing for *H pylori* in patients with GERD or functional dyspepsia; this approach, therefore, is still not common in the Netherlands. Not advising to test is consistent with guidelines developed with a primary care perspective but differs in fundamental ways from guidelines formulated by specialists.^{11,12} The role of *H pylori* in esophagitis and reflux disease is not clear.¹³ Whether successful eradication of *H pylori* leads to exacerbation of esophagitis because of the absence of acid buffering by *H pylori*-derived urease production has been debated.¹⁴ In our study, one third of the patients suffered from GERD, which is easy to control, but not to cure; patients often experience a relapse after tapering of ASDs. Intermittent treatment with ASDs and the use of antacids as an escape medication may be an effective approach for managing patients with uncomplicated GERD and reducing the use of ASDs.^{15,16}

There is little difference in the pattern of ASD prescribing for patients with ulcer, GERD, or functional dyspepsia. This similarity is particularly interesting because most studies of patients with functional dyspepsia have shown no benefit with the use of ASDs or with the eradication of *H pylori*.¹⁷⁻²² In these patients it may be sensible to taper the use of ASDs gradually, supported by antacid use; to explore the level of psychosocial distress; and to advise on lifestyle improvement.²³ Long-term medication was prescribed as a preventive measure for the remaining 25% of all long-term users and to patients not given

an endoscopy or barium study. The guidelines advise further investigation after several empirical treatments and again before a long-term ASD is prescribed.

One notable finding was that the patient's sex appeared to influence whether investigations were ordered. The fact that ulcer disease is overall less often diagnosed in women might explain why the GPs did not perform further diagnostic investigations in women. Anxiety for endoscopy in men or women is another reason for not having a confirmed working diagnosis. A small number of anxious patients who have underlying ulcer disease might benefit from a test-and-treat approach to *H pylori* infection. However, serology cannot differentiate between either present or past *H pylori* infection and between ulcer or nonulcer disease.

Patients often experience a fast relapse of symptoms after discontinuation of therapy that may be related to rebound acid hypersecretion.^{24,26} It is possible that the prescription pattern of physicians in a subset of dyspeptic patients, especially in those with acid-related dyspepsia, leads to dependence on long-term therapy.

CONCLUSIONS

The use of ASDs, especially proton-pump inhibitors, is becoming increasingly common. In general practice in the Amsterdam region, 2% of patients used long-term ASDs. Patients with ulcer disease may stop taking ASDs after apparently successful *H pylori* eradication. Other patients require additional proof of underlying disease and *H pylori* status to determine the subsequent treatment approach. Tapering strategies in patients with mild reflux disease or functional dyspepsia need to be developed. Research is also needed in the general practice setting to develop strategies for tapering ASDs in chronic dyspeptic patients.

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