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ORIGINAL ARTICLE

Risk factors of incomplete response to proton pump inhibitor therapy in patients with mild erosive esophagitis

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KEYWORDS
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Summary *Background:* Incomplete symptom resolution to proton pump inhibitor (PPI) therapy is a common problem in the treatment of gastroesophageal reflux disease (GERD). The aims of this study were (1) to examine the rate of incomplete symptom response following 8-week PPI therapy in patients with mild erosive esophagitis (Los Angeles Grade A/B erosive esophagitis) and (2) to determine the independent factors predicting incomplete symptom response in patients with mild erosive esophagitis.
Methods: From January 2010 to July 2012, symptomatic GERD patients with endoscopic findings of Los Angeles Grade A or B erosive esophagitis were recruited for the study and received esomeprazole 40 mg daily for 8 weeks. The characteristics of eligible patients including clinical factors, endoscopic findings, *Helicobacter pylori* status, and *CYP2C19* (cytochrome P450 2C19) genotype

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were checked on enrollment. Patients were asked to record symptoms with diary cards during the follow-up period. The major outcome measurement was incomplete symptom response.
Results: In total, 232 patients (male/female, 126/106) participated in this study. Following 8-week esomeprazole therapy, 50 (21.6%) of the patients had incomplete symptom response. Univariate analysis showed that sex, alcohol consumption, underlying diseases, regurgitation of food, chest pain, globus, and insomnia were associated with incomplete symptom response ($p = 0.049$, $p = 0.006$, $p = 0.023$, $p = 0.010$, $p = 0.013$, $p = 0.009$, and $p < 0.001$, respectively). Multivariate analysis with stepwise logistic regression revealed that only globus [95% confidence interval (CI): 1.185–4.897; $p = 0.015$] and insomnia (95% CI: 1.289–3.018; $p = 0.002$) were independent risk factors for incomplete symptom response with odds ratio (OR) = 2.4 and OR = 2.0, respectively.
Conclusion: Of the patients with Los Angeles Grade A/B erosive esophagitis, 21.6% failed to have complete symptom resolution following 8-week PPI therapy. Globus and insomnia are two independent factors predicting incomplete symptom response in patients with mild erosive esophagitis.
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Introduction

Gastroesophageal reflux disease (GERD) is a common acid-peptic disorder characterized by recurrent troublesome reflux symptoms and esophageal injury. It is the strongest known risk factor for esophageal adenocarcinoma [1,2]. Many studies indicated that the prevalence of GERD is markedly higher in Western populations than in Asian populations [3–6]. However, the prevalence of GERD has increased in Asia in recent decades [7,8]. Our studies demonstrated that the recent prevalence of GERD in the general population and erosive esophagitis in patients undergoing health check-ups in Taiwan were 25% and 17%, respectively [7,8]. The reasons for the increasing prevalence of erosive esophagitis in Asia remain unclear, but are probably related to the changes in lifestyles, westernization of diet, lack of exercise, aging of population, and a decrease in *Helicobacter pylori* infection [9].

Currently, therapy for erosive esophagitis largely focuses on the pharmacological reduction of gastric acid secretion. Reducing the acidity of gastric juice ameliorates reflux symptoms and allows esophagitis to heal [10–12]. Nonetheless, incomplete symptom resolution to proton pump inhibitor (PPI) therapy is a common problem in the treatment of GERD and affects a significant proportion of patients who use a PPI once daily [13]. The putative mechanisms for poor symptom response to PPIs include poor compliance, improper timing of PPI consumption, reduced PPI bioavailability, non-acid reflux, visceral hypersensitivity, delayed gastric emptying, psychological comorbidity, and concomitant functional bowel disorders [13,14]. Recently, Cheong et al [15] showed that an abnormal Hill's gastroesophageal flap valve (GEFV) was a significant factor predicting poor response of GERD to PPI treatment. However, whether other factors including pretreatment symptom profiles, rapid PPI metabolism, obesity, metabolic syndrome, and *H. pylori* infection status play important roles in poor symptom response in GERD patients is unclear.

The aims of this study were (1) to examine the rate of incomplete symptoms response following 8-week PPI therapy in patients with mild erosive esophagitis (Los Angeles Grade A/B) and (2) to determine the independent factors predicting incomplete symptom response in patients with mild erosive esophagitis.

Methods

Patients

This study was a multicenter trial. From January 2010 to July 2012, patients between the ages of 15 years and 80 years with (1) clinical symptoms of acid regurgitation, heartburn, or feeling of acidity in the stomach and (2) endoscopic examination showing Los Angeles Grade A or B erosive esophagitis [16] were recruited for the study. Criteria for exclusion included (1) coexistence of peptic ulcer or gastrointestinal malignancies, (2) coexistence of serious concomitant illness (for example, decompensated liver cirrhosis and uremia), (3) previous gastric surgery, (4) allergy to esomeprazole (Nexium, Astrazeneca, 21F, No. 207, Dunhua South Road, Section 2, Taipei City), (5) symptom score of a validated questionnaire (Chinese GERDQ) < 12 [17], (6) pregnancy, (7) frequent (> 3 times/wk) use of hypnotics. Written informed consent was obtained from each patient.

Study design

On enrollment, patients were requested to complete a Chinese GERDQ [17]. In the scoring system, the GERD symptoms included acid regurgitation, heartburn, and feeling of acidity in the stomach. The severity and frequency of symptoms were graded on a 5-point Likert scale as follows: none (no symptoms/none in the past year); mild (symptoms can be ignored/$<$ once monthly); moderate (awareness of symptoms but tolerated easily/ $\geq$ once

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