

PROLONGED TREATMENT WITH OMEPRAZOLE DOES NOT IMPROVE THE ERADICATION RATE OF *HELICOBACTER PYLORI* INFECTION - A SHORT HISTORY

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ABSTRACT

Omeprazole has been shown to have a suppressive effect on Helicobacter pylori. The aim of this study was to determine if prolonged treatment with omeprazole would result in a higher eradication rate than short course treatment.

Twenty patients with endoscopy proven duodenal ulcers and unequivocal evidence of Helicobacter pylori (HP) infection based on culture, histology, urease test and Gram's stain of a fresh tissue smear were treated with omeprazole 40 mg om for 2-4 weeks. Following ulcer healing, patients received either maintenance omeprazole 20 mg om or placebo for up to one year. All 20 patients had healed ulcers following a 2-4 week course of omeprazole 40mg om. All were negative for HP at the end of treatment. Thirteen patients received short course therapy with omeprazole only, followed by placebo. On follow-up endoscopy at 3 months, only one of 13 (7.7%) had eradicated the bacteria. Seven patients received maintenance treatment with omeprazole 20mg om for one year. Following completion of treatment, patients were followed up at 1, 3 and 6 months. Only one of 7 (14.3%) patients had eradicated the infection on long term follow-up.

The eradication rates of HP with both short and long course omeprazole monotherapy were low.

Keywords: omeprazole, *Helicobacter pylori*, duodenal ulcers, eradication, relapse

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INTRODUCTION

Omeprazole, a potent acid-suppressing agent is an efficient ulcer healing drug. Reports of its effect in clearing or suppressing *Helicobacter pylori* (HP)⁽¹⁻⁸⁾ have obviously generated much interest worldwide especially with the increasing recognition of the role of HP in peptic diseases and in ulcer relapse⁽⁹⁾.

Hitherto reports⁽¹⁻⁸⁾ have however been on short course treatment with omeprazole. The aim of our study was to determine the effect of short course and prolonged treatment with omeprazole of up to one year in the eradication of HP in duodenal ulcer (DU) patients.

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PATIENTS AND METHOD

Patients selected had endoscopy proven duodenal ulcers of a minimum diameter of 5 mm and were HP positive. They received omeprazole 40mg om for 2 weeks and were reendoscoped at completion of treatment. If the ulcers were not healed, patients received a further 2-week course of omeprazole 40mg om and were endoscoped again at the end of that period. Patients with healed ulcers received either maintenance omeprazole 20mg om or placebo for one year. Patients were seen every 3 months or whenever there was recurrence of ulcer symptoms. At every endoscopy, antral biopsies were taken for HP diagnosis by rapid urease test, culture, histology and a Gram's stain of a fresh tissue smear as described previously⁽¹⁰⁾. A positive diagnosis of HP infection was made when culture was positive or when two of the above-mentioned tests were positive, one of which was histology. Eradication was defined as absence of bacteria in all the above tests performed on antral biopsies, at least four weeks after cessation of therapy.

The endoscopist, microbiologist and histopathologist were blind to each other's report until final analysis.

STATISTICAL ANALYSIS

Fisher's exact test was used for statistical analysis.

RESULTS

A total of 20 patients were enrolled into the study. The male/female ratio was 3:2. The mean age of the patients was 43 years (range 26-70) and the ethnic distribution was as follows: Malays 1; Chinese 15; Indians 4.

Ulcer healing

Seventeen patients (85%) had healed ulcers after 2 weeks of omeprazole and 3 following a further 2 weeks of treatment.

HP status

All patients were proven to have HP infection prior to commencement of treatment. Immediately following

completion of treatment, all patients were shown to be negative for HP.

Thirteen patients received short course treatment with omeprazole for 2-4 weeks followed by placebo. Within 3 months following cessation of treatment, 12 patients had symptomatic recurrence of ulcer pain and were detected to have a relapse of the infection as well as relapse of duodenal ulcers. The single patient who remained clear of HP was seen at 3 and 6 months following completion of treatment and remained ulcer-free and HP negative. The eradication rate with short course omeprazole was therefore only 7.7% (1/13).

Seven patients received long-term maintenance omeprazole 20mg om for one year following a short ulcer healing course of omeprazole 40 mg om for 2-4 weeks. Patients were reviewed 3 monthly; while on treatment, ulcers remained healed and HP was not detected in the antral biopsies of any of the patients. One month after cessation of treatment, HP had recurred in 6 of 7 patients and ulcer relapse in 4. The single patient who remained clear of HP was seen again at 3 and 6 months and continued to be HP negative and free from ulcers. The eradication rate following prolonged treatment with omeprazole was 14.3% (1/7). There was no significant difference in the eradication rates ($p=0.589$). Overall, only 2 of 20 patients (10%) who received short-course or prolonged treatment with omeprazole had eradication of HP on long term follow-up of up to 6 months after cessation of therapy.

Gastritis

All patients had histological changes of chronic active gastritis before the start of treatment. The histological picture improved markedly on treatment with disappearance of markers of acute inflammation on completion of treatment. With relapse of the infection there was reappearance of features of chronic active gastritis. Patient compliance to medication was good and in general, patients did not complain of any side-effects.

DISCUSSION

The action of omeprazole on HP is not entirely clear as omeprazole has not been shown to possess any antibacterial activity *in-vitro*⁽¹¹⁾ although a related compound, lansoprazole, has been shown to have such antimicrobial properties⁽¹²⁾. It has been postulated that the profound acid-suppression achieved with omeprazole may cause the bacteria to become more vulnerable or that the higher gastric pH may potentiate the effect of concomitantly administered antibiotics⁽¹³⁾.

It is however clear nonetheless that omeprazole used as a single agent is not effective in eradicating the bacteria although as shown in our study there was promising effect in the temporary suppression of the bacteria. Conventional methods of diagnosis have been shown to be insensitive in patients treated with omeprazole especially when the HP status is checked immediately on cessation of therapy. In one study, electron microscopy demonstrated presence of HP in possibly dormant forms in 7 of 15 patients where histology and culture were negative⁽⁷⁾.

We have also shown that prolonged treatment with omeprazole up to one year does not improve the eradication

rate and that the infection relapses just as quickly on stopping the medication. Recent reports on long term omeprazole treatment are consistent with our findings^(14,15).

The value of omeprazole in the eradication of HP infection has, as with bismuth compounds, been shown to be best exploited in combination therapy with antibiotics⁽¹⁶⁾.

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