Acquisition of Helicobacter pylori infection and reinfection after its eradication are uncommon in Indian adults

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Background: Eradication of Helicobacter pylori infection is known to decrease the recurrence rate of peptic ulcer disease. Data from India on the acquisition rate of H. pylori infection and reinfection after eradication are scant. Aim: To study the rates of acquisition of H. pylori infection and of reinfection after eradication in Indian adult patients. Methods: We evaluated 116 consecutive patients with dyspepsia undergoing endoscopy. Sixty-four of them were H. pylori-positive on gastric antral biopsy (rapid urease test and histology). Patients diagnosed to have H. pylori infection were treated with a four-drug regimen (omeprazole, bismuth subcitrate, tetracycline, furazolidone) for 2 weeks; those failing H. pylori eradication were treated with a second regimen (lansoprazole, amoxicillin, secnidazole) for one week. Patients who were H. pylori-negative to begin with and those who had successful H. pylori eradication were followed up clinically and endoscopically every 3 months for a median of one year. Results: Ninety-six patients (50 H. pylori-positive) were available for study; the other 20 were lost to follow up after the first endoscopy. Fifty of the 96 (52%) were H. pylori-positive; four of these 50 patients did not follow up after first treatment. The eradication rate with the four-drug regimen was 89.1% (41/46). Four of the 5 non-responders eradicated H. pylori with the second regimen. At the end of median one year follow-up (range 9-15 months), one of the 45 patients (2.2%) who eradicated the organism developed reinfection; none of the 46 patients who were initially H. pylori-negative acquired new infection. Conclusions: The risk of reinfection after eradication is low in Indian subjects at the end of one year. The rate of acquisition of new infection is also low in the adult population. [Indian J Gastroenterol 2000;19:172-174]

Key words: Acid-peptic disease, peptic ulcer disease

Helicobacter pylori has a causal role in the pathogenesis of chronic gastritis, duodenal and gastric ulcers, gastric lymphoma, and gastric adenocarcinoma. Eradication of H. pylori is known to decrease the recurrence rate of duodenal and gastric ulcers and heal early MALT lymphoma.2,3

Reinfection after H. pylori eradication is reported to be rare in developed countries.4 In less developed countries like India, the likelihood of reinfection is suspected to be high because of high prevalence of H. pylori infection. However, Indian data regarding reinfection rates are scanty. This information is important for deciding about advisability of using H. pylori eradication regimens as treatment for peptic ulcer disease.

We treated patients with dyspepsia with eradication regimens for H. pylori, and followed them up to observe for reinfection. We also studied the rate of acquisition of new infection.

Methods

During the period January 1996 to March 1997, we evaluated 116 consecutive patients (mean age 30 years, range 18-65; 69 men) attending our out-patient section who had dyspepsia of at least six months' duration. The following subjects were excluded: a) those with history of intake of NSAIDs, antibiotics, histamine H2-receptor antagonists or proton pump inhibitors in the previous 4 weeks; b) patients who had undergone surgery for peptic ulcer disease; and c) those with debilitating co-morbid illnesses. The protocol was approved by the institution's ethics committee; the subjects were included after informed written consent.

Protocol

After detailed clinical evaluation, patients were subjected to diagnostic upper gastrointestinal endoscopy (Olympus, Japan). Standard aseptic precautions were followed during all endoscopic procedures. Endoscopic evidence of gastritis or gastric or duodenal ulcer was noted. Ulcer was defined as breach in mucosal continuity exceeding 5 mm in its largest diameter; endoscopically, gastritis was diagnosed when the mucosa showed erythema, fine granularity, loss of luster or punctate exudate.

Biopsies were obtained from the gastric antrum; one specimen was subjected to the rapid urease test using an in-house kit (standardized earlier with comparison to commercial kits; unpublished data). Two specimens were paraffin-embedded, sectioned and stained with hematoxylin-eosin and alcian blue PAS at pH 2.5. The slides were interpreted by a histologist who was blinded to the clinical and endoscopic findings. Histologic findings were de-
scribed as superficial gastritis, atrophic gastritis and intestinal metaplasia.

At entry, patients were considered positive for _H. pylori_ if both the rapid urease test and histology were positive, and negative if either test was negative. Patients diagnosed as _H. pylori_-positive were treated with omeprazole 20 mg bid, bismuth subcitrate 240 mg bid, tetracycline 500 mg qid and furazolidine 100 mg qid for 14 days. They underwent repeat endoscopy four weeks after completion of this therapy. If _H. pylori_ was still positive by either the rapid urease test or histology, they were treated with lansoprazole 30 mg bid, amoxycillin 500 mg qid and secnidazole 1 g bid for 7 days. Subjects who remained _H. pylori_-positive by either test 4 weeks after the second therapy were terminated from the study. Patients who were negative for _H. pylori_ at entry or after either of these regimens were treated symptomatically with anti-ulcer drugs and/or proton pump inhibitors depending on symptoms.

All patients who were _H. pylori_-negative at entry or after treatment underwent follow-up endoscopy every 3 months and biopsies were taken as at entry, irrespective of the endoscopy findings. If they remained _H. pylori_-negative, they continued to be on endoscopy follow up; if biopsy showed _H. pylori_ positive at any visit, the study was terminated for that patient.

**Results**

Of the 116 patients with dyspepsia who were recruited, 64 were _H. pylori_-positive. Twenty patients (14 _H. pylori_-positive, six negative) were lost to follow up after the first endoscopy. Thus, 50 _H. pylori_-positive and 46 _H. pylori_-negative patients were available for the study.

A majority (43 of 50) of the _H. pylori_-positive subjects had endoscopic antral gastritis. Two patients had duodenal ulcer and one gastric ulcer on endoscopy; three patients had duodenitis. Four patients had normal endoscopy. Of the 46 _H. pylori_-negative patients, 30 had normal endoscopy, 13 had antral gastritis, and three patients had duodenal ulcer.

Histologically, all 50 _H. pylori_-positive patients had antral gastritis; these included 22 with chronic superficial gastritis and 28 with chronic atrophic gastritis. All these patients had polymorphonuclear infiltration; four patients had evidence of intestinal metaplasia. In the _H. pylori_-negative group, 20 of 46 had evidence of chronic superficial gastritis and rest had normal histology.

Two _H. pylori_-positive patients did not follow up after the first post-treatment endoscopy; two patients developed skin rash and diarrhea on treatment and therapy was discontinued in them. _H. pylori_ was eradicated in 41 of the remaining 46 patients (89.1%) after the first course of therapy (triple regimen). Of the 5 non-responders, four responded to the second course (triple regimen); _H. pylori_ could not be eradicated in one patient despite the two regimens.

**Follow-up**

The 45 patients who had eradicated _H. pylori_ infection were followed up for a median period of 12 (range 9-15) months. Only one of them (who had eradicated the organism with the quadruple regimen) acquired _H. pylori_ reinfection, at the third follow-up endoscopy; no treatment was given to him at this stage as he was asymptomatic. All the initial _H. pylori_-negative patients followed up; none of them acquired _H. pylori_ infection during a median follow-up period of 12 (range 9-15) months.

**Discussion**

The long-term effects of _H. pylori_ eradication have been well documented in the Western population. Eradication leads to drastic decrease in the duodenal ulcer recurrence rates, from a high of 70% to nearly zero, at the end of one year. There are scant data regarding _H. pylori_ reinfection rates, and ulcer recurrence rates, in Indian patients.

After eradication of _H. pylori_ infection, we observed a reinfection rate of 2.4% (1 of 45) at one year; no patient contracted this infection anew during the same period. Ours is probably the first Indian study to prospectively study reinfection with _H. pylori_ and acquisition of new infection on follow-up. Nanivadekar et al. and Dayal et al. studied patients with duodenal ulcer to document the recurrence rate of ulcer after eradication of _H. pylori_; their reports did not provide _H. pylori_ reinfection rates. A recent analysis of three Indian reports published as Abstracts mentioned a reinfection rate of 16% (range 11%-40%) per patient-year among 75 _H. pylori_-eradicated subjects. One of the reasons for the variability in reported reinfection rates is the confusion with recurrence of uneradicated organisms. This factor can be negated by confirming absence of infection one month after the attempt at eradication, as in our study.

By current evidence, _H. pylori_ appears to be transmitted predominantly by the fecal-oral route; close person-to-person contact and shared utensils or equipment are other suspected risk factors. Overcrowding and unhygienic surroundings have also been implicated. In these circumstances, reinfection rates should be higher in the less developed countries and in the lower socioeconomic strata. Our study suggests that, even in these circumstances, the risk of infection in adult subjects may be rather low. Acquisition of immunity, complete or partial, against infection by _H. pylori_ by the host may be a possible cause of low reinfection rates.

A low reinfection rate has also been reported from other less developed countries. A South African study reported 4% reinfection rate, and a recent study from
Bapat, Abraham, Bhandarkar, Phadke, Joshi

Helicobacter pylori eradication and reacquisition

Chile reported a reinfection rate of 3% at the end of one year. On the other hand, Sabbatini et al. reported a reinfection rate of 27% in an Italian group with non-ulcer dyspepsia, who had been treated with bismuth citrate and amoxycillin or metronidazole. Another Italian study reported a reinfection rate of 20%.

An incidental finding in our study was the 89% eradication rate of H. pylori that we obtained with a quadruple-drug regimen that included omeprazole, bismuth, tetracycline and furazolidine. We chose this combination for two reasons: its low cost (approximately Rs. 400 for 14 days) and to circumvent any resistance to nitroimidazole derivatives. We do not recommend this as the ideal regimen; other regimens have been reported to give over 95% eradication rates, and the likelihood of unpleasant side effects may be higher with a four-drug regimen like the one we used. But we had excellent compliance and no adverse event.

There is no recommendation in India for treating dyspeptic patients without ulcer for H. pylori infection; we did this only with the intention of determining the outcome of the infection.

We conclude that the risk of reinfection after H. pylori eradication is low in Indian adult subjects at the end of one year; the rate of acquisition of new infection is also low. Low reinfection rate has important implications on treatment strategies for H. pylori infection. Attempt at H. pylori eradication may be undertaken as a viable option even in patients from developing countries.

References


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174 Indian Journal of Gastroenterology 2000 Vol 19 October - December