Kaohsiung Journal of Medical Sciences (2016) 32, 255–260

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.kjms-online.com

ORIGINAL ARTICLE

Comparison of vonoprazan and proton pump inhibitors for eradication of *Helicobacter pylori*

Satoshi Shinozaki [a], Hiroaki Nomoto [b], Yoshie Kondo [b], Hirotsugu Sakamoto [c], Yoshikazu Hayashi [c], Hironori Yamamoto [c], Alan Kawarai Lefor [d], Hiroyuki Osawa [c,*]

[a] *Shinozaki Medical Clinic, Utsunomiya, Japan*
[b] *Department of Gastroenterology, Haga Red Cross Hospital, Moka, Japan*
[c] *Division of Gastroenterology, Department of Medicine, Jichi Medical University, Shimotsuke, Japan*
[d] *Department of Surgery, Jichi Medical University, Shimotsuke, Japan*

Received 11 January 2016; accepted 18 April 2016
Available online 21 May 2016

KEYWORDS
Antibiotics;
Gastric acid;
Helicobacter pylori;
Proton pump inhibitors;
Treatment outcome

Abstract Alternative eradication therapies for *Helicobacter pylori* infection are needed because of an increasing failure rate over the past decade. The aim of this study was to determine if vonoprazan, a new potassium-competitive acid blocker, showed superiority to existing proton pump inhibitors for primary eradication of *H. pylori* in routine clinical practice. Data for 573 patients who underwent primary *H. pylori* eradication therapy were retrospectively reviewed. Regimens included clarithromycin 200 mg, amoxicillin 750 mg, and an acid-suppressing drug [lansoprazole 30 mg (LAC), rabeprazole 10 mg (RAC), esomeprazole 20 mg (EAC), or vonoprazan 20 mg (VAC)] twice daily for 1 week. Eradication was successful in 73% (419/573) of patients using intention-to-treat (ITT) analysis and 76% (419/549) of patients in per-protocol (PP) analysis. The VAC group had a significantly superior eradication rate compared with the LAC and RAC groups in ITT (VAC 83%, LAC 66% and RAC 67%, $p < 0.01$) and PP analysis (VAC 85%, LAC 69% and RAC 70%, $p < 0.01$), and had a similarly high eradication rate to the EAC group (83% in ITT and 87% in PP). Although the eradication rate in the VAC and EAC groups was not significantly higher than in the LAC and RAC groups in patients with mild gastric atrophy with both ITT and PP analyses, it was significantly higher in patients with severe gastric atrophy ($p < 0.01$). The VAC group had a significantly higher *H. pylori* eradication rate

Conflicts of interest: Author S.S. has received honoraria from Takeda and Eisai Pharmaceuticals. Author Y.K. received honoraria from AstraZeneca Pharmaceuticals. Author H.S. received a research grant from Takeda. Author Y.H. has received honoraria from AstraZeneca, Eisai and Daiichi Sankyo Pharmaceuticals. Author H.Y. has received research grants and honoraria from Takeda, Otsuka, AstraZeneca, Eisai and Daiichi Sankyo Pharmaceuticals. Author H.O. received research grants and honoraria from Takeda, AstraZeneca and Daiichi Sankyo Pharmaceuticals. The funding source had no role in the design, practice or analysis of this study. Other authors have no conflicts of interest to report.

* Corresponding author. Division of Gastroenterology, Department of Medicine, Jichi Medical University, 3311-1 Yakushiji, Shimotsuke, Tochigi, 329-0498, Japan.
E-mail address: osawa@jichi.ac.jp (H. Osawa).

http://dx.doi.org/10.1016/j.kjms.2016.04.009

than the LAC and RAC groups, and a > 80% eradication rate regardless of the degree of atrophy.

Introduction

Curative therapy for *Helicobacter pylori* infection has become a major interest for gastroenterologists over the past 2 decades, because eradication of *H. pylori* decreases the incidence of future gastric cancer as well as gastroduodenal ulcers [1]. In Japan, standard triple therapy has been approved for the treatment of *H. pylori*-infected peptic ulcer by the national health insurance system since 2000, and consists of using a proton pump inhibitor (PPI) with amoxicillin and clarithromycin twice daily for 1 week. At that time, three kinds of PPIs including omeprazole, lansoprazole, and rabeprazole were available in Japan. In 2013, the Japanese health insurance system began reimbursement for primary *H. pylori* eradication therapy in patients with *H. pylori* gastritis diagnosed by esophagogastroduodenoscopy (EGD). Since that time, the number of patients receiving eradication therapy has been increasing.

However, the primary *H. pylori* eradication rate has been decreasing to an unacceptable level over the past decade [2,3]. The recent subsequent increase in bacterial resistance to clarithromycin in Japan led to a decline in successful eradication using first-line therapy [4]. Therefore, a novel strategy for primary *H. pylori* eradication has been sought. Esomeprazole (an S-isomer of omeprazole), a second generation PPI, suppresses gastric acid secretion more strongly, resulting in improved susceptibility to antibiotics by *H. pylori*. In 2011, this drug was released in Japan and made available for *H. pylori* eradication therapy. A meta-analysis showed the superiority of esomeprazole in the primary eradication of *H. pylori* compared with other PPIs [5]. In 2015, vonoprazan, a member of a new class of potassium-competitive acid blockers (P-CAB), was released and approved for use in *H. pylori* eradication in Japan. Although PPIs decrease gastric acid secretion by inhibiting H^+, K^+-ATPase in parietal cells, P-CABs do this by directly inhibiting H^+-K^+ exchange on the gastric luminal surface. Vonoprazan suppresses gastric acid secretion through this alternative mechanism [6].

Recently, the superiority of vonoprazan over lansoprazole for primary *H. pylori* eradication therapy was reported, with an eradication rate of 93% for vonoprazan and 76% with lansoprazole ($p < 0.01$) [7]. However, few reports are available regarding the rate of eradication employing both PPIs and P-CAB. The aim of this study was to determine if this new P-CAB shows superiority to existing PPIs for the primary eradication of *H. pylori* in routine clinical practice.

Patients and methods

Study population

We retrospectively reviewed the medical records of 573 patients who underwent standard primary *H. pylori* eradication therapy at Haga Red Cross Hospital (Moka, Japan) and Shinozaki Medical Clinic (Utsunomiya, Japan) between April 2013 and July 2015. Abstracted data include age, sex, *H. pylori* presence test used, prior PPI or vonoprazan use, type of PPI or vonoprazan used for eradication, EGD findings, and side effects. All patients underwent EGD because the Japanese national health insurance system requires the diagnosis of *H. pylori* gastritis by EGD prior to performing an *H. pylori* presence test. Positive *H. pylori* status was established by a rapid urease test, histology, stool antigen test, serology (serum IgG), or ^{13}C-urea breath test (UBT). The degree of atrophy was endoscopically evaluated based on the Kimura—Takemoto classification, in which closed and open types correspond to mild and severe atrophy, respectively [8]. The Institutional Review Board approved this study.

Primary H. pylori eradication

Standard triple therapy in Japan includes clarithromycin 200 mg, amoxicillin 750 mg, and an acid suppression drug [lansoprazole 30 mg (LAC), rabeprazole 10 mg (RAC), esomeprazole 20 mg (EAC), or vonoprazan 20 mg (VAC)] twice daily for 1 week. The choice of acid-suppressing drug was made by the physician in charge. Data regarding vonoprazan have been gathered since its release in Japan in February 2015. Based on previous favorable eradication data using vonoprazan [7], its use has predominated since early 2015. For the evaluation of successful eradication, a UBT or stool antigen test was used at least 8 weeks after the eradication period. The cut-off value for the UBT was 2.5‰. Before the UBT, PPI or vonoprazan intake was suspended for at least 2 weeks for a patient taking a PPI or vonoprazan. Successful primary *H. pylori* eradication therapy was determined by a negative UBT or stool antigen test. The stool antigen test was mostly used for patients who had undergone distal gastrectomy. The success rate of eradication was assessed by intention-to-treat (ITT) and per-protocol (PP) analyses. Exclusion criteria for PP analysis included: (1) patients who showed poor compliance (< 50%); and (2) patients who did not return to the clinic to receive a UBT or stool antigen test for evaluating the results of eradication therapy. All patients treated, but not included in the PP analysis, were considered to have failed eradication.

Statistical analysis

Statistical analysis was performed using BellCurve for Excel 2015 software (Social Survey Research Information Co., Ltd. Tokyo, Japan). Categorical data were assessed using Fisher's exact test. Differences in data with $p < 0.05$ are considered statistically significant.