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Original Article

Comparison of the effect of a single dose of omeprazole or lansoprazole on intragastric pH in Japanese participants: A two-way crossover study

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Abstract

Background: It is known that the pharmacokinetic profile of proton pump inhibitors (PPIs) after postprandial administration may differ among PPIs. The purpose of this study was to compare the inhibitory effects of gastric acid secretion by PPIs administered after a meal, based on a 24-hour intragastric pH monitoring.

Methods: Ten healthy men who provided written informed consent participated in the study. They were given a 20-mg omeprazole tablet and a 30-mg lansoprazole orally dispersing tablet in a two-way crossover manner. At baseline, the anti-HP-IgG antibody levels in blood and the pepsinogen (PG) I/II ratio were measured. Participants were given a standardized meal and 200 mL of water at 9:30 AM, 13:30 PM, and 18.30 PM. Participants took the PPI after breakfast.

Results: Two of the ten participants tested positive for *Helicobacter pylori* infection. The PG I/II ratio indicated negative gastric atrophy in all the participants. The percentage 24-hour intragastric pH $>$ 4 holding times (median, range) with omeprazole and lansoprazole were 29.3, 19.3−50.0% and 27.8, 13.0−42.3%, respectively, which shows that with the administration of omeprazole, the pH was maintained at $>$4 for a longer period ($p < 0.05$). Each median intragastric pH value per hour at 3, 17, and 18 hours after a dose of omeprazole was significantly higher than that of lansoprazole ($p < 0.05$).

Conclusion: Compared with lansoprazole, a single postprandial dose of omeprazole showed a more rapid and sustained acid-inhibitory effect.

Keywords: gastric pH; gastroesophageal reflux disease; nocturnal gastric acid breakthrough; on demand; proton pump inhibitor

1. Introduction

Proton pump inhibitors (PPIs) are potent inhibitors of gastric acid secretion, and are used as a first-line treatment in patients with gastroesophageal reflux disease (GERD) and other acid-related diseases. Because PPIs are activated in the presence of a high concentration of hydrogen ions, preprandial administration is recommended for PPIs in Western countries so that the peak blood concentration of the PPIs occurs when gastric acid is actively secreted by the parietal cells of the gastric mucosa after the meal.[1] In Japan, by contrast, a questionnaire survey on the timing of administering PPIs that included 127 gastroenterologists revealed following: 79% recommended postbreakfast, 13% recommended postevening meal, 3% recommended at bedtime, and 6% recommended prebreakfast.[2] Another report has described that many clinicians recommend postbreakfast administration of PPIs, and approximately 50% of patients with GERD do not take PPIs at an appropriate time of the day.[3] The inhibitory effect of PPIs on gastric acid secretion is known to correlate with the area under the blood concentration−time curve. Although the absorption of omeprazole is not affected when administered before or after a meal,[4,5] the absorption of lansoprazole is reduced when administered after a meal,[6,7] which indicates that the pharmacokinetic profile after postprandial administration may differ among PPIs.

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Therefore, we conducted a crossover study in which a single postprandial dose of 20-mg omeprazole or 30-mg lansoprazole (orally disintegrating tablet) was administered to determine their effects on intragastric pH by 24-hour intragastric pH monitoring.

2. Methods

2.1. Participants

Healthy Japanese men who volunteered to participate in this study were recruited between July 2010 and June 2011. Exclusion criteria included having upper gastrointestinal symptoms, a history of upper gastrointestinal surgery, history of gastrointestinal or hepatobiliary diseases, and use of medications known to influence gastric acid secretion.

This study was conducted in accordance with the Declaration of Helsinki and the Japanese Ethical Guidelines on Human Genome and Genetic Analyses, and was approved by the Ethics Committee of Aichi Medical University Hospital, Aichi, Japan. Written informed consent was obtained from all the participants before their participation.

2.2. Helicobacter pylori infection

The participants underwent blood tests to determine the status of their *Helicobacter pylori* infection (serum anti-*H. pylori* antibody) and the degree of gastric mucosal atrophy [pepsinogen (PG) I level, PG II level, and PG I/II ratio] (SRL, Inc., Tokyo, Japan). PG I/II ratio positively correlated with acid output.[8] Participants with a PG I/II ratio < 2.0 were considered to have positive gastric mucosal atrophy.

2.3. Twenty-four-hour intragastric pH monitoring

The participants were not allowed to eat from 21:00 PM the day before the test. Before each recording session, a glass electrode (Multi-use pH catheter, SYNECTICS MEDICAL, Stockholm, Sweden) was calibrated in buffer solutions at pH 1.07 and 7.01. At 9:00 AM, the pH electrode was inserted through the nose and the tip was fluoroscopically positioned in the upper portion of the gastric corpus (10 cm below the gastroesophageal junction) and connected to a portable digital recorder (Digitrapper pH400, Sierra Scientific Instruments, Los Angeles, CA, USA). At 9:30 AM, after the insertion of pH electrode, the participants were given a standardized meal for breakfast. From this time onward, measurement of the intragastric pH commenced that continued for 24 hours. The participants were provided standardized meals [total calories: 1102 kJ/d (proteins, 14.6 g; lipids, 16.9 g; and carbohydrates, 222.8 g)] and 200 mL of tap water at fixed times (lunch at 13:30 PM, dinner at 18:30 PM, breakfast at 9:30 AM). They also had to drink 200 mL of water at 15:00 PM and 22:00 PM. No restrictions were imposed in terms of daily activities. The pH values obtained were analyzed using the commercially available EsopHogram software program (Gastrosoft, Stockholm).

2.4. Study design and procedure

This was a prospective, open-label, two-way crossover study. Each participant received either 20-mg omeprazole (OMEPRAL; AstraZeneca, Osaka) or a 30-mg orally dispersing (OD) tablet of lansoprazole (TAKEPRON; Takeda Pharmaceutical Co., Tokyo). PPIs were given to the participant immediately after breakfast. The 20-mg omeprazole tablet was given with approximately 100 mL of water. The 30-mg OD tablet of lansoprazole was given after drinking approximately 100 mL of water. The drugs were given with an interval of at least 1 week to allow for the excretion of the previously administered PPI. Intragastric pH was monitored two times in each participant, that is, once with omeprazole and the other with lansoprazole. The inhibitory effect of gastric acid secretion was compared between the two drugs using the pH data recorded every 10 seconds, specifically regarding the percentage (%) of total time of pH > 4 (pH > 4 holding time) during the 24-hour period and the median intragastric pH per hour.

2.5. Statistical analysis

The percent of pH > 4 holding time during 24 hours and median intragastric pH per hour after dosing of each drug were compared by the Wilcoxon signed-rank test. Statistical analysis was performed using StatView 4.54 (Abacus Concepts, Berkeley, CA, USA). A p value <0.05 was considered to be statistically significant.

Table 1
Characteristics of the participants who took part in this study.

Participant	Age	Body mass index	*Helicobacter pylori*	Pepsinogen I	Pepsinogen II	Pepsinogen I/II ratio
1	34	23.6	–	49.2	8.5	5.8
2	44	20.2	–	71.8	8.1	8.9
3	36	22.5	–	31.7	9.2	3.4
4	31	22.4	–	39.6	6.1	6.5
5	25	20.4	–	37.1	6.8	5.5
6	25	21.5	+	74.5	29.9	2.5
7	22	23.3	–	23.7	4.9	4.8
8	20	22.5	–	42.3	9.2	4.6
9	21	20.6	–	54.4	8.4	6.5
10	32	21.8	+	80.1	36.4	2.2

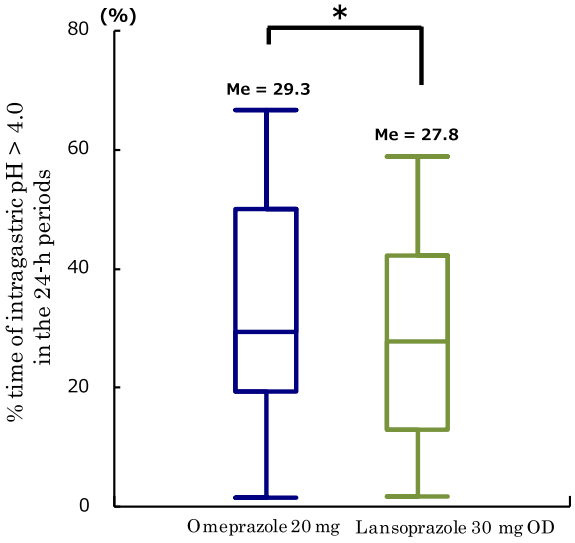

Fig. 1. Box–whisker plots of the percent of time that intragastric pH was above 4.0 during 24 hours after the administration of 20-mg omeprazole and 30-mg lansoprazole orally dispersing to healthy participants (*$p < 0.05$ by Wilcoxon signed-rank test between the two groups). In this box–whisker plot, the median values are indicated as the transverse line within the box, the interquartile range as the vertical extent of the box, and total range as the whiskers. Me = median.

3. Results

A total of 10 healthy volunteers aged between 20 and 44 years (mean: 29 years) with a body mass index of 20.2–23.6 kg/m^2 (mean: 21.9 kg/m^2) and having no history of eradication therapy participated in this study. *H. pylori* infection was detected in two of the ten participants. The PG I/II ratio was found to be negative in all the participants (Table 1). No adverse events occurred during the study, which was completed according to the protocol by all the participants.

The percentage of pH > 4 holding times after the administration of each PPI is shown in Fig. 1. After the administration, the percentage intragastric pH > 4 holding time [median and range (25–75%)] were 29.3 and 19.3–50.0% with omeprazole and 27.8 and 13.0–42.3% with lansoprazole, with the pH maintained significantly higher with omeprazole ($p < 0.05$).

The 24-hour intragastric pH (median pH per hour) profiles after the administration of each PPI are shown in Fig. 2. After the start of the intragastric pH measurement, administration of omeprazole showed a rapid increase in pH. Three hours after the start of pH measurement (i.e., at 12:30 PM), omeprazole showed a significant increase in pH, compared with lansoprazole ($p < 0.05$). Also at 17 and 18 hours after the start of pH measurement (i.e., 2:30 AM and 3:30 AM), a significantly higher pH was observed with the administration of omeprazole compared with lansoprazole ($p < 0.05$).

4. Discussion

In the treatment of GERD, rapid acid suppression is important to control unpleasant reflux symptoms quickly.[9,10] In contrast, patients with GERD tend to discontinue their medication once their symptoms are controlled. A 2000 Gallup survey showed that 45% of patients who were prescribed omeprazole or lansoprazole once daily took the PPI substantially less frequently.[11] In a study conducted in the United Kingdom, only 21% of 209 patients on long-term PPI therapy actually complied with the once-daily regimen. Therefore, there has been an increasingly recognized proclivity of many reflux patients to take their medications on demand.[12,13]

Oral administration of omeprazole led to a rapid increase in intragastric pH, with significantly increased pH compared with lansoprazole at 3 hours after the start of pH measurements, which indicates a rapid onset of the effectiveness even in the on-demand use. In addition, while some reports have described that nocturnal gastric acid breakthrough (NAB), which refers to transient decrease in intragastric pH during nighttime on PPI therapy in general and is typically observed

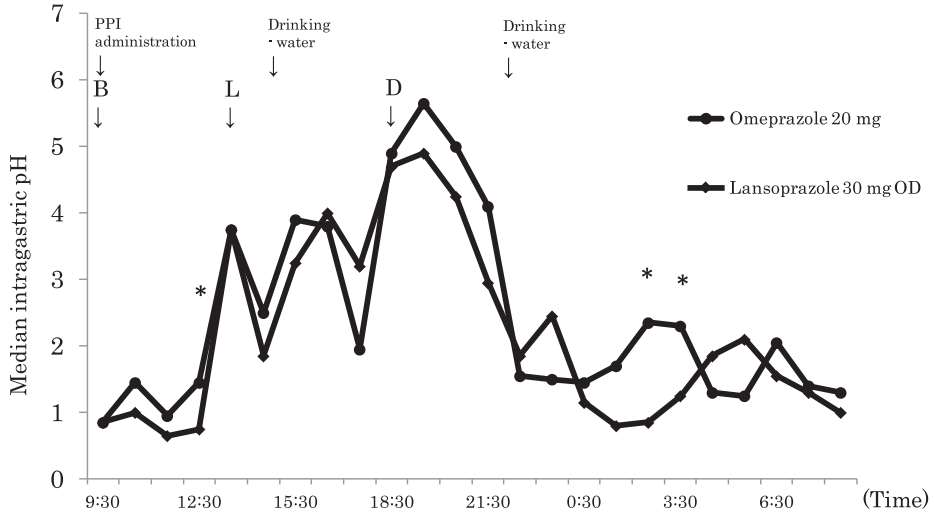

Fig. 2. Profiles of 24-hour intragastric pH (median pH per hour) in healthy participants who were administered 20-mg omeprazole and 30-mg lansoprazole orally dispersing (OD) after breakfast (*$p < 0.05$ by Wilcoxon signedl-rank test between the two groups). B = breakfast; D = dinner; L = lunch; PPI = proton pump inhibitor.

in *H. pylori*-negative patients,[14,15] plays a role in the onset of GERD.[16,17] This study has demonstrated significantly increased pH with omeprazole administration than with lansoprazole between 2:30 AM and 3:30 AM, thereby indicating the beneficial effect of the administration of omeprazole against NAB.

Based on the results from this study of single postprandial dosing of PPIs, the usefulness of omeprazole was demonstrated in terms of more rapid and sustained inhibition of gastric acid secretion and reduction of NAB. Omeprazole also appears to be suitable for patient-driven on-demand therapy that should improve patient satisfaction with the treatment.

5. Limitations of the study

One of limitations of this study was that there were no data on intragastric pH while taking these two kinds of PPIs before breakfast. Another limitation of the study was lack of information about *CYP2C19* genetic polymorphism. Although a previous report documented that there is no difference between omeprazole and lansoprazole in terms of pharmacokinetic variations depending on *CYP2C19* genetic polymorphism,[18] more detailed information of genetic polymorphism might more precisely show their influence on intragastric pH values. Therefore, the study result could not completely reflect the difference of intragastric pH control between a 20-mg omeprazole tablet and a 30-mg lansoprazole OD.

In conclusion, in this study, we used 24-hour intragastric pH monitoring to compare the pH in the stomach after a single postprandial dose of a 20-mg tablet of omeprazole and a 30-mg OD tablet of lansoprazole in a crossover manner. Postprandial administration of omeprazole, compared with lansoprazole, demonstrated more rapid and sustained inhibitory effect on intragastric acidity.

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