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Six-year follow-up after *Helicobacter pylori* eradication in peptic ulcer disease

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Abstract

Background The longterm outlook after *Helicobacter pylori* (*H. pylori*) eradication in peptic ulcer disease is unclear.

Aim This study documents *H. pylori* recurrence, dyspeptic symptoms and anti-secretory therapy in peptic ulcer patients six years or more after *H. pylori* eradication.

Methods Peptic ulcer patients with *H. pylori* eradication between 1990 and 1992 were included. Infection recurrence was diagnosed by 13-carbon urea breath test (UBT). Dyspeptic symptoms and anti-secretory therapy use were assessed by questionnaire.

Results Sixty-one patients completed the study protocol. Mean follow-up after eradication was 6.1 years (range 4.8-8.3). Four patients had a positive UBT. *H. pylori* recurrence rate was 6.6% or 0.02% per patient per year. Forty-two patients (69%) had dyspeptic symptoms. Heartburn and belching were more common than pain (*p*<0.001). All four patients with *H. pylori* recurrence had symptoms compared with 38 of 57 *H. pylori*-negative patients (*p*>0.05). Ten of 61 patients (16.4%) were taking anti-secretory therapy and their dyspepsia scores were higher.

Conclusions Despite a low *H. pylori* recurrence rate, longterm dyspeptic symptoms were common in peptic ulcer patients after *H. pylori* eradication. The symptoms are mainly reflux in type and require anti-secretory therapy in only a minority of patients.

Introduction

Eradication of *H. pylori* is accepted as the treatment of choice in *H. pylori*-positive peptic ulcer disease. Cure of infection accelerates healing, prevents ulcer bleeding, improves quality of life and significantly reduces ulcer relapse. Data are sparse however on the longterm outcome following *H. pylori* eradication and concerns have been raised about the development of reflex oesophagitis following cure of *H. pylori* in peptic ulcer disease.

The aim of this study was to document *H. pylori* recurrence, dyspeptic symptoms and the use of anti-secretory medication in a cohort of peptic ulcer patients more than six years after eradication of *H. pylori* with bismuth triple therapy.

Methods

Patients

Patients were eligible for inclusion if they had peptic ulcer disease diagnosed at endoscopy between 1990 and 1992 and had *H. pylori* infection successfully eradicated using bismuth triple therapy. This consisted of colloidal bismuth subcitrate 120mg four times daily for 28 days combined with tetracycline 500mg three times daily and metronidazole 400mg three times daily for the first seven days of therapy. This patient group originally participated in a previous study from this unit on the effect of *H. pylori* eradication on peptic ulcer healing.

*H. pylori* status before treatment was established using a combination of CLOtest (Delta West, Perth, Australia) for the presence of preformed urease activity in gastric biopsies and histological examination of modified Giemsa-stained sections, as previously described. *H. pylori* eradication was defined as the inability to detect evidence of infection on both the CLOtest and histological evaluation of gastric antral and corpus biopsy specimens at least four weeks after completing eradication therapy.

Patients were contacted by letter giving an outline of the proposed follow-up study and invited to participate. Patients who agreed to participate gave written informed consent.

*H. pylori* recurrence

Recurrence of *H. pylori* infection was confirmed by 13-carbon (*¹³C*) urea breath test (UBT). Patients were requested to discontinue anti-secretory therapy for at least two weeks prior to the test. Patients fasted for at least four hours before the UBT, and at the start of the test were given 200ml of orange juice to delay gastric emptying. Patients were then given 100mg of *¹³C* urea dissolved in water and duplicate breath samples were collected before and 30 minutes after administration of the *¹³C* urea. Breath samples were mailed and analysed at the HP Testing Unit at the Adelaide/Meath Hospital, Dublin. The *¹³C*/¹²C ratio in the CO₂ was measured by isotope mass spectrometry and an increase of five per million in the *¹³CO₂* after
ingestion compared with baseline measurement was considered positive for *H. pylori* infection. Patients with a positive UBT were invited to undergo upper gastrointestinal endoscopy and gastric biopsies.

**Dyspepsia and anti-secretory therapy**

Dyspeptic symptoms were assessed prior to the UBT using a validated questionnaire designed to measure the severity, frequency and duration of three key symptoms: epigastric pain, heartburn, and belching. Epigastric pain was defined as upper abdominal pain or discomfort. Severity of symptoms was graded on a five-point Likert scale from none to very severe. Frequency was graded as less than three episodes per week, more than three episodes per week, daily, or almost continuous. Duration was graded as lasting less than 10 minutes, 10–30 minutes, or more than 30 minutes. The total symptom score was calculated by adding the scores for severity, frequency and duration of each symptom (see Table 1).

Patients were also asked to provide details of current medications and specifically asked about use of antacids, H₂ antagonists, and proton pump inhibitors.

**Table 1.** Details of the dyspepsia questionnaire and scoring system used to assess epigastric pain, heartburn and belching

<table>
<thead>
<tr>
<th>Severity</th>
<th>Score</th>
<th>Frequency</th>
<th>Score</th>
<th>Duration</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1</td>
<td>&lt;3 episodes/week</td>
<td>1</td>
<td>1–10 minutes</td>
<td>1</td>
</tr>
<tr>
<td>Mild*</td>
<td>2</td>
<td>&gt;3 episodes/week</td>
<td>2</td>
<td>10–30 minutes</td>
<td>2</td>
</tr>
<tr>
<td>Moderate*</td>
<td>3</td>
<td>&gt;3 episodes/day</td>
<td>3</td>
<td>&gt;30 minutes</td>
<td>3</td>
</tr>
<tr>
<td>Severe*</td>
<td>4</td>
<td>Almost continuous</td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Very severe*</td>
<td>5</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Maximum score for each symptom = 12
Maximum total dyspepsia score = 36
*Mild = can be ignored when you do not think about it
*Moderate = cannot be ignored
*Severe = influences concentration on daily activities
*Very severe = markedly affects daily activities and/or rest

**Statistical analysis**

Differences in the frequency and severity of symptoms between patient groups were tested for statistical significance using the Chi-squared test with Yates' correction and the rank sum test for unpaired data. A p value of <0.05 was considered significant.

**Results**

Seventy-three peptic ulcer patients who had *H. pylori* success-fully eradicated were eligible to participate in the study, but 12 did not attend. One patient had died in a road traffic accident, one had a stroke, three had left the area and seven declined to participate. Details of the 61 patients who completed the study protocol are shown in Table 2. The mean follow-up after *H. pylori* eradication was 6.1 years, range 4.8–8.3 years, giving a total of 371 patient years of follow-up.

**H. pylori recurrence**

A positive UBT was detected in four male patients (mean age, 39) between 6.3 and 7 years after eradication therapy giving a total *H. pylori* recurrence rate of 6.6% or 0.02% per patient per year. Three of the four patients with a positive UBT underwent endoscopy and all three were *H. pylori*-positive on CLOtest and histological examination of gastric biopsies. One patient had an active duodenal ulcer, one had an ulcer scar in the duodenal cap and the other had erosive oesophagitis.

**Dyspeptic symptoms**

Dyspeptic symptoms were reported by 42 of 61 patients (69%). Heartburn was reported by 27 patients (44.3%), belching by 27 (44.3%), and epigastric pain by 9 (14.8%). Heartburn and belching were each more frequently reported symptoms than epigastric pain (p<0.001). The combination of epigastric pain and heartburn was reported by six patients (9.8%), the combination of belching and epigastric pain by five patients (8.2%), and the combination of belching and heartburn by 14 patients (23%). The combination of belching and heartburn was more frequent than the combination of belching and epigastric pain (p<0.05). Four patients (6.6%) reported all three symptoms. In the patients who reported symptoms, the median scores for epigastric pain, heartburn, and belching were 6, 5, and 5 respectively (p<0.05). All four patients with a positive UBT had dyspepsia compared with 38 of the 57 patients (66.6%) with a negative UBT (p<0.05).

**Anti-secretory therapy**

Ten of the 61 patients (16.4%) were taking anti-secretory therapy at the time of the study: antacids 3; H₂ antagonists 4; and proton pump inhibitors 3. Two of the 10 patients taking anti-secretory therapy (20%) had a positive UBT compared with two of the 51 patients (3.9%) not taking anti-secretory therapy (p<0.05). Dyspeptic symptoms were reported by nine of the 10 patients (90%), compared with 33 of the 51 patients not taking medication (64.7%) (p<0.05). However, the median dyspepsia score in the group taking anti-secretory therapy was significantly higher than that in the dyspeptic patients not taking anti-secretory therapy (12 vs 6, p<0.01).

**Discussion**

The aim of our study was to assess the long-term outcome for peptic ulcer patients after *H. pylori* therapy, particularly symptomatic outcome and the need for anti-secretory therapy. Patients enrolled were more than six years, on average, after successful *H. pylori* eradication using bismuth triple therapy, the