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Esomeprazole Versus Pantoprazole for Healing Erosive Oesophagitis

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A B S T R A C T

The aim of this study was to compare the efficacy of esomeprazole and pantoprazole with regard to healing and relief from gastroesophageal reflux disease-related symptoms. I this multicentre, randomized, single-blind study 180 patients (ITT population) diagnosed with endoscopically proven GERD grade A,B,C received esomeprazole (40 mg once daily (o.d.), n=90) or pantoprazole (40 mg o.d., n=90). Healing and relief from GERD-related symptoms were assessed at first and final visit (after 4 or 8 weeks of treatment). Esomeprazole 40 mg provided significantly greater healing than pantoprazole 40 mg after 4 weeks of treatment in patients with EE (77.8% vs. 72.2%). Esomeprazole-treated patients were healed after up to 8 weeks of treatment similar those treated with pantoprazole (92.2% vs. 91.1%). The proportion of heartburn-free days was similar in patients treated with esomeprazole and to those treated with pantoprazole.

Key words: *gastroesophageal reflux disease, GERD, esomeprazole, pantoprazole*

Introduction

Gastroesophageal reflux disease (GERD) is an extremely common clinical problem accounting for a large proportion of physician visits regarding gastrointestinal problems.

GERD is associated with severe and frequently life-long symptoms that lead to a marked reduction in normal function and well-being[1]. Up to 50% of patients with chronic GERD develop erosive oesophagitis (EE)[2]. GERD and/or EE are associated with complications such as peptic stricture, bleeding and Barrett's oesophagus; the latter is a risk factor for oesophageal adenocarcinoma[3]. Patients with GERD have a diverse range of symptoms, the most common of which is heartburn[4]. The goals of management in patients with GERD are healing of EE, resolution of symptoms and prevention of complications[5]. The most effective and established drugs to inhibit gastric acid secretion are proton pump inhibitors (PPIs), which are nowadays recommended as the treatment of choice for GERD[6].

The aim of this study was to compare esomeprazole 40 mg with pantoprazole 40 mg for healing and symptom relief in patient with EE. The results presented here relate to the acute treatment phase of a management study.

Methods

Patients with EE were enrolled into this randomized, single blind, multi-centre study. The study was undertaken in accordance with the Declaration of Helsinki and with the prior approval of local ethics committees. Informed consent was obtained from all patients prior to study entry. The study was conducted at 3 centres in Croatia.

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Inclusion criteria included: history of GERD symptoms for at least 6 months immediately prior to enrolment, confirmed by endoscopy and graded using the LA grading system[7].

Exclusion criteria included: other significant upper gastrointestinal disorders (including Zollinger-Ellison syndrome, gastric or duodenal ulcer, oesophageal stricture, history of dysplasia in Barrett's oesophagus); intake of medication liable to affect the outcome of the study (including non-steroidal anti-inflammatory drugs); pregnancy, childbearing potential (unless taking suitable precautions) or lactation; alcohol and/or drug abuse; PPI use within 4 weeks prior to the first endoscopy.

At visit 1 (baseline) physical examination was carried out and the investigator assessed GERD symptoms. These symptoms were on a fourpoint severity scale: none, mild, moderate or severe. The number of days with symptoms of heartburn over the previous 7 days was also recorded. Patients were then randomized to receive esomeprazole 40 mg or pantoprazole 40 mg once daily for up to 8 weeks. Treatment compliance was determined by counting unused capsules at the end of the study. Patients taking 75–110% of prescribed doses were deemed to have been compliant with the dosing protocol.

At 4 weeks, patients underwent a further endoscopy and their GERD symptoms were assessed in the same way as at visit 1. Patients with unhealed EE and/or with moderate or severe heartburn or acid regurgitation in the prior 7 days, as assessed by investigators, continued treatment for a further 4 weeks, after which EE and GERD symptoms were re-assessed. From baseline to the 4-week visit, patients were instructed to record the severity of heartburn on daily diary cards. Heartburn was assessed using a four-graded scale: none, mild, moderate or severe. Adverse events were recorded on each control visit.

TABLE 1
BASELINE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE INTENT-TO-TREAT POPULATION (180 PATIENTS TO TREATMENT WITH EITHER ESOMEPRAZOLE 40 mg OR PANTOPRAZOLE 40 mg)

Characteristics	Esomeprazole 40 mg (N=90) n (%)	Pantoprazole 40 mg (N=130) n (%)
Gender – male	57 (63.3%)	59 (65.6%)
Age (years)		
< 65	77 (85.6%)	79 (87.8%)
X (SD)	51.2 (14.5)	49.4 (13.9)
LA grade oesophagitis		
A	37 (41.1%)	35 (38.9%)
B	40 (44.4%)	39 (43.3%)
C	13 (14.4%)	16 (17.8%)
Barrett s oesophagus,		
Absent	84 (93.3%)	85 (94.4%)
Present	6 (6.7%)	5 (5.6%)
Helicobacter pylori status		
negative	68 (75.6%)	70 (77.8%)
positive	22 (24.4%)	20 (22.2%)

Statistical analyses

The study was planned to include 180 patients calculated by assuming 8 week healing rates of 96% and 92% for esomeprazole and pantoprazole, respectively, using a two-sides chi-squared test with 5% significance level and a power of 95%. The assumptions about healing rates for esomeprazole and pantoprazole were based on data from previous studies[8–12]. Time to sustained resolution of heartburn symptoms (defined as a period of seven consecutive days without heartburn) based on patient daily diary cards, with differences analysed by log-rank test and the difference between treatment groups for the proportion of heartburn-free days analysed by analysis of variance (ANOVA).

No formal statistical analysis was planned on adverse event reports.

Results

In total, 180 patients were randomised to treatment with either esomeprazole 40 mg or pantoprazole 40 mg. 2 patients were excluded from the intent-to-treat (ITT) population because of intake of an unknown study drug, and a further 2 patients because of study protocol violations. The baseline demographic and clinical characteristics of the ITT population are shown in Table 1. There were no clinically relevant differences between the two treatment groups. Overall treatment compliance rates were similar for the two treatment groups (esomeprazole 40 mg: 87.6%, pantoprazole 40 mg: 88.2%).

Esomeprazole 40 mg provided significantly greater healing than pantoprazole 40 mg after 4 weeks of treatment in patients with all grades of EE severity at baseline (Table 2).

Esomeprazole-treated patients were healed after up to 8 weeks of treatment similar those treated with pantoprazole. Healing rates at 8 weeks, by LA grade at baseline, are provided in Table 3.

TABLE 2
HEALING RATES OF EROSIVE OESOPHAGITIS (EE) AFTER 4 WEEKS TREATMENT WITH EITHER ESOMEPRAZOLE 40 mg OR PANTOPRAZOLE 40 mg BY BASELINE LOS ANGELES (LA) GRADE SEVERITY (INTENT-TO-TREAT POPULATION). χ^2 TEST (ESOMEPRAZOLE VS. PANTOPRAZOLE)

LA grade	Esomeprazole 40 mg n (%)	Pantoprazole 40 mg n (%)
A	31 (83.8%)	29 (82.8%)
B*	31 (77.5%)	28 (71.8%)
C**	8 (61.5%)	8 (50.0%)
All patients*	70 (77.8%)	65 (72.2%)

*p<0.05, **p<0.01

TABLE 3
HEALING RATES FOLLOWING UP TO 8 WEEKS TREATMENT WITH ESOMEPRAZOLE 40 mg (N=130) OR PANTOPRAZOLE 40 mg (N=130) BY BASELINE LOS ANGELES (LA) GRADE OF EROSIVE OESOPHAGITIS (EE) SEVERITY. χ^2 TEST (ESOMEPRAZOLE VS. PANTOPRAZOLE)

LA grade	Esomeprazole 40 mg n (%)	Pantoprazole 40 mg n (%)
A	35 (94.6%)	33 (94.3%)
B	38 (95.0%)	37 (94.9%)
C	10 (76.9%)	12 (75.0%)
All patients	83 (92.2%)	82 (91.1%)

The proportion of heartburn-free days was similar in patients treated with esomeprazole 40 mg and to those treated with pantoprazole 40 mg (mean values – esomeprazole: 70.2%; pantoprazole: 69.8%). Time to sustained heartburn resolution (the first of seven consecutive days with no heartburn) was equally short for patients treated with esomeprazole 40 mg and with pantoprazole 40 mg (median days – 6).

Safety

A total of 12% patients in the esomeprazole group and 11% in the pantoprazole group had adverse events. The most commonly reported of these were, in esomeprazole group, nausea, dizziness and headache. In the pantoprazole group, headache, diarrhoea and nausea.

All these adverse events were considered mild or moderate in intensity and none were considered treatment--related.

Discussion

Comparative studies with PPIs are relatively few, but some have shown advantages, albeit small, for esomeprazole and pantoprazole. In a study comparing esomeprazole (20 mg and 40 mg daily) with omeprazole (20 mg daily), both esomeprazole doses proved significantly superior to omeprazole in terms of oesophagitis healing after 8 weeks[13]. In terms of daytime symptom resolution, esomeprazole 40 mg was superior to both esomeprazole 20 mg and omeprazole 20 mg. However, in terms of night-time heartburn symptom relief both doses of esomeprazole were significantly better than omeprazole. Compared with lansoprazole (30 mg daily), esomeprazole (40 mg daily) proved superior in terms of both healing of oesophagitis and night-time symptom resolution[14].

In another comparative study, pantoprazole (40 mg daily) was compared with omeprazole (40 mg daily) in terms of healing of oesophagitis and symptom relief. No significant differences were noted between the two treatment groups. No distinction was made between daytime and night-time heartburn[15]. Pantoprazole (40 mg daily) was compared with lansoprazole (30 mg daily) and omeprazole (20 mg daily) in the resolution of heartburn symptoms. Both omeprazole and pantoprazole were superior to lansoprazole in the relief of heartburn symptoms[16]. Using continuous intra-gastric pH-metry, it was demonstrated that equal doses of pantoprazole and omeprazole have similar potency to inhibit gastric acid secretion[17,18].

In a study pantoprazole (40 mg daily) and esomeprazole (40 mg daily) have an equivalent effect on intra-oesophageal pH after repeated intake. Both drugs were safe well tolerated[19]. Gillessen et al.[20] and Scholten et al.[21] have reported similar effectiveness for esomeprazole 40 mg and pantoprazole 40 mg, or even greater effectiveness for latter drug in terms of speed of symptom resolution. In these studies however »GERD-related symptoms» included gastric complaints, feeling of satiety and flatulence. As these symptoms are not generally accepted as specifically related to GERD, and the studies lacked statistical power to detect differences between treatments, the studies added little information of the two treatments in resolving classical GERD symptoms.

Crossover studies in healthy subjects and patients with symptoms of GERD have shown that esomeprazole is more effective than all other PPI for providing greater time with pH>4[22,23]. The results of large comparative study demonstrate a therapeutic advantage of esomeprazole 40 mg over pantoprazole 40 mg for healing of EE and providing resolution of associated heartburn[12]. This result may be predicted, as healing of EE is inversely related to gastric acidity[24], and esomeprazole has been shown to provide greater suppression of gastric acidity than standard doses of all other PPIs[22].

The results of this study demonstrate a therapeutic advantage of esomeprazole 40 mg over pantoprazole 40 mg for providing healing of EE after 4 weeks, but not after 8 weeks.

The proportion of heartburn-free days was similar in patients treated with esomeprazole 40 mg and to those treated with pantoprazole 40 mg (mean values – esomeprazole: 70.2%; pantoprazole: 69.8%). Time to sustained heartburn resolution (the first of seven consecutive days with no heartburn) was equally short for patients treated with esomeprazole 40 mg and with pantoprazole 40 mg (median days – 6).

Treatment with esomeprazole and pantoprazole was well tolerated. Similar rates of adverse events occurred in both treatment groups.

In conclusion, the present study demonstrated that esomeprazole 40 mg provides more effective healing of EE than pantoprazole 40 mg after 4 weeks of treatment. But, after 8 weeks of treatment esomeprazole and pantoprazole 40 mg daily are equally effective in the treatment of GERD.

Similar rates of adverse events occurred in both treatment groups. Both study drugs were well tolerated, safe and had high patient compliance.

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ESOMEPRAZOL NASUPROT PANTOPRAZOLU U CIJELJENJU EROZIVNOG EZOFAGITISA

SAŽETAK

Cilj ovog rada je bio komparirati učinkovitost esomeprazola i pantoprazola u cijeljenju erozivnog ezofagitisa (EE) i nestanku simptoma gastroezofagealne refluksne bolesti (GERB). U ovu multicentričnu, randomiziranu, jednostruko slijepu studiju je bilo uključeno 180 bolesnika s endoskopski dijagnosticiranim GERB-om i dobivali su esomeprazol 40 mg/dan (90 bolesnika) ili pantoprazol 40 mg/dan (90 bolesnika). Nakon 4. i 8. tjedna terapije kontrolirani su radi dokaza cijeljenja EE i nestanka simptoma GERB-a. Esomeprazol bio je statistički značajno učinkovitiji od pantoprazola u cijeljenju EE nakon 4 tjedna liječenja (77.8% nasuprot 72.2%). Nakon 8 tjedana liječenja učinkovitost im je bila podjednaka (92.2% nasuprot 91.1%). Postotak bolesnika bez simptoma GERB-a je bio podjednak nakon 4. i 8. tjedna liječenja u obje skupine.