A Randomized, Double Blinded, Clinical Trial to Assess the Efficacy and Cost Effectiveness of Omeprazole Compared to Rabeprazole in the Maintenance Therapy of Patients With Gastroesophageal Reflux Disease

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Background/Aims
The aim of this study was to evaluate the efficacy and cost efficiency of omeprazole 10 mg and rabeprazole 10 mg once daily for 24 weeks in the maintenance therapy.

Methods
This was a randomized, open-label study enrolling 279 patients with erosive esophagitis A or B (Los Angeles classification) and typical gastroesophageal reflux disease symptoms. Patients who showed complete endoscopic and symptomatic healing after 8 weeks of proton pump inhibitor treatment were randomly allocated to maintenance treatment with omeprazole 10 mg once daily or rabeprazole 10 mg once daily for 42 weeks. The primary efficacy endpoint was the proportion of patients with symptomatic remission at 42 weeks.

Results
At the end of 42 weeks of maintenance therapy, 96.4% of omeprazole and 95.1% of rabeprazole treated patients remained symptom free (P > 0.05). Two drugs were also comparable with regard to the severity and frequency of reflux symptoms during the maintenance phase (P > 0.05). By the cost-minimization analysis, the mean total costs per patient for remaining symptom-free for 6 months were 241,775 won for omeprazole and 287,115 won for rabeprazole, respectively.

Conclusions
Omeprazole 10 mg appeared to have similar efficacy in maintaining symptom remission as rabeprazole 10 mg, but was superior to rabeprazole 10 mg in terms of cost efficiency in the maintenance therapy of gastroesophageal reflux disease symptoms.


Key Words
Cost-benefit analysis; Gastroesophageal reflux; Maintenance

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Introduction

Gastroesophageal reflux disease (GERD) is a major public health problem in Korea. GERD affects approximately 3.4-3.8% of the Korean population and its incidence is on the increase. Generally, treatment of GERD begins with suppression of acid secretion by proton pump inhibitors (PPIs). PPI therapy relieved symptoms and healed the esophagitis in more than 80% of patients within 8 weeks of treatment, and it was better than placebo and histamine 2 receptor antagonist therapy as the treatment for esophagitis at 4-8 weeks. However, due to the recurring nature of GERD, most patients require additional long-term maintenance therapy.

Management options for the long-term management of GERD are either daily therapy or on-demand therapy of PPI. On-demand therapy is an adequate option for patients with non-erosive reflux disease (NERD) and uninvestigated GERD without alarm features. In contrast, continuous treatment is effective in the maintenance of healing in patients with esophagitis. And also, continuous treatment was preferred over on-demand therapy in patients with esophagitis, in the elderly and in patients with Barrett’s esophagus since on-demand treatment is less cost-saving in patients with esophagitis and symptomatic relapses occur frequently in severe grades.

Continuous PPI therapy for reflux esophagitis is associated with a large economic burden. Therefore, it is important to use the most cost effective PPIs at the adequate dose. Omeprazole is the oldest PPI approved for clinical use in the treatment and prevention of reflux esophagitis. Although new PPIs have been developed since, omeprazole 20 mg is still as effective as the new PPIs including rabeprazole 20 mg, lansoprazole 30 mg and pantoprazole 40 mg in the acute treatment of reflux esophagitis and prevention of the relapse of esophagitis.

In terms of half dose omeprazole, maintenance treatment with omeprazole 10 mg daily keeps about 60% of patients with erosive esophagitis free of relapse and half dose omeprazole was recommended in the prevention of relapse of esophagitis. However, little information is available about its effectiveness compared with other newer half dose PPI drugs in continuous PPI therapy for reflux esophagitis.

Therefore, in this study, we tried to determine the efficacy and cost effectiveness of maintenance therapy with omeprazole 10 mg compared with rabeprazole 10 mg in patients with reflux esophagitis who experienced symptom resolution after an 8 week course of continuous omeprazole therapy.

Materials and Methods

Patients

Subjects with typical GERD symptoms such as heartburn, regurgitation or epigastric pain for 2 days or more during the last 7 days were enrolled in the healing phase of the trial if they met the following eligibility criteria: were 18 to 75 years of age with a history of reflux symptoms for 6 months or longer, and had endoscopically proven erosive esophagitis (Grade A or B using Los Angeles [LA] classification of esophagitis). All participants either underwent esophagogastroduodenoscopy (EGD) at baseline, or had undergone EGD within 2 weeks prior to enrollment. Exclusion criteria were as follows: endoscopically proven Grade C or D esophagitis; presence of another organic lesion on endoscopy such as peptic ulcer or Barrett’s esophagus; past history of gastric or esophageal surgery; signs of gastrointestinal bleeding at the time of EGD; chronic alcoholism ( > 40 g alcohol/day); heavy smoking ( > 2 packs/day); pregnancy or lactation; presence of abnormal liver function test ( > 2× normal AST and ALT); known hypersensitivity to any component of omeprazole or rabeprazole; and concomitant diseases that might affect the results such as epilepsy or manic-depressive disorder. Patients were also excluded if they had received PPI or histamine 2 blocker therapy within 15 days before the screening date, or had received other medications that might affect the interpretation of the treatment outcome (quinidine, high dose corticosteroid, nonsteroidal anti-inflammatory, warfarin, anticholinergic, prostaglandin analogue or salicylate [except low dose aspirin]).

Study Design

This was a multi-center, randomized, double blinded, non-inferiority study consisting of a healing phase and a maintenance phase (Fig. 1). All patients received open-label oral omeprazole 20 mg once daily for 8 weeks. Repeat EGD was performed at the end of 8 weeks. This study was undertaken according to the principles of the Declaration of Helsinki and local ethics committee approval was obtained before the start of the study. Patients whose esophagitis was healed and were asymptomatic started maintenance treatment with omeprazole 10 mg q.d. or rabeprazole 10 mg q.d. for 24 weeks. 'Healing' was defined as no macroscopic mucosal breaks based on the LA classification, and 'asymptomatic' was defined as having complete resolution of reflux symptoms.