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Original Article

Vonoprazan treatment improves gastrointestinal symptoms in patients with gastroesophageal reflux disease

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Outcome measure

Abstract The effects of vonoprazan, a new potassium-competitive acid blocker, on gastroesophageal reflux disease (GERD) symptom are not fully elucidated. The aim of this study is to determine the effect of vonoprazan on GERD and associated gastrointestinal symptoms. We retrospectively reviewed 88 *Helicobacter pylori* negative patients with GERD treated with vonoprazan 10 mg daily. Symptoms were evaluated using the Izumo scale, which reflects quality of life related to various abdominal symptoms. The rates of improvement and resolution of GERD symptoms were 86% (76/88) and 57% (50/88), respectively. Improvement and resolution in patients with erosive esophagitis was higher than in those with non-erosive reflux disease (91% vs 83%, $p = 0.260$ and 71% vs 47%, $p = 0.025$, respectively). We attempted to identify factors which predict the effects of vonoprazan. Multivariate analysis identified advanced age (≥60-year-old) (odds ratio [OR] 7.281, 95% confidence interval [CI] 2.056–25.776, $p = 0.002$), obesity (BMI ≥ 24) (OR 3.342, 95%CI 1.124–9.940, $p = 0.030$) and erosive esophagitis (OR 4.368, 95%CI 1.281–14.895, $p = 0.018$) as positive predictors of resolution of GERD symptoms. Alcohol use (OR 0.131, 95%CI 0.027–0.632, $p = 0.011$) and history of *H. pylori* eradication (OR 0.171, 95%CI 0.041–0.718, $p = 0.015$) were identified as negative predictors. Vonoprazan also improved epigastric pain (73%), postprandial distress (60%), constipation (58%) and diarrhea (52%) in patients with GERD. In conclusion, vonoprazan 10 mg daily is effective in improving GERD symptoms. Advanced age, obesity, erosive esophagitis, alcohol use and

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history of *H. pylori* eradication influence the resolution of GERD symptoms. Treatment with vonoprazan favorably affects gastrointestinal symptoms in patients with GERD.

Introduction

Gastroesophageal reflux disease (GERD) is a common disorder frequently diagnosed by community-based physicians, with an increasing incidence [1]. GERD is caused by reflux of acidic or non-acidic fluid from the stomach into the esophagus and/or pharynx. GERD includes erosive esophagitis (EE) and non-erosive reflux disease (NERD) diagnosed by esophagogastroduodenoscopy (EGD), but the severity of symptoms are not necessarily proportional to the degree of mucosal injury [2]. Recently, the beneficial effects of proton pump inhibitors (PPI) have been confirmed in patients with both EE and NERD [2,3], and patients with EE showed 20% greater improvement of GERD symptoms than patients with NERD [2,4].

Previous reports of the effect of acid suppression on patients with GERD included a sizable number of patients with *Helicobacter pylori* (*H. pylori*) infection [5–7]. Gastric acid secretion is higher in patients without *H. pylori* infection than in those with the infection [8]. Hiyama et al. reported that the absence of *H. pylori* infection is a risk factor for PPI-resistant NERD [9]. The number of people who are *H. pylori* negative is increasing in Japan, because the Japanese health insurance system began reimbursement for *H. pylori* eradication therapy in patients with *H. pylori* gastritis in 2013. Since successful *H. pylori* eradication therapy increases the incidence of reflux esophagitis by increasing acid secretion [10,11], the number of people with GERD will increase gradually as the number of people undergoing eradication increases.

Vonoprazan, a new potassium-competitive acid blocker, was released and approved for use in patients with GERD in Japan starting in February 2015. Unlike existing PPIs which inhibit H^+, K^+-ATPase in parietal cells, vonoprazan directly inhibits H^+—K^+ exchange on the gastric luminal surface. As a result, vonoprazan has greater acid inhibition via this alternative mechanism compared with existing PPIs [12]. We previously reported a high rate of success in primary *H. pylori* eradication therapy using vonoprazan 20 mg twice daily [13]. Administration of 20 mg once daily can also heal endoscopically more than 90% of EE in only two weeks [6]. Subsequently, a dose of 10 mg is used for patients with persistent GERD symptoms after a long period of clinical use, although it is unknown whether this dose is effective in patients with symptoms related to GERD, especially those with NERD and PPI-resistant GERD. Approximately 80% of patients with GERD symptoms also have other gastrointestinal (GI) symptoms [14]. Thus, it is important to clarify the effect of vonoprazan on other GI symptoms including epigastric pain, postprandial distress, constipation and diarrhea. The aim of this study is to determine the effect of vonoprazan on GERD and other GI symptoms in patients without *H. pylori* infection using the Izumo scale.

Patients and methods

Study population

One-hundred thirty-four patients with GERD were treated with vonoprazan 10 mg daily from January 2016 to March 2017 at Shinozaki Medical Clinic. All patients underwent EGD prior to starting vonoprazan. GI symptoms were evaluated using the Izumo scale which is useful to assess quality of life related to abdominal symptoms [15]. We reviewed the medical records and abstracted the following data: medical history, clinical findings, alcohol consumption, smoking habits, medications, endoscopic findings, *H. pylori* infection status and history of *H. pylori* eradication therapy. Izumo scale scores for patients that is routinely used in clinical practice were reviewed before and one month after starting vonoprazan treatment. Alcohol use was defined as more than 20 g per day. Smoking was defined as more than ten cigarettes per day. To avoid bias, patients who treated with PPI within four weeks before starting vonoprazan were excluded from this study. If acotiamide was used for the treatment of functional dyspepsia, vonoprazan was added to the acotiamide. Endoscopic findings of esophagitis were graded by the Los Angeles (LA) classification where grade A and above was considered as EE [16]. NERD was diagnosed when EGD did not show EE. Based on the Kimura-Takemoto classification, we endoscopically assessed the degree of gastric atrophy where closed and open types correspond to mild and severe atrophy, respectively [17]. No additional medications for the treatment of GI symptoms were added during the study period. The Institutional Review Board approved this retrospective review (No. 28-R001).

Of 134 patients treated with vonoprazan, 27 patients who treated with PPI within four weeks before starting vonoprazan, 15 patients who were not followed for one month, three patients with current *H. pylori* infection and one patient who underwent distal gastrectomy were excluded from the study. A total of 88 patients were included in the final cohort.

Symptom assessment and diagnosis of GERD

The severity of GI symptoms was scored using the Izumo scale, a validated and widely used questionnaire about quality of life related to various abdominal symptoms [14,15,18]. The Izumo scale has good internal consistency and correlation with the Gastrointestinal Symptom Rating Scale [14]. It has five domains: GERD, epigastric pain, postprandial distress, constipation and diarrhea. Each domain is scored with three items. There are 15 items, each scored 0 to 5 on a Likert scale according to the degree of symptoms as follows: 0 = not bothered, 1 = not so

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