7

SUCCESSFUL TREATMENT OF ELDERLY PATIENTS WITH EROSIVE ESOPHAGITIS (EE) USING PANTOPRAZOLE 40 mg

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Purpose: Elderly patients (≥65 years old) have more frequent complications of GERD such as erosive esophagitis and Barrett's esophagus (Collen MJ, AJG 1995;90:1053–7). Elderly patients may have a variety of anatomical and functional alterations in the upper gastrointestinal tract that may result in an increased risk of more severe GERD. The goal of this analysis is to determine the efficacy of pantoprazole 40 mg in healing EE in this high risk population.

Methods: This retrospective analysis was based on combined data from two prospective, double-blind, multicenter, randomized trials in which 254 patients were randomized to the pantoprazole 40 mg arms of the studies; 82 patients received placebo in one study and 82 patients received nizatidine 150 mg bid in the other study. Patients with EE (grade ≥2, Hetzel-Dent (HD) scale) were treated with study medication daily in the morning and followed with repeat endoscopy at 4 and 8 weeks (if not healed at 4 weeks). Patients with HD grades 3 and 4 were considered to have severe EE. Biopsies were obtained of the gastric antrum and body to evaluate for *H. pylori.*

Results: In these studies, 44 elderly patients (≥65 years old) and 210 younger patients (age <65) were treated with pantoprazole 40 mg. There was no difference in the rate of *H. pylori* positivity in elderly vs younger patients (19% vs 20%). Healing rates at 8 weeks on pantoprazole 40 mg for the elderly group were 96% (22/23) for HD grade 2; 76% (16/21) for HD grades 3 & 4; and 86% (38/44) for all grades. These results are not different from the younger group who had healing rates of 87% (122/140) HD grade 2; 74% (52/70) HD grades 3 & 4; and 83% (174/210) for all grades. Elderly patients with EE treated with pantoprazole 40 mg had a significantly higher healing rate compared with the combined placebo/nizatidine group ($p<0.001$). Elderly patients with severe EE (grades 3 & 4) had a healing rate on placebo of 20% (1/5) and on nizatidine of 0% (0/7).

Conclusions: Healing rates of EE in elderly patients treated with pantoprazole 40 mg are similar to those in patients less than 65 years old treated with pantoprazole 40 mg and superior to healing in elderly patients treated with placebo or nizatidine. Pantoprazole 40 mg once daily provided excellent healing of mild and severe grades of EE in the elderly as well as younger patient groups.

8

ESOMEPRAZOLE MAINTAINS CONTROL OF UPPER GI SYMPTOMS IN PATIENTS ON NSAID THERAPY

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Purpose: All NSAIDs, including COX-2 selective NSAIDs, cause upper GI adverse events, ranging from symptoms to ulcers. Two recent studies1 demonstrated that 4 weeks' esomeprazole treatment is effective in relieving symptoms in NSAID users without ulcers. Given the importance of maintaining symptom relief during continuous, long term NSAID therapy, we compared esomeprazole with placebo in preventing upper GI symptom relapse over 6 months.

Methods: Patients who achieved upper GI symptom relief (none/mild for last 7 days, maximum 2 days rated as mild) in the acute studies1 were re-randomized into two identical, multicenter, placebo-controlled, double-blind studies. Patients received esomeprazole 40 mg (E40), esomeprazole 20 mg (E20) or placebo (P) qd orally for 6 months. Upper GI symptoms were recorded on patient daily diary cards. Relapse was defined as moderate or severe symptoms (a score of 3–6 on a 7-graded scale for ≥3 days in any 7 day period). Symptom (heartburn, acid regurgitation, upper abdominal bloating and nausea) severity was investigator assessed at 1, 3 and 6 months on a 4-point scale (last values carried forward if missing). The primary endpoint was the proportion of patients with relapse of upper GI symptoms through 6 months of treatment.

Results: In the pooled ITT population of 594 patients, both doses of esomeprazole were significantly more effective than placebo in preventing the relapse of upper GI symptoms (table). Compared with placebo, E40 and E20 treatment resulted in significantly ($p<0.05$) more patients with no (investigator-assessed; 'none' on a 4-point scale) heartburn (E40: 81.3%, E20: 75.5%; P: 62.4%) or acid regurgitation (E40: 86.5%, E20: 78.1%, P: 67.3%) at 6 months.

Cumulative proportion of patients with relapse of upper GI symptoms (diary card).

Pooled ITT population	E40 Estimated (%) rate (95%CI)	E20 Estimated (%) rate (95%CI)	P Estimated (%) rate (95%CI)
Month 1	11.2 (6.7–15.7)	14.8 (9.8–19.9)	31.5 (25.1–37.9)
Month 3	20.3 (14.4–26.3)	20.9 (15.0–26.9)	35.9 (29.2–42.6)
Month 6	26.1 (19.4–32.9)	29.3 (22.3–36.2)	39.1 (32.2–46.0)
Logrank test, p-value vs placebo	0.0006	0.0059	

Conclusions: Esomeprazole 40 mg and 20 mg qd are significantly more effective than placebo in preventing relapse of upper GI symptoms in non-selective and COX-2 selective NSAID users over 6 months.

1. Yeomans N, et al. Gastroenterology 2003; 124(4, suppl 1): A107

9

PANTOPRAZOLE EFFECTIVELY DECREASES THE NUMBER OF LONG REFLUX EPISODES BY DAY 1 OF THERAPY

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Purpose: Erosive GERD patients with more severe disease frequently have prolonged esophageal mucosal contact of the refluxate. The lack of clearance results in increased exposure to acid that causes mucosal damage. Therefore, decreasing the number of reflux episodes lasting longer than 5 minutes should be an important factor in healing severe disease and treating associated symptoms. This analysis was performed to assess the effect of pantoprazole on the number of long reflux episodes in patients with severe erosive GERD.

Methods: Patients with endoscopically documented erosive GERD participated in a 24-hour esophageal pH-monitoring screen followed by pantoprazole 40mg qd for 5 days. Repeat esophageal pH monitoring was performed on days 1 and 5 of treatment. Evaluation of the number of long reflux episodes (LRE; defined as number of times esophageal pH ≤ 4.0 lasting 5 minutes or longer) was performed to determine if active therapy decreased these episodes during daytime and nighttime (when the patient was supine) hours. Also, the number of heartburn-related symptoms was recorded at baseline, day 1, and day 5.

Results: A total of 35 patients (23 M /11 F, ages 24–51) were enrolled and completed therapy. The total number of reflux episodes over 24 hours was 159 at baseline, and only decreased to 129 and 134 after day 1 and day 5 of therapy, respectively. However, median number of LRE over 24 hours significantly decreased from a baseline of 9 to 2 and 1 at days 1 and 5, respectively (both $p<0.001$). During daytime hours, pantoprazole decreased the median number of LRE from a baseline of 6 to1on days 1 and 5 (both $p<0.001$). More importantly, nighttime LRE were decreased from