Once-daily Dose Dexlansoprazole-Levofloxacin-based Quadruple Therapy for Helicobacter pylori Eradication: A Randomized Controlled Study

Introduction

Helicobacter pylori (HP) infection affects 70–90% of the population in developing countries and 25–50% in developed countries and remains a significant cause of morbidity and mortality(1). It is a major cause of gastric diseases such as chronic gastritis, gastroduodenal ulcers, gastric adenocarcinoma, mucosal-associated lymphoid tissue lymphoma (MALT lymphoma) and other extragastric diseases. It is well known that the eradication of HP infection
is important in preventing and treating these gastric diseases (2, 3). Therefore, a safe and effective eradication regimen for this infection is imperative (4). Triple therapy (TT) regimens including proton pump inhibitors (PPIs), clarithromycin and amoxicillin has regarded as a first-line HP eradication regimen for a long time. However, eradication rate of TT has declined primarily due to increased bacterial resistance to clarithromycin. From this reason, several regimens have proposed as an alternative to eradicate HP infection (5). Levofloxacin-based quadruple therapy for HP eradication has shown to increase cure rate with minimal side effects and has used as a second line treatment for HP infection. Proton pump inhibitor (PPI) is one of the key drugs in anti-HP regimens. It has anti-H pylori activity by increasing bioavailability and activity of some antibiotics by reducing gastric acid secretion (6, 7). All PPIs have been used as twice-daily dosing for HP eradication. Dexlansoprazole is a new-generation proton pump inhibitor and exhibiting high efficacy in the treatment of symptoms and lesions associated with erosive esophagitis caused by gastroesophageal reflux disease (GERD)(8). It has dual release of the active drugs that resulting in two peak concentrations at various times, and has long acid suppression activity up to 24 hour. However, one of the study from Thailand showed the excellent eradication rate of dexlansoprazole-based quadruple therapy (more than 95%) (9). From its long duration of acid suppression activity by its dual delayed release formulation. This study was designed to test weater dexlansoprazole can be used as once-daily for HP eradication.

Materials and Methods

Patients and Study Design

A prospective, randomized, open-label, parallel design clinical trial, was conducted from January 2017 to September 2017 at Ramathibodi hospital, Bangkok, Thailand. Eligible patients aged 18-75 years who were diagnosed as HP positive by one of the following two methods: 1) a positive rapid urease test (CLO test).2) histologic evidence of HP by modified Giemsa staining were enrolled to the study. Exclusion criteria were 1) Patients with previous history of HP eradication therapy; 2) patients who has taken drugs that could influence the study results such as a PPI, H2 blocker, mucosal protective agent, or antibiotics within the prior 4 weeks; 3) patients with previous gastric surgery; 4) patients with active malignancies; 5) patients with decompensated liver cirrhosis; 6) patients who have abnormal renal function or chronic kidney disease; 8) patients with previous history of contraindications or allergic reactions to the study drugs; 9) patients with mental disorders or alcohol or drug addiction; 10) pregnancy or lactation or refusal to use an appropriate method of contraception throughout the course of the study; 11) patients with any conditions that might affect the evaluation of the clinical results in the judgment of the principal investigator or sub-investigator. The study protocol was approved by ethic committee of Faculty of Medicine Ramathibodi hospital, Mahidol university.

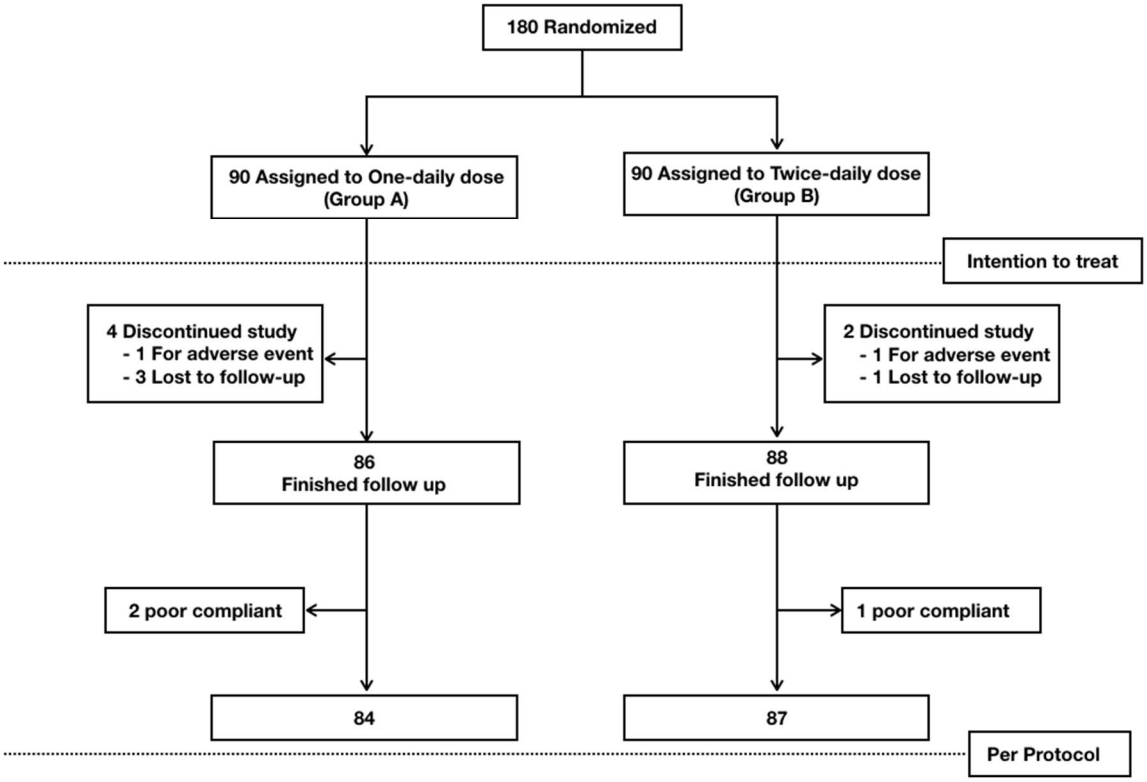

Fig. 1 Flowchart of participants

The diagnosis of HP infection

During the endoscopy, 4 biopsy samples, 2 from gastric antrum and 2 from gastric body were obtained for rapid urease test and histological examination. The presence of HP was defined as: positive tests (rapid urease test or histology). After obtaining informed consent, each enrolled patient was randomly assigned to receive Once-daily (60 mg od) or Twice-daily (60 mg bid) dose dexlansoprazole based on quadruple therapy (levofloxacin 500 mg once daily, amoxycilin 1000 mg twice daily, bismuth subsalicylate 1048 mg twice daily) for 14 days. A 13C urea breath test was performed to confirm HP eradication at least 6 weeks after treatment to evaluate the result. All the enrolled patients were tested for HP eradication rate in intention to treat (ITT) analysis. Patients who stopped taking the medication due to severe adverse effects, poor compliance, or loss to follow-up were excluded from the per protocol (PP) analysis.

Therapeutic regimens

Randomization was generated by reference to a computer-generated list. The subjects were randomized in a 1:1 ratio by a block of four randomization method to receive either Once (60 mg) or Twice (120 mg)-daily dose Dexlansoprazole based on quadruple therapy (levofloxacin 500 mg OD, Amoxycilin 1000 mg bid, bismuth subsalicylate 1048 mg bid).

Post-therapy follow-up

At least 6 weeks after completion of therapy, 13C-urea breath test (UBT) was test in all patients to assess HP eradication. Successful eradication was defined as a negative result from UBT. Pill count was used and drug consumption over 85% was defined as good compliance. Side effects were assessed by personal interview using open-ended questions. The potential adverse events listed in the questionnaires were diarrhea, taste distortions, nausea, vomiting, abdominal pain, dizziness and skin rashes. New symptoms and exacerbation of pre-existing symptoms during the treatment period were considered to be therapy-related adverse events. Serious adverse events were defined as events that disturbed on daily activities.

Sample size and Statistical analysis

The students's t-test, Pearson's chi-squared test and Fisher's exact test were used to determine the parametric difference and nonparametric proportions between the two study groups. Because the eradication rate of the quadruple therapy was found to be 96.0 % in a previous Thai report (9) the

eradication rate of the Once-daily dose dexlansoprazole based on quadruple therapy was assumed to be similar to that of the Twice-daily dose dexlansoprazole based on quadruple therapy if the rate difference between the two regimens was less than 15 %. All tests of significance were two-tailed with a p value less than 0.05