Clinical Study

Comparison between Single-Dose Esomeprazole- and Pantoprazole-Based Triple Therapy on the Effectiveness for Helicobacter pylori Eradication in Taiwanese Population

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Background and Study Aims. To compare the effectiveness of two regimens, single-dose esomeprazole- and pantoprazole-based triple therapy, for Helicobacter pylori (H. pylori) eradication. Patients and Methods. A total of 453 patients were enrolled for H. pylori eradication. They were randomly assigned to either EAC group (Esomeprazole 40 mg once daily, Amoxicillin 1 g twice daily, Clarithromycin 500 mg twice daily for 7 days) or PAC group (Pantoprazole 40 mg twice daily, Amoxicillin 1 g twice daily, Clarithromycin 500 mg twice daily for 7 days). Follow-up endoscopy or urea breath test was scheduled 12–16 weeks after the eradication to evaluate the therapeutic response. Results. Higher eradication rate in EAC group than PAC group was shown by intention-to-treat analysis (EAC 72% versus PAC 55%, \( P < 0.05 \)) and per-protocol analysis (EAC 91% versus PAC 72%, \( P < 0.05 \)). The incidence of adverse effects (EAC 19% versus PAC 17%, \( P = 0.712 \)) and the compliance (EAC 87% versus PAC 91%, \( P = 0.083 \)) were comparable between these 2 groups. Conclusions. Single-dose esomeprazole-based triple therapy is effective for H. pylori eradication.

1. Introduction

Chronic Helicobacter pylori (H. pylori) infection is responsible for gastritis, peptic ulcer disease, gastric mucosa-associated lymphoid tissue lymphoma (MALT lymphoma) [1], and gastric adenocarcinoma [2]. Consequently, eradication of H. pylori is indicated for patients with peptic ulcer disease, low-grade gastric MALT lymphoma, atrophic gastritis. First-degree relatives of gastric cancer patients and some extraintestinal diseases, for example, unexplained iron deficiency anemia, and chronic idiopathic thrombocytopenic purpura may benefit from H. pylori eradication as well [2]. According to the Maastricht III Consensus Report, the recommended first-line treatment of H. pylori eradication is triple therapy with a proton pump inhibitor (PPI), clarithromycin, and amoxicillin or metronidazole given twice daily [2].

Proton pump inhibitor (PPI) is superior to H2 blocker for H. pylori eradication [3] because PPI is the most potent drug to inhibit gastric secretion to enhance the bioavailability of the antibiotics in the stomach [4]. PPI is metabolized via hepatic enzyme cytochrome P450 system,
especially S-mephenytoin 4’-hydroxylase (CYP 2C19) and CYP 3A4 [5]. Single-nucleotide polymorphism (SNP) of these enzymes may lead to variable plasma level of PPI and affect intragastric pH level as a result. Esomeprazole is the S-enantiomer of omeprazole. This single enantiomer is shown to be more efficacious than the racemic mixture of omeprazole. Although esomeprazole and its metabolites are indistinguishable from omeprazole, a single oral dose of 40 mg esomeprazole generally results in peak plasma esomeprazole concentrations of 0.5–1.0 mg/L within 1–4 hours [6]. Theoretically, esomeprazole (40 mg once daily) should be as effective and economic for H. pylori eradication as the regular bid dose of PPI, suggested by Maastricht III consensus. Although some studies showed the effectiveness of esomeprazole-based triple therapy for H. pylori eradication, they studied esomeprazole 40 mg twice daily [7, 8], instead of esomeprazole 40 mg once daily. Therefore, we conducted the study to evaluate the effectiveness of single-dose 40 mg once daily esomeprazole based triple therapy for H. pylori eradication.

2. Patients and Methods

2.1. Patients and Study Design. A total of 501 dyspeptic patients were included and 453 patients (192 men and 261 women, mean age 52.48 years old, 16–83 years old) were enrolled at the Outpatient Department of the Division of Gastroenterology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, from March 2005 to March 2009. Exclusion criteria were recent use of antibiotics, bismuth, or PPIs within the prior 4 weeks; history of gastric surgery; allergy to the study medication; serious comorbid illness (decompensated liver cirrhosis, renal failure); women who are pregnant and breastfeeding; previous H. pylori eradication therapy. All of them received esophagogastroduodenoscopy (EGD). In addition, all of the patients were interviewed by a trained interviewer for the personal and medical history obtained by a standardized questionnaire. Once the status of H. pylori infection was confirmed, participants were randomly assigned to two groups: EAC group (esomeprazole 40 mg once daily, amoxicillin 1 g twice daily, clarithromycin 500 mg twice daily for 7 days) or PAC group (panpoxprazole 40 mg twice daily, amoxicillin 1 g twice daily, clarithromycin 500 g twice daily for 7 days). Follow-up endoscopy or urea breath test was scheduled 12–16 weeks after the eradication to evaluate the therapeutic response and PPI was withheld 2 weeks beforehand. This study was approved by Institutional Review Board and Ethical committee of Kaohsiung Medical University Hospital and we obtained written informed consents from all the participants.

2.2. Questionnaire. The standardized questionnaire consisted of demographic data, underlying diseases, use of nonsteroidal anti-inflammatory drug (NSAID) and personal history about smoking and alcohol, coffee, or tea drinking. Smokers were defined as consumption of more than one pack of cigarettes per week. Drinkers were defined as consumption of more than one glass of alcoholic beverage per day. Compliance was defined as good (taking more than 70% of all administered medication) and poor [9]. The adverse events included diarrhea, constipation, abdominal pain, anorexia, nausea, vomiting, skin rash, headache, dizziness, taste perversion, and fatigue. The adverse events were further divided into positive adverse events defined as those who considered the adverse events disturbing the quality of daily life and negative ones defined as those who did not experience the events or did not consider them troublesome [9].

2.3. Diagnosis of H. pylori Infection. Culture, histology, rapid urease test, and 13C-urea breath test (UBT) were used in this study. Endoscopic biopsy specimens were rubbed on the surface of a Columbia blood agar plate for culture. Positive culture was considered if one or more colonies showed Gram negative, oxidase(+), catalase(+), urease(+), or spiral or curved rods in morphology. The presence of H. pylori in the pathology of gastric biopsy specimens was also evaluated by experienced pathologists. The result of rapid urease test (sensitivity 93–97%, specificity 98%) [10], CLO test (Delta West Bentley, WA, Australia), was interpreted as positive if the color turned to pink or red at room temperature 6 hours after the EGD examination. The 13C-urea breath test used in the study was manufactured by the Institute of Nuclear Energy Research, Taiwan. H. pylori infection was defined as positive either culture was positive or at least two positive results of rapid urease test, histology, or UBT [11].

2.4. Statistical Analysis. The primary outcomes were rates of eradication, adverse events, and compliance. The difference of the age of the patients was analyzed by Student’s t-test. The eradication rate, adverse effects and compliance between EAC and PAC groups were analyzed by Chi-square test. The patient disposition according to CONSORT statement was shown (Figure 1) [12].

3. Results

3.1. Demographic Characteristics. The demographic characteristics, including age, gender, smoking, alcohol consumption, ingestion of coffee or tea or both and no significant difference demonstrated, and endoscopic diagnosis of both groups (EAC group and PAC group) were analyzed (Table 1). No significant difference was found between the two groups except age and alcohol consumption (Table 1). The patient disposition according to CONSORT statement was shown (Figure 1) [12].

3.2. Eradication Rate. The eradication rate of H. pylori between the two groups was shown in Table 2. The eradication rate in the EAC group was significantly better than the PAC group in both the intention-to-treat (ITT) and the per-protocol (PP) analyses.

3.3. Adverse Events and Compliance. There was no difference regarding adverse effects during the treatment (EAC versus PAC, 19% versus 17%) (Table 2). In our study, adverse
events included abdominal symptoms (diarrhea, constipation, abdominal pain, nausea, vomiting), taste perversion, anorexia, dizziness, headache, fatigue, and skin rash. Of all the adverse events tasted perversion (EAC group 12 patients (15.4%); PAC group 29 patients (11.9%)) was the most common, followed by dizziness (EAC group 12 patients (5.8%); PAC group 11 patients (4.5%)). Fatigue (EAC 4.8%) and diarrhea (PAC 4.1%) also topped the list (Table 3). As for the compliance, 87% in the EAC group and 91% in the PAC group were noted. No significant difference was noted.

4. Discussion

Our study demonstrated higher eradication rate of *H. pylori* with single-dose esomeprazole based triple therapy (esomeprazole 40 mg once daily, amoxicillin 1 g twice daily, clarithromycin 500 mg twice daily for 7 days) than pantoprazole-based triple therapy (pantoprazole 40 mg twice daily, amoxicillin 1 g twice daily, clarithromycin 500 mg twice daily for 7 days). Similar prevalence of adverse events and compliance were observed between the two groups. Proton pump inhibitors (PPIs) are primarily metabolized via hepatic cytochrome P450(CYP)2C19 pathway. Genetic polymorphisms in CYP2C19 has been shown to have great influence on the metabolism of the PPIs. In our study, esomeprazole, s-isomer-omeprazole, is less influenced than pantoprazole.

Another issue which matters with the potency of PPI is to tackle the increasing antibiotic resistance. Increasing prevalence of resistant strain of *H. pylori* to clarithromycin was demonstrated in some studies. According to Vakil the prevalence of clarithromycin-resistant strain in the United States was 10–12% and wider range of 1–21% in the Europe. In Asia, a study from Hong Kong disclosed that
and alcohol consumption had positive effects, respectively, and the values of pantoprazole are 3.83.

The other explanation for the higher eradication rate in the EAC group was still as high as 91%. As mentioned above, PPIs are metabolized primarily via CYP2C19 pathway. According to the results of some studies from the United States, the eradication rate of H. pylori for first-line therapy (PPI + Amoxicillin + Clarithromycin) is decreasing in recent years from 75% (Laine, 1998) to 65% (Bochenek, 2003) [17]. As shown from our study the eradication rate in the EAC group was still as high as 91%. As mentioned above, PPIs are metabolized primarily via CYP2C19 pathway. According to the polymorphism of CYP2C19, individuals can be divided into extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is more frequent in Asian population (15–23%) than Caucasian population (2–5%) [24]. The therapeutic effect of PPI in terms of H. pylori eradication is better in PM individuals. This observation might explain the higher eradication rate in our study than studies from the United States. In addition, another major determinant for successful eradication is body mass index (BMI). According to Hsu et al. [9] the average body weight of the Asian is less than the Caucasian. Therefore, it is not surprising that higher eradication rate is found Asian populations, if the same dose of proton pump inhibitor and antibiotics are used.

In conclusion, our study show that single-dose esomeprazole in the morning and clopidogrel in the evening or at bedtime during H. pylori eradication for reducing the interaction. According to Hsu et al. esomeprazole doesn’t have negative effect on clopidogrel about platelet aggregation [27]. Single-dose esomeprazole-based triple therapy is a better option than pantoprazole for patients coprescribed clopidogrel.

In conclusion, our study show that single-dose esomeprazole-based first line triple therapy (esomeprazole 40 mg once daily, amoxicillin 1 g twice daily, clarithromycin 500 mg twice daily) is an effective regimen for H. pylori eradication in Taiwan.

Conflict of Interests

All authors have no conflict of interest to declare.

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