Original Article

IMPACT OF HELICOBACTER PYLORI ERADICATION ON DYSPEPTIC SYMPTOMS IN THE COMMUNITY

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ABSTRACT:

Background: Eradication of Helicobacter pylori (Hp) will cure most Hp positive duodenal ulcers (DU). However, after such treatment, patients often continue to get dyspeptic symptoms. The effects of Hp eradication in patients with proven DU on gastro-oesophageal reflux disease (GORD) symptoms are controversial.

Aims: To study any changes in patient's symptoms following eradication of Hp in the setting of chronic DU and its effects on the need for continuing treatment for acid suppression.

Methods: Eighty out of 85 patients (94%) from general practice with documented successfully eradicated Hp with a week long triple therapy regimen. Their symptoms and requirement for acid suppression treatment were studied at enrolment and after successful eradication of Hp for a median of 17 months.

Results: Eighty one percent patients had improvement in ulcer-type symptoms. 21% developed new GORD symptoms. 68% discontinued long-term acid-suppression treatment. 79% requiring continued acid suppression therapy had new or continued GORD symptoms.

Conclusion: Patients in the community with Hp positive DU disease after eradication, 81% patients got symptomatic improvement, two third discontinued their acid suppressing therapy but 21% developed new GORD symptoms. Among those who required continued acid suppression, 79% had GORD symptoms.

KEYWORDS: Helicobacter pylori, eradication, duodenal ulcer, community, dyspepsia, gastro-oesophageal reflux disease.

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INTRODUCTION

The association of Helicobacter Pylori (Hp) infection and peptic ulcer disease (PUD) is very well established. The National Institute of Health Consensus Development Conference Statement, The Maastricht Consensus Report by European Helicobacter Pylori Study Group (EHPSG) and The Maastricht 2 Consensus Report therefore strongly recommend eradicating Hp in all infected PUD patients including those in remission or receiving long-term anti-secretory therapy[1-4], However, the interrelation between H. pylori infection and gastro-oesophageal reflux disease (GORD) is complex, controversial, not yet fully understood, and the evidence often seems to be

conflicting[5-8]. This study attempted to explore the effects of successful eradication of Hp on the symptoms of ulcer-type dyspepsia and GORD and the continued need for anti-secretory therapy.

PATIENTS AND METHODS

One hundred patients with previously documented chronic DU, were identified from general practice by the Cornwall GP Trainers Workshop from the computerized practice records. After obtaining informed consent to participate in the study, 80/85 patients with active Hp infection as suggested by positive serology and C14 Urea Breath Test (UBT), successfully eradicated the bacteria as diagnosed by a negative repeat UBT 6-8 weeks following the treatment. The regimen used was clarithromycin 250 mg, omeprazole 20 mg and either tinidazole 500 mg or metronidazole 400 mg - all twice daily for one week. They included 67 men and 13 women with an average age of 60 years (range 31-79).

Patients were asked about ulcer-type dyspepsia (abdominal pain or discomfort after eating with or without associated nausea) and GORD symptoms (position dependent heartburn or regurgitation of bitter fluid or burning/warm sensation arising in the upper abdomen and radiating towards throat) on enrolment into the study and about ulcer-type dyspepsia at 6-8 weeks after eradication treatment at the time of the second UBT. A further follow-up telephone/postal survey was performed at a median time interval of 17 months (range = 3 – 23) post-treatment. These symptoms were graded as 0 = none (symptoms absent), 1 = mild (symptoms present, but causing little discomfort), 2 = moderate (symptoms annoying but do not interfere with daily activity) and 3 = severe (symptoms causing marked interference with daily activity). 75 out of 85 patients (88%) responded to the telephone/postal survey. Of these, 70 patients had successful eradication therapy.

Exclusion criteria

1. Patients under 18 or over 80 years of age.
2. Patients who had previous Hp eradication therapy.
3. Patients who needed to continue receiving drugs which may interact with the study drugs eg warfarin, carbamazepine and lithium.
4. Patients with hypersensitivity to the study drugs.
5. Pregnant and breast-feeding mothers.
6. Patients with mental impairment who could not comply or consent

Statistical analysis

Ninety-five percent Confidence Intervals (95% CI) were calculated.

Ethical committee approval for this study was obtained from the Cornwall Ethics Committee.

RESULTS

Seventy-four (87.05%) and 52 (61.1%) patients out of 85 with DU had ulcer-type dyspepsia and GORD symptoms respectively before the eradication treatment. Six to eight weeks after the successful eradication, 59 patients out of 69 (85.5%, 95% CI = 77.2 – 93.8) in the group with ulcer-type dyspepsia who had successfully eradicated Hp reported either a complete [46 (66.7%; 95% CI = 55.5 – 77.8)] or a partial [13 (18.8%; 95% CI = 9.6 – 28.1)] relief in ulcer-type dyspepsia symptoms. The symptoms remained unchanged in ten patients (14.5%; 95% CI = 6.2 – 22.8). Four of the eleven patients (36.4%) without ulcer-type dyspepsia before the treatment, reported development of new ulcer-type dyspepsia symptoms after Hp eradication (figure 1).

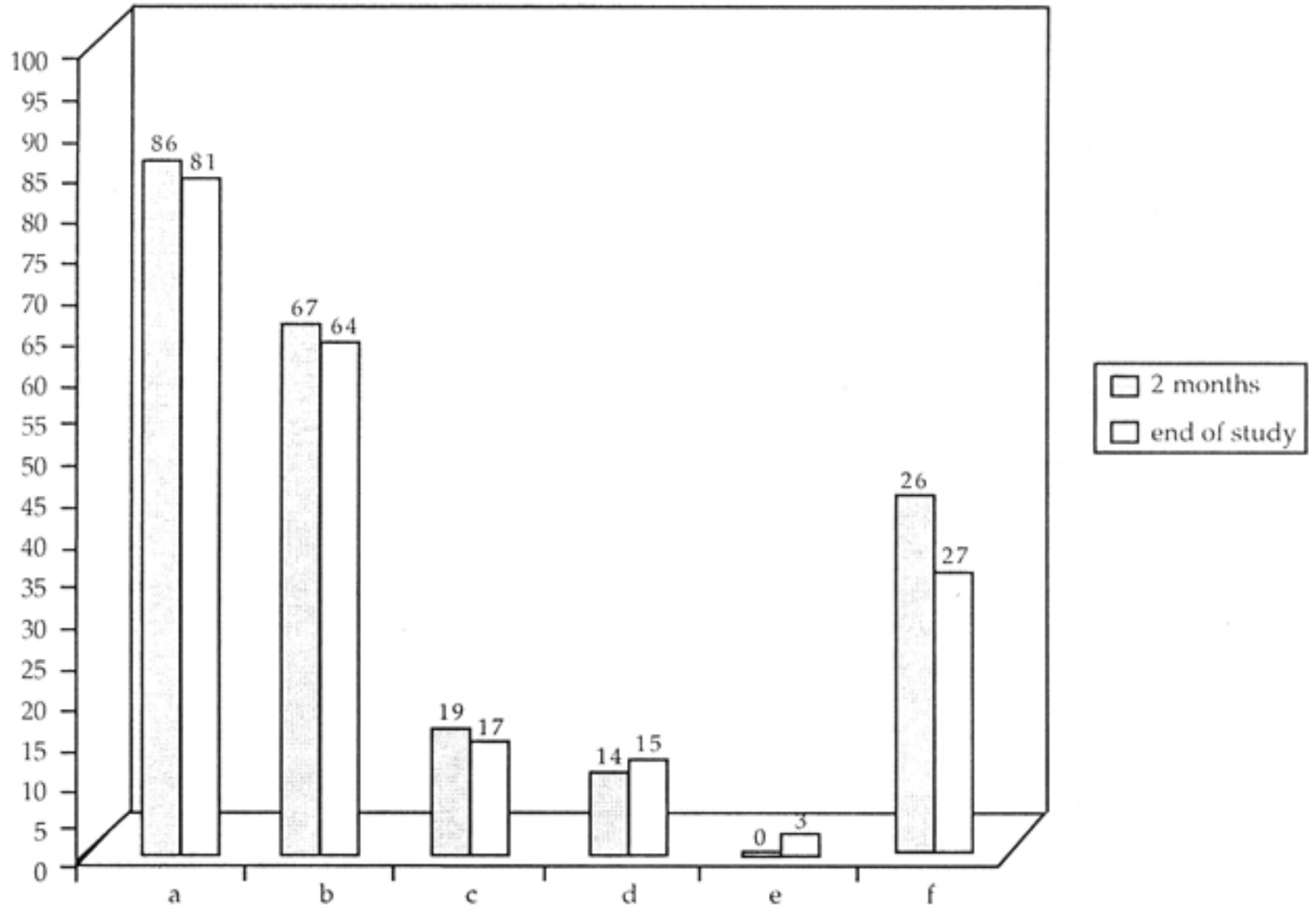
Seventy-five patients responded to the telephone/postal survey which was carried out after a median time interval of 17 months (range = 3-23) post-eradication therapy. 70/75 had their Hp successfully eradicated. 59 (84.2%) of these 70 patients had ulcer-type

dyspepsia on enrolment into the study. At the end of the study period, 48 of the 59 ulcer-type dyspeptic patients (81.4%; 95% CI = 71.4 – 91.3) reported relief in their symptoms – either partial [10 patients (17%; 95% CI = 7.4 – 26.5)], or complete [38 patients (64.4%; 95% CI = 52.2 – 76.6)]. 2 (3.4%) had some worsening of the symptoms and the symptoms remained unchanged in 9 patients (15.3%; 95% CI = 6.1 – 24.5) (figure 1). 3 of the 11 patients (27.3%) who did not have ulcer-type dyspepsia before the eradication therapy, reported development of new such symptoms.

Forty-one of the 70 patients (58.5%) who responded to the survey (and had successful eradication of Hp) had GORD symptoms before the eradication treatment. Thirty of these 41 patients (73.2%; 95% CI = 59.6 – 86.8) reported either a complete [25 patients (61%; 95% CI = 46.1 – 75.9)], or a partial [5 patients (12.2%; 95% CI = 2.2 – 22.2)] resolution of their GORD symptoms. However four patients (9.8%) had worsening of their pre-existing symptoms. The symptoms score for GORD remained unchanged for 7 patients (17.1%; 95% CI = 5.6 – 28.6). Six of the 29 patients who had no GORD symptoms at enrolment (20.7%; 95% CI = 16.0 – 25.4) developed new GORD symptoms after the successful eradication of Hp (figure 2).

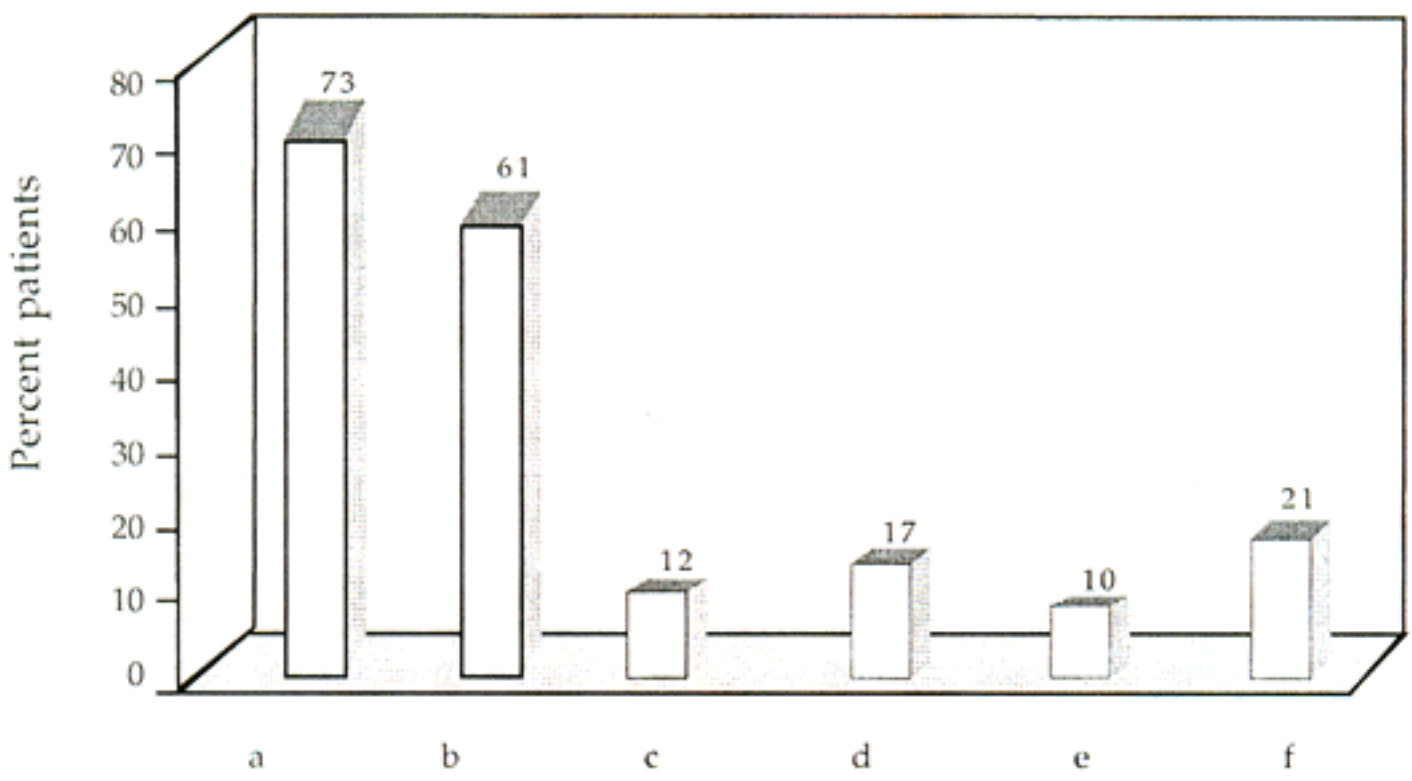
Before the eradication treatment, 60 of the 70 patients (85.7%; 95% CI = 77.5 – 93.9%) in the successful treatment group were taking acid-suppression medications (10 on proton pump inhibitors, 50 on H-2 receptor blockers). Following successful eradication therapy, 41 of these patients (68.3%; 95% CI = 56.5 – 80.1) had not required acid suppressing medication during the follow up period. Of the 19 patients who continued the acid-suppression treatment, 15 (78.9%; 95% CI = 54.4 - 93.9) had GORD symptoms.

Figure-1



Changes in ulcer-type dyspepsia after Hp eradication at 2 months and after median 17 months follow up (3 - 23); a=overall improvement, b=completely better, c=partial improvement, d=unchanged, e=worse, f=new ulcer-type dyspepsia.

Figure-2



Changes in GORD symptoms after Hp eradication:
a=overall improvement, b=completely better, c=partial improvement, d=unchanged, e=worse, f=new reflux.

DISCUSSION

Successful Hp eradication results in significant reduction in ulcer-type dyspepsia symptoms and allows majority of Hp infected patients to discontinue long-term acid-suppression treatment after eradication[9,10]. However, despite the fact that a large number of patients with chronic DU disease are cared for in the community by their GPs, often without much involvement of hospital gastroenterologists, this is one of the very few studies conducted in this setting to investigate the effects of the Hp eradication on patients symptoms[11]. This study shows that 81% patients reported an improvement in ulcer-type dyspepsia symptoms upto the end of study period, which was at a median of 17 months after successful Hp eradication treatment. 68.3% of all the patients who had successfully eradicated Hp, were able to discontinue their long-term acid-suppression treatment. Some previous studies have also reported a flare-up of dyspepsia symptoms in a significant number of patients and a need for further pharmacological anti-secretory treatment in a significant proportion of Hp eradicated patients with PUD at their follow-up[10,12,13].

If the symptoms of food – or posture-related heartburn and regurgitation are the patients' predominant complaint, they are said to be 90% specific for the diagnosis of GORD[14]. Clinicians and research workers have therefore used this positive correlation to diagnose GORD on clinical grounds without using invasive investigations[12,13].

The inter-relationship between Hp infection and GORD is curious but as yet not fully understood. Patients with DU have an increased acid output and thus there is a high prevalence of symptomatic or Endoscopic GORD (30-72%) in patients with DU at initial presentation[15,16]. In contrast, Hp infection leads to atrophic gastritis and thus a decreased acid output may actually protect against GORD[17]. Reflux oesophagitis has been shown to occur more commonly in the absence of Hp infection and gastric hyposecretion. Hp may therefore prevent reflux oesophagitis by inducing hypoacidity[18]. There is some evidence that Hp infection produces ammonia and volatile amines. Ammonia has a high pKa of 9.1 and is a

neutralizing agent at elevated pH but less effective at low pH. Therefore it could represent a powerful neutralizing substance in the oesophagus. This acid-neutralising system disappears after cure of Hp infection which may result in development of reflux oesophagitis[19-22]. Indeed, oesophagitis has been reported as a new feature in a significant number of Hp infected patients with or without PUD after successful eradication of Hp[13,19,23-26]. The risk of developing reflux oesophagitis seems to be high during the first year after eradication, after which it seems to be similar to the patents with ongoing infection.[19]

Another argument put forward in favour of the hypothesis for the increased risk of GORD after Hp eradication in patients with duodenal ulcer is one of weight gain. Individuals who, after years of food-related pain, could finally eat what they liked, may overeat and so put on weight. Weight gain or, more likely, a higher intake of dietary fat and larger meals leading to weight gain, may increase the risk of GORD[19].

Conversely, it has also been shown that symptomatic reflux in some patients with PUD may improve from cure of the infection[5,12,27]. In this study, 73% patients reported improvement in their GORD symptoms whereas 21% developed new GORD symptoms after successfully eradicating Hp. It therefore appears that although pre-existing symptoms of GORD are likely to improve, there is some risk of developing new GORD symptoms with successful Hp eradication in patients with DU. It is interesting to note that at the end of the study nearly 80% of the patients requiring continuing acid suppression therapy had GORD symptoms.

It has been suggested that certain Hp strains, e.g. vac A and cag A genotypes are associated with PUD but protect against he development of GORD, with associated Barrett's oesophagus and malignant complications. On the contrary, patients with GORD infected with Hp mostly carry less virulent strains[28-32]. We did not determine the genotyping of the Hp in our patients, but this may, in part, explain the apparent discrepancy of improvement in GORD symptoms in the majority of patients, whereas development of new reflux symptoms in some others in this study and some previous reports[16].

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