

Original Article

Clinical, endoscopic and histologic evaluation of gastroesophageal reflux disease in patients treated with proton pump inhibitor: a prospective study

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Abstract

This study was done to demonstrate the histological changes in gastroesophageal reflux disease (GERD) before and after proton pump inhibitor (PPI) therapy as well as, to evaluate the efficacy of PPI in patients with GERD and to find out the healing rate of erosion in erosive reflux disease after PPI therapy. This hospital based prospective study was conducted among 57 patients suffering from gastroesophageal reflux disease who were recruited from the outpatient department of gastroenterology of Bangabandhu Sheikh Mujib Medical University. It was carried out from May 2008 to December 2008. Most of the GERD patients had non erosive disease (63.2% vs 36.8%). PPI was effective to relieve the major symptoms of GERD. In erosive group (n=21), at the end of 28th day, heartburn was present in 3(14.3%) patients. In non-erosive group (n=36), at the end of 28th day heartburn was present in 6(16.7%) patients. Changes in histological parameters were also found to be significant before and after therapy. GERD patients had characteristic histologic changes in lower esophagus and after 4 weeks of treatment with PPI, there was significant improvement of symptoms, endoscopic and histological features of reflux disease.

Key words: GERD, esomeprazole, erosive reflux disease, non-erosive reflux disease.

Introduction

Gastroesophageal reflux disease (GERD) is the failure of the normal antireflux barrier to protect against frequent and

abnormal amounts of gastroesophageal reflux. GERD is a spectrum of disease usually producing symptoms of heartburn and regurgitation.¹ Studies done by Rokonuzzaman SM and Shahed MM shows that the prevalence of GERD in rural and urban population of Bangladesh is 19.4% and 18.1% respectively.^{2,3} Upper GI endoscopy, which is often the investigation of first choice, is useful if there are erosive changes in the lower esophagus or complications of GERD. However, the absence of macroscopic esophagitis does not exclude GERD.⁴ Most GERD patients do not have any endoscopically visible damage to their mucosa. These patients have non erosive reflux disease(NERD).⁵ Histological changes in the lower esophagus have been described in GERD. It has been suggested that the detection of these changes on esophageal biopsy affords a quick, inexpensive and reliable method of diagnosing nonerosive GERD. In erosive reflux disease patients, there is strong correlation between severity of GERD and histological parameters.⁶ Acid suppression by proton pump inhibitors (PPI) is the mainstay for treating GERD.⁷ Objectives of this study were to evaluate the efficacy of PPI in patients with GERD, to find out the healing rate of erosion in erosive reflux disease after PPI therapy and to demonstrate the histological changes in gastroesophageal reflux disease before and after PPI therapy.

Methods

This was a prospective study. Patients suffering from GERD were recruited from the outpatient department of gastroenterology of Bangabandhu Sheikh Mujib Medical University. It was carried out from May 2008 to December 2008. A structured questionnaire was used to select the patients. Informed written consent was taken from each study subject. Upper GI Endoscopy was done on those subjects who had a positive symptom score (3 or more) and biopsies were taken 2 cm above the gastroesophageal junction from all the subjects. Repeat endoscopy and biopsy were done 4 weeks after giving esomeprazole therapy (40 once daily). Clinical assessments were done at baseline, at 2nd and 4th week. NERD patients were identified by the absence of mucosal breaks while erosive reflux disease was identified by presence of mucosal injury on upper GI endoscopy. At endoscopy 3 biopsies were taken from the esophagus; 2 cm above the gastroesophageal junction. The specimens were assessed by calculating the thickness of the

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basal cell layer and the elongation of the papillae as a percentage of the whole epithelial thickness. All biopsies were scrutinized by an experienced histopathologist who was unaware of the endoscopy or symptom score. For the purpose of this study, a daily diary was maintained which recorded daily presence of heartburn, regurgitation, dysphagia, epigastric or chest pain and nausea. Patients were instructed to take drugs (esomeprazole) once daily half an hour before breakfast for 28 days and come for follow up in every week and maintain their daily diary. Compliance of treatment was monitored by completion of daily diary. All patients were assessed on 2nd and 4th week by analyzed daily diary, maintained by the patients. Data were collected from daily diary and analysed by SPSS.

Results

The present study included 60 patients. Of them, 3 did not complete the treatment and hence were excluded from the study. The findings of the study obtained from data analyses were documented here. At day 1, heartburn was almost equally distributed between erosive and non-erosive diseases (47.6% and 47.2% respectively). After 4 weeks of treatment the symptoms were substantially reduced to 14.3% and 16.7% in erosive and non-erosive disease groups respectively. Although erosive group responded better than the non-erosive group, the difference was not statistically significant (p = 0.463). At day 1, about 43% of the erosive disease subjects complained of regurgitation which reduced to 9.5% after 4 weeks of treatment. In non-erosive group about 42% of the subjects had regurgitation which decreased to 13.8% after 4 weeks following intervention. Erosive group responded significantly better than their non-erosive counterpart (p=0.034).

Out 57 subjects of GERD, 36.8% had erosive diseases at baseline which decreased significantly to 5.3% after 4 weeks of intervention with esomeprazole (p = 0.020). (Table-I)

Table-I: Endoscopic Changes in erosive disease

Erosion at baseline	Erosion after 4 weeks of treatment		Total
	Present	Absent	
Present 21	03	18	21(36.8%)
Absent 36	00	36	36(63.2%)
Total 57	03(5.3%)	54(93.7%)	57

Figures in the parentheses denote corresponding percentage.

Chi-square (χ^2) Test was done to analyse the data; $\chi^2 = 5.429$; p = 0.020.

Papillary length of the subjects with erosive disease was 63% which reduced to 51.2% after 4 weeks of treatment (p < 0.001). The papillary length of non-erosive disease also responded well to treatment reducing from 52.1% at baseline to 29.3% after 4 weeks of treatment (p < 0.001). (Table-II)

Table-II: Changes in Papillary length

GERD	Papillary length		P value
	At baseline	After 4 weeks	
Erosive disease (%) (n = 21)	63.0 ± 6.7	51.2 ± 9.9	<0.001
Non-erosive disease (%) (n = 36)	52.1 ± 6.7	29.3 ± 7.4	<0.001

Data were analysed using Wilcoxon Signed Rank Test and were presented as mean ± SD.

The thickness of basal cell layer also responded well to treatment with esomeprazole in both erosive and non-erosive diseases. Thickness of basal cell layer in erosive disease group reduced from 16.9% at baseline to 6.6% after 4 weeks of treatment (p < 0.001) and that in non-erosive disease from 11.2% at baseline to 7.5% after 4 weeks of treatment (p < 0.001).

Table-III: Changes in Thickness of basal cell layer

GERD	Thickness of basal cell layer		P value
	At baseline	After 4 weeks	
Erosive disease (%) (n = 21)	16.9 ± 13.7	6.6 ± 2.0	<0.001
Non-erosive disease (%) (n = 36)	11.2 ± 2.5	7.5 ± 2.3	<0.001

Data were analysed using Wilcoxon Signed Rank Test and were presented as mean ± SD.

Discussion

There is paucity of data on GERD in Bangladesh. This was a prospective study to assess the efficacy of PPI in improving the symptoms, endoscopic and histological features of patient with GERD. For this study 60 patients were selected for the trial and 57 patients completed the trial; 3 patients dropped out.

This study showed that PPI is effective to relieve the major symptoms of GERD. In erosive group (n=21), heartburn was present in 10(47.6%) patients in day 1. At the end of 14th day heartburn was present in 9(42.9%) patients and at the end of 28th day heartburn was present in 3(14.3%) patients. In non-erosive group (n=36), heartburn was present in 17(47.2%) patients in day 1. At the end of 14th day heartburn was present in 12(33.3%) patients. At the end of 28th day heartburn was present in 6(16.7%) patients. Although erosive group responded better than the non-erosive group, the difference was not statistically significant ($p = 0.463$). This findings are consistent with the study done by Edson Pedro et al where at the end of 4th week of treatment with esomeprazole, 10% patients had heartburn.⁸ Biswjit Dutt, in his study, had shown resolution of heartburn by omeprazole in 76% patients.⁹ David and Pierre, in a randomized control comparison study, showed that PPI (pantoprazole) resulted in higher complete resolution of heartburn compared to placebo therapy in GERD patients but relief of heartburn was not significantly different between the erosive and nonerosive GERD.¹⁰ Carlsson et al used 20 mg of omeprazole to treat both endoscopic negative and endoscopic positive patients with GERD symptoms. After 4 weeks of treatment resolution of heartburn was approximately same in both groups.¹¹

At day 1, 9 (43%) of the erosive disease subjects complained of regurgitation which reduced to 5 (23.8%) after 2 weeks of treatment and to 2 (9.5%) after 4 weeks of treatment. In non-erosive group 15 (42%) of the subjects had regurgitation which decreased to 9 (25%) after 2 weeks and 4 (13.8%) after 4 weeks following intervention. Edson Pedro et al, in their study found that at the end of 4th week of treatment with esomeprazole, 10% patients had regurgitation.⁸ Carlsson et al. showed that after 4 weeks of treatment with omeprazole, symptoms of acid regurgitation, epigastric pain, nausea and dysphagia were resolved more often in endoscopy positive patients than in those without endoscopic finding.¹¹ Bishwajit D. showed that acid regurgitation improved in 90% of patients in both endoscopy positive and negative groups.⁹ In this study, erosive group responded significantly better than their non-erosive counterpart ($p = 0.034$). Out of 57 patients of this study 21 (36.8%) had erosive and 36 (63.2%) had non erosive disease. This is higher than that of some Asian study. In this study, it was seen that out of 21 patients with erosive disease 18 (85.7%) patients had their erosions healed at the endpoint. KD Bardhan et al showed that the healing rate was 74.8% at the end of 4th week of treatment with 40 mg of esomeprazole and 75% with 40 mg of pantoprazole.¹²

Edson et al found that the healing rate was 82.5% at 4th week and 93.6% at 8th week of treatment with once daily 40 mg esomeprazole treatment.⁸ Proton pump inhibitor therapy has been reported to reduce proliferative changes of esophagus significantly in GERD. In this study, proliferative changes of the squamous epithelium was assessed histologically by measuring thickness of basal cell layer and elongation of the papilla as percentage of whole epithelial thickness. After intervention with esomeprazole, papillary length reduced significantly in both erosive and non-erosive group. In patients with erosive disease mean length reduced to 51.2% of total epithelial thickness to 63% ($p < 0.001$) and in patients with non-erosive disease reduced to 29.3% from 52.1% ($p < 0.001$). The thickness of basal cell layer also responded well to treatment with esomeprazole in both erosive and non-erosive diseases. The thickness of basal cell layer in erosive disease group reduced from 16.9% at baseline to 6.6% after 4 weeks of treatment ($p < 0.001$) and that in non-erosive disease from 11.2% at baseline to 7.5% after 4 weeks of treatment ($p < 0.001$). This study showed that PPI is highly effective in treating gastroesophageal reflux disease. After 4 weeks of treatment with esomeprazole, there was significant improvement of symptoms, endoscopic and histological features of reflux disease. The drawbacks of the study were that it had no control arm and small sample size. Further randomized controlled study with large sample is needed to verify the significance.

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