

The role of screening for *Helicobacter pylori* in patients with duodenal ulceration in the primary health care setting

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SUMMARY

Background. It is known that at least 90% of duodenal ulcers are caused by infection with the bacterium *Helicobacter pylori*. Eradicating this organism usually results in complete resolution of the disease. Testing for *H pylori* was introduced relatively recently, and thus, many patients known to have uncomplicated peptic ulcer disease who continue to need long-term treatment with ulcer-healing drugs have never been tested for the infection or offered eradication therapy. In modern computerized practices, this subgroup of patients can readily be identified by reference to morbidity and repeat prescribing data. Eradication of *H pylori* infection in this group of patients has great potential benefit for the individuals concerned as well as cost-saving benefit for the National Health Service.

Aim. The aim of this prospective study was to determine whether it is worthwhile screening for and treating *H pylori* infection in patients in a general practice population with previously diagnosed duodenal ulcer disease taking ulcer-healing drugs long term.

Method. In 1994, in a practice of 7100 patients, morbidity and repeat prescribing data were used to identify 40 patients (0.6%) with proven duodenal ulcer disease taking ulcer-healing medication long term and with uncertain *H pylori* status. Twenty-nine of the 40 subjects agreed to undergo serology testing for *H pylori* antibodies. Of 20 (69%) who were positive, 18 (eight women, median age 63.8 years) were given eradication therapy. Seventeen patients received omeprazole 40 mg once daily and amoxicillin 500 mg three times daily for 14 days with metronidazole 400 mg three times daily for the first 7 days; for the remaining patient metronidazole was inadvertently omitted. [¹³C]Urea breath testing was carried out at the local hospital at least one month after therapy to determine whether eradication treatment had been successful. Subjects were also personally followed up by telephone after 1 and 4 months to assess the success of treatment subjectively.

Results. [¹³C]Urea breath testing showed that *H pylori* eradication was successful in all 17 patients (100%) who received the intended eradication regimen. *Helicobacter pylori* was not eradicated in the patient who received only omeprazole and amoxicillin. Four months after successful *H pylori* eradication, 13 of the 17 (76%) patients remained completely asymptomatic. Two of the four patients who had some recurrent dyspepsia had known gastro-oesophageal reflux and their ongoing symptoms after eradication therapy seemed, on close questioning, to be more

attributable to this than to duodenal ulcer disease.

Conclusion. Testing for and eradication of *H pylori* is worthwhile in general practice in those patients with previous proven duodenal ulceration who need long-term ulcer-healing medication. The high rate of eradication of *H pylori* achieved with the regimen used in this study compares very favourably with that of other treatment regimens. However, in patients with duodenal ulcers there may be coexisting pathology, and *H pylori* eradication does not necessarily result in complete disappearance of dyspeptic symptoms. Thus, when monitoring the outcome of treatment it is important to assess improvement of symptoms as well as objective evidence of eradication.

Keywords: peptic ulcers; *Helicobacter pylori* infections; screening diagnosis.

Introduction

SINCE the bacterium *Helicobacter pylori* (*H pylori*) was first cultured in 1983, major changes in the treatment of peptic ulcer disease have been instituted. It has been found that over 90% of duodenal ulcers are caused by *H pylori*.^{1,2} The case is less clear cut with gastric ulcers; certainly in 70% of cases *H pylori* is found.

Peptic ulcers can usually be cured by treatment with H₂-receptor antagonists or proton pump inhibitors, but at least 80% will recur within one year of stopping treatment.^{2,3} An overview of trials found that only a minority (0–20%) of duodenal ulcers recur after successful *H pylori* eradication.² It remains unclear whether eradication of *H pylori* will affect the relapse rate of gastric ulcers.² Eradication therapy for patients with *H pylori* infection who do not have underlying peptic ulcer disease has generally not been advocated.^{4,5} However, in view of recent work suggesting a long-term benefit of *H pylori* eradication in patients with non-ulcer dyspepsia,⁶ this approach should perhaps be revised.

The aim of this study was to evaluate the benefit of *H pylori* eradication therapy in general practice among patients known to have duodenal ulcer disease who are receiving long-term continuous/intermittent ulcer-healing medication. All those offered eradication therapy were found on serological testing to have *H pylori* antibodies in their blood and had, on previous investigation, been found to have peptic ulcer disease.

Method

The study took place in the spring of 1994 in a general practice of 7100 patients in Solihull in the West Midlands. Using computer repeat prescribing data, 277 patients (3.9% of the practice population) were identified as taking long-term continuous or intermittent courses of H₂-receptor antagonists or proton pump inhibitors for dyspeptic symptoms. Of these, almost half (137) had at some time been investigated by barium meal or endoscopy for symptoms of dyspepsia. Of these, 49 (35.8%) had been found to have peptic ulceration, of whom 45 had had a duodenal ulcer. Of these, five were excluded as they had already been tested for *H pylori* by

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biopsy at the time of endoscopy and treated accordingly.

The remaining 40 patients were contacted by telephone (or letter if unavailable by telephone) and, after a detailed explanation, invited for serological *H pylori* antibody testing at the surgery. Three patients did not reply to letters and eight refused antibody testing for the following reasons: recent severe ill-health (three subjects), a wish to continue long-term ulcer-healing treatment (three subjects) or currently being asymptomatic off treatment (two subjects). The rest agreed (and were keen) to take part in the study as they had all experienced troublesome dyspepsia requiring ongoing long-term ulcer-healing drugs, although none had experienced a change in symptoms that might have warranted urgent investigation.

Thus, after giving informed consent, 29 patients were accepted for serological testing for *H pylori* IgG antibodies, of whom 20 (69%) were positive. These patients were offered treatment with omeprazole 40 mg once daily and amoxicillin 500 mg three times daily for two weeks and metronidazole 400 mg three times daily for the first seven days of therapy. To improve compliance, subjects were provided with written information describing how and when to take their medication and what side-effects might be expected. Two patients (aged 62 and 81 years) decided against starting eradication therapy because they felt it was too complicated and were happier to continue long term on their current medication.

Altogether 18 patients (eight women, median age 63.8 years, range 38–85 years) with previous proven duodenal ulcers (one of whom had also had a proven gastric ulcer) took specific eradication treatment. Inadvertently, one patient received only omeprazole and amoxicillin.

All patients were contacted by phone 1 and 4 months after completion of eradication therapy to ascertain subjectively the success of treatment.

Those who had received eradication therapy were also invited to undergo [¹³C]urea breath testing at the local hospital in Solihull, having taken no antibiotics in the previous 2 weeks, to assess objectively the success of *H pylori* eradication. This was carried out at least one month after completion of eradication therapy to avoid false-negative results. *H pylori* can easily be detected by this simple breath test. A small amount of radiolabelled liquid is taken orally after a 6-h fast. The presence of *H pylori* in the stomach rapidly breaks down [¹³C]-labelled urea to produce [¹³C]-labelled carbon dioxide, which is expelled in the breath.

Results

On close questioning after completion of the eradication treatment all patients had apparently been fully compliant. Two patients had experienced troublesome nausea and increased frequency of bowel movements, but no other patients complained of any serious side-effects.

Of the 17 patients with previous proven duodenal ulceration who had undergone the eradication regimen as intended, 15 (88.2%) at one month and 13 (76.5%) at 4 months remained completely asymptomatic. After 4 months, two patients had restarted regular ulcer-healing medication because of the return of dyspeptic symptoms. A further two patients felt symptomatically much better but still needed occasional antacid or H₂-receptor antagonist therapy. Of these four patients, two had known hiatus hernia associated with reflux oesophagitis that may have caused ongoing symptoms. After eradication therapy symptoms certainly suggested reflux oesophagitis rather than duodenal ulcer.

[¹³C]Urea breath testing at least one month after treatment

confirmed that *H pylori* infection had been successfully eradicated in all 17 (100%) patients who received the intended treatment regimen.

In the patient who inadvertently received only omeprazole and amoxicillin, symptoms did not improve after eradication therapy and [¹³C]urea breath testing showed that this patient still carried *H pylori* infection.

Discussion

In the study group, 20 out of 29 (69%) patients with known previous duodenal ulcer had *H pylori* antibodies. According to other studies, at least 90% of patients with active duodenal ulcer have *H pylori* infection. The reason for the lower than predicted rate of *H pylori* infection in this study is unclear. Duodenal ulcer disease runs a chronic course with intermittent exacerbations, eventually resolving. It is possible that a proportion of patients who had been treated long term with ulcer-healing drugs in fact no longer had active duodenal ulcer disease.

Table 1 shows *H pylori* status in relation to time since duodenal ulcer diagnosis and Table 2 shows the relationship between time elapsed since duodenal ulcer diagnosis and symptomatic improvement in *H pylori* carriers after successful eradication therapy. Unfortunately, the numbers are small and it is not possible to draw useful conclusions.

It is also possible that the large number of patients who were negative for *H pylori* infection reflects a high false-negative rate of serology testing, and it would have been interesting to have also carried out comparative [¹³C]urea breath testing in these patients. However, several studies have shown that both [¹³C]urea breath testing and serology are simple, reproducible, highly specific and sensitive tests and are acceptable to patients in establishing the presence of *H pylori* infection.⁷⁻¹⁰ Serology testing may be preferable to [¹³C]urea breath testing in general practice, provided laboratory facilities for identification of antibodies are available locally, as it is cheaper for the practice and less time-consuming for the patient. Unfortunately, after successful eradication therapy *H pylori* antibody titres are slow to fall and therefore [¹³C]urea breath testing was used in this study to establish the effectiveness of treatment. However, a study found that a 20% reduction in antibody titres at 6 months was associated with successful eradication of *H pylori*, and it was concluded that serology is a potentially useful way to monitor the success of treatment.¹¹

Currently there is no general agreement on the best method of eradicating *H pylori*, and the variety of eradication regimens used reflects this uncertainty. Standard 'triple therapy' using a bismuth salt together with metronidazole and amoxicillin or tetracycline has been widely used with an overall success rate of around 80–90%.¹²⁻¹⁴

More recently, eradication using omeprazole and antibiotics has been found to be effective and better tolerated by patients.¹³⁻¹⁶ Following a literature review, a regimen of omeprazole 40 mg once daily and amoxicillin 500 mg three times daily for two weeks with metronidazole 400 mg three times daily for the first seven days was chosen for *H pylori* eradication in this study. In the study group, this regimen resulted in a 100% eradication rate when assessed objectively by [¹³C]urea breath testing. Although the study group was small, these figures are encouraging and suggest a high degree of compliance among the patients. A study showed quite clearly that compliance is the most important factor predicting success.¹⁷ This study involved only well-motivated patients who took part after a clear verbal and written explanation of the treatment regimen and potential side-effects.

Thirteen out of 17 patients previously receiving long-term

ulcer-healing treatment felt that dyspeptic symptoms which they had attributed to a proven duodenal ulcer had completely resolved 4 months after eradication therapy. However, four patients in whom *H pylori* infection was successfully eradicated continued to experience symptoms of dyspepsia. In view of the very low relapse rate of duodenal ulcer after eradication of *H pylori*, it must be assumed that in this subgroup symptoms were probably not caused by ulceration, and indeed two of the four patients had known gastro-oesophageal reflux, which may have been responsible for ongoing intermittent dyspepsia. In some patients with duodenal ulcer, high acid output and lax cardiac sphincters a significant proportion of the symptoms of dyspepsia result from reflux, and hence, may persist after successful *H pylori* eradication. An attempt should be made to assess this clinically at the time of eradication therapy, although it may be difficult to distinguish possible underlying causes of dyspepsia on the basis of the history alone. However, this illustrates the importance of asking patients about recurrence of symptoms after eradication therapy rather than basing success of treatment purely on objective results. In patients with a history of duodenal ulcer disease, *H pylori* eradication does not necessarily result in the disappearance of dyspeptic symptoms.

In conclusion, many patients with duodenal ulcer disease receiving long-term ulcer-healing treatment will not have been offered eradication therapy because their ulcer was diagnosed before testing and treatment for *H pylori* were generally available. Clearly, even although in some of these patients the disease will no longer be active, there is a strong case for identifying individuals with *H pylori* infection so that eradication therapy may be offered.

Eradication of the organism would reduce morbidity from both the disease and treatment side-effects. Although only a comparatively small number of patients might be identified in a single practice population, a regional general practice policy would considerably help reduce the National Health Service drugs bill for ulcer-healing medication. There may also be long-term benefits of *H pylori* eradication given accumulating evidence that *H pylori* may play an important role in both the development of non-ulcer dyspepsia and gastric carcinogenesis.

Target patients are easily identified in the primary health care setting by reference to repeat prescribing and morbidity data, made all the easier since the widespread introduction of computers in general practice. To make patient contact easier, a leaflet explaining the role of *H pylori* in peptic ulcer disease and extending an invitation to attend for *H pylori* testing could be attached to repeat prescriptions awaiting collection. Serological *H pylori* antibody testing for these individuals is quick, cheap, acceptable to the patient, easy to perform in the primary health care setting and has a high sensitivity and specificity.

In this study, the treatment regimen of omeprazole, amoxicillin and metronidazole resulted in a high (100%) *H pylori* eradication rate in a well-motivated and highly compliant although small patient group. The majority remained symptom free four months after treatment, although longer follow up is required. However, in spite of successful *H pylori* eradication, a minority of patients continued to have some dyspeptic symptoms. When monitoring the outcome of eradication therapy, to assess long-term effects, it is important to take into account patients' symptoms as well as objective test results.

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