Effect of Single-Dose v.s. Divided-Dose Drug Administration on Eradication of Helicobacter pylori in Patients with Peptic Ulcers

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Introduction

Antibiotic therapy is commonly used to treat Helicobacter pylori (H. pylori) infection in patients with peptic ulcers. With antibiotic treatment alone,
the eradication rates for amoxicillin and clarithromycin are approximately 20% and 40%, respectively. Proton pump inhibitors (PPIs) markedly increase the efficacy of eradication therapy against *H. pylori*. When amoxicillin or clarithromycin therapy is complemented with PPIs, eradication rates are approximately 60% and 70%, respectively. PPIs have a direct antimicrobial effect that interferes with a number of *H. pylori*’s physiological mechanisms in vitro. In addition to proton pump inhibitors, H2 receptor antagonists that have no direct antimicrobial activity also enhance the eradication effect of antibiotics. The postantibiotic effect is now a well-established pharmacodynamic parameter manifest as an antibacterial effect that lasts longer than expected, given the active concentration at the infection site. The most significant factor is the specific combination of antimicrobial drugs, followed by the concentration and the duration of exposure to the drugs. Other factors that influence the postantibiotic effect are pH, hyperbaric oxygen, and temperature. The acidic environment of the stomach has a profound effect on antibiotic action. The intragastric pH is already known to be an important predictor of the success of *H. pylori* eradication. In a recent in vitro study, omeprazole, lansoprazole, and erythromycin demonstrated concentration-dependent eradication of *H. pylori*. However, it remains unclear whether high peak serum drug levels or prolonged exposure to antimicrobials given with PPI in patients with peptic ulcers results in the most effective eradication of *H. pylori*.

We designed the current study to determine whether there are any differential effects on *H. pylori* eradication when treatment is administered as one dose as opposed to a divided dose. The primary hypothesis tested in this study is that antibiotics and lansoprazole administered to peptic ulcer patients once per day cause a higher serum peak level, leading to a higher *H. pylori* eradication rate, than treatment administered as a divided dose, increasing the duration of exposure to antimicrobials. We have also studied whether there is a difference in the intragastric pH of patients in the single-dose group as compared to patients in the divided-dose group, and whether the intragastric pH affects the eradication rate of *H. pylori* in patients with peptic ulcers.

**Methods**

1. Study populations

Fifty-six patients previously diagnosed with peptic ulcers were enrolled into this randomized study according to two inclusion criteria: a history of endoscopically-confirmed peptic ulcer disease, and *H. pylori* infection confirmed by histological analysis and a rapid urease test. Patients were excluded from the study if they were over 70 years of age and if they exhibited any of the following: a history of ulcer surgery, coexisting pyloric stenosis, cirrhosis of the liver, renal failure, alcoholism, pregnancy, or lactation. Patients who had taken NSAIDs, proton pump inhibitors, bismuth salts, or antibiotic treatment during the two months prior to initiation of the study, or who showed a hypersensitivity to one of the study drugs, were also excluded from the study. All patients provided written informed consent. The protocol for the study was approved by the Institutional Review Board of Human Research at the Catholic University of Korea.

2. Study design

Before eradication treatment was initiated, and after four weeks of treatment, an upper gastrointestinal endoscopy was performed on each patient. *H. pylori* infection was confirmed with a rapid urease test (CLOtest™ Delta West, Australia) and histological assessment (Whartin Starry silver stain). The rapid urease test was performed on two biopsy specimens from each patient (one from the antrum,