

RELAPSE OF PEPTIC ULCER AFTER ERADICATION OF *HELICOBACTER PYLORI* WITH LOW DOSE, SHORT TERM ONE-WEEK TRIPLE THERAPY

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ABSTRACT: Relapse of peptic ulcer after healing and eradication of *Helicobacter pylori* by low dose, short term 7-day triple therapy was assessed on one-year follow-up. Thirty-five endoscopically confirmed patients of peptic ulcer with *Helicobacter pylori* infection diagnosed on the basis of urease test and histology (Giemsa stain) were selected. All selected patients received Lansoprazole 30 mg o.d., Clarithromycin 250 mg b.i.d. and Tinidazole 500 mg b.i.d. for 7 days. Four weeks after completion of therapy, healing was seen in all patients with eradication of *H. pylori* in 93.5% cases. Patients were followed up for one year and endoscopy, urease test and histology repeated. Relapse was seen in 4.2% patients during this duration.

KEY WORDS: Peptic Ulcer *Helicobacter pylori* Proton pump/inhibitors

INTRODUCTION

Relapse of peptic ulcer is an important issue. The healing rate of different H₂ receptor antagonists has been reported as between 76-90% after 6-8 weeks of therapy¹⁻³ and that of proton pump inhibitors (PPI) as 80-96% after 2-4 weeks of therapy⁴. No significant difference has been observed in the healing rate of H₂ receptor antagonists and PPI⁵. Most of the ulcers have a relapse within one year, and relapse rates with PPI are reported to be higher as compared to H₂ antagonists⁶. It has been observed that 90-100% of duodenal ulcers are associated with *Helicobacter pylori*⁷. It has an established role in the pathogenesis of chronic active type B gastritis and of duodenal ulceration⁸⁻¹⁰. Eradication of *Helicobacter pylori* has decreased the relapse rate of peptic ulcer and is now being strongly recommended¹⁰. Many drug combinations are now in use and give eradication rates varying from 70-90%¹¹⁻¹⁴. Many of them have lower compliance and several side effects. We tested the new, low dose, short term, one-week triple therapy consisting of lansoprazole 30 mg o.d., clarithromycin 250 mg b.i.d. and tinidazole 500 mg b.i.d. for one week (LCT-1) for *Helicobacter pylori* eradication and ulcer healing with encouraging results¹⁵. This study presents the one-year follow-up of the same patients to document relapse rates with this new regimen.

PATIENTS AND METHODS

Patients presenting with symptoms of acid peptic disease at Chandka Medical College, Larkana and at the private clinic of the chief author during the period of July 1994 and June 1996 were subjected to Oesophago-gastro-duodenoscopy (OGD) after taking informed consent. Patients with history of intake

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of H₂ receptor antagonists, PPI, Clarithromycin or Tinidazole during past 2 weeks, patients of chronic liver or renal disease and pregnant or lactating women were excluded. The procedure was performed observing standard technique and precautions¹⁶ using Midazolam for sedation. Ulcer was defined as a localized defect in gastric or duodenal mucosa of at least 5 mm in diameter with perceptible depth, whereas smaller lesions were considered as erosions. Ulcer dimensions were measured with the standard biopsy forceps, with the fully open spoon being equivalent to 5 mm. Two biopsy specimens were taken from the ulcer edges, two from antrum and one each from body and fundus. One antral biopsy was immediately inoculated in locally prepared Urease gel with sensitivity and specificity equal to that of imported kit¹⁷, while the rest were kept in 10% formaline for histological assessment with Giemsa stain. Urease test was read at 30 minutes after insertion of biopsy, reviewed at 24 hours and the results recorded. The patients with either Urease positivity or histologic evidence of *Helicobacter pylori* were inducted into the trial. Selected patients were given the drugs (LCT-1) as under:

Lansoprazole	30 mg	o.d.	for 7 days.
Clarithromycin	250 mg	b.i.d.	for 7 days.
Tinidazole	500 mg	b.i.d.	for 7 days.

Four weeks after completion of therapy patients were again subjected to OGD and Urease test. The patients in whom *Helicobacter pylori* was eradicated and the ulcer healed, were followed up for one year. OGD and Urease test were repeated in these patients after one year or whenever symptoms suggested a relapse. The patients in which either ulcer did not heal or *Helicobacter pylori* was not eradicated were excluded from further evaluation. All results for continuous variables were expressed as means \pm SD. The Mann-Whitney U test and t-test were used to compare continuous variables between

different groups. The p values for comparison of categorical variables were generated by the chi-square test for proportions with appropriate degrees of freedom, and p values of less than 0.05 according to the two-sided McNemar test were considered to indicate statistical significance. All calculations were done with SPSS 7.0 (SPSS, Chicago).

RESULTS

Thirty five patients with endoscopically proven peptic ulcer who were also positive for *Helicobacter pylori* by Urease test¹⁷ were selected for the study. Out of these 32 (91.43%) were also positive for *Helicobacter pylori* on histology. There were 28 males (mean age 33.2±2.2 years) and 7 females (mean age 29.6±2.2 years) as shown in Table I. No significant difference was observed between the ages of two sexes.

Four weeks after completion of specified therapy; OGD, Urease test and histopathology were performed to assess healing and *H.pylori* eradication. Four patient did not report for OGD and were excluded from the study. Ulcer healing was seen in the remaining 31 (100%) patients¹⁵. Urease test became negative in 29 (93.5%) patients, while histological clearance of *Helicobacter pylori* at this stage was seen in 30 (96.8%) patients. Two patients in whom Urease test remained positive were also excluded from further evaluation. Patients were followed up for one year for occurrence of relapse. Five patients were lost to follow up at one year and excluded from further analysis. One (4.2%) patient out of 24 had a relapse of ulcer during the followup period after ten months of eradication therapy. Details are tabulated in Table II. Side/adverse effects reported were trivial in nature and included diarrhoea (2%), skin rashes/itching (1.4%), decreased appetite (2.5%) and abnormal taste (3%).

TABLE I Clinical and demographic details of patients (n=35)

Criteria	Number
Mean age±SD (years)	29.4±5.4
Weight±SD(kg)	68.4±3.3
Height±SD(meters)	1.7±0.2
Duration of Symptoms (days)	30.0±5.0
Smokers	6
History of UGI Bleeding	3

TABLE II Healing and relapse rates in two groups

Criteria	Number
Total patients	35
Follow up loss after 4 weeks	4
Ulcer healing after 4 weeks	31/31 (100.0%)
<i>H.pylori</i> eradication after 4 weeks	29/31 (93.5%)
Follow up loss after 1 year	5
Relapse after 1 year	1/24 (4.2%)

DISCUSSION

Helicobacter pylori has been implicated in the pathogenesis of many diseases like chronic gastritis, peptic ulcer⁶⁻⁹, gastric malignancy^{18,19}, coronary heart disease^{20,22} and hepatic encephalopathy^{23,26}. Its eradication has shown to decrease the relapse of peptic ulcers¹⁰. Many combinations are being tried to give better response with simple and easy to take regimens.

The new low dose regimen in peptic ulcer healing and eradication of *Helicobacter pylori* LCT-1 has shown promising results as reported by us earlier on¹⁵. We now report the one year follow up of the same patients treated with LCT-1, and found a very low relapse rate of only 4.2%. The relapse rates of duodenal ulcer without *Helicobacter pylori* eradication have been reported as 79% with ranitidine and 100% with omeprazole, on one year follow up⁵. Thus the relapse rate with LCT-1 are significantly low on one year follow-up. Various doses of clarithromycin have been tried in search of optimal dose. Reports with 250mg and 500mg of clarithromycin for 1-week in combination with PPI and another antibiotic have failed to show any advantage of using 500 mg b.i.d. dose over 250mg b.i.d. in terms of ulcer healing and *Helicobacter pylori* eradication. Even the side effects were less frequent with the 250mg dosage regimen²⁷. Different regimens comprising various combinations of PPI with two antibiotics have been tried for 1-week with equally good results in ulcer healing and *Helicobacter pylori* eradication^{27,30}. Lansoprazole when used alone has shown to have activity against *Helicobacter pylori* at the usual clinical doses leading to its eradication in 54.5% to 66.7% of cases³¹. Thus eradication regimens based on Lansoprazole would give better results. Recently, a National Institute of Health, Consensus Development Conference has recommended that all patients of gastric or duodenal ulcer who are infected with *Helicobacter pylori* should be treated with antimicrobials including patients presenting with an ulcer for the first time³². There is growing evidence that eradication of *Helicobacter pylori* leads to a lower relapse rate³³⁻³⁶. We conclude that the LCT-1 therapy for *H.pylori* positive peptic ulcer is simple, effective and has a low relapse rate.

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