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Proton Pump Inhibitor Ameliorates Taste Disturbance among Patients with Laryngopharyngeal Reflux: A Randomized Controlled Study

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Patients with laryngopharyngeal reflux (LPR) were reported to suffer from hypogeusia that affects quality of life. Proton pump inhibitor (PPI) is a useful drug in the treatment of LPR, but its effect on hypogeusia is not known. We therefore assessed the effects of PPI or a histamine H2 receptor antagonist (H2 blocker) on hypogeusia among patients with LPR. Both PPI and H2 blocker could inhibit acid reflux. LPR was diagnosed with reflux finding score and reflux symptom index. The visual analogue scale (VAS) of taste disturbance symptoms and the gustatory tests were assessed before and 8 weeks after treatment with esomeprazole, a PPI (20 patients, aged 50.0 ± 1.7 years) or famotidine, a H2 blocker (20 patients, aged 47.1 ± 1.8 years). There were no significant differences in VAS scores and recognition thresholds for four basic tastes between the two groups before treatment. Only PPI therapy significantly decreased the VAS scores, suggesting the improvement of taste perception. Moreover, PPI therapy significantly decreased recognition thresholds for bitter taste in the anterior tongue (chorda tympani nerve area) and the thresholds in the posterior tongue (glossopharyngeal nerve area) for salty, sour, and bitter tastes. By contrast, H2-blocker therapy caused no significant changes of thresholds in the anterior tongue, but improved the threshold only for bitter in the posterior tongue, the value of which was however significantly higher than that in PPI group. In conclusion, PPI could ameliorate hypogeusia by improving bitter, salty, and sour tastes among patients with LPR.

Keywords: gastroesophageal reflux disease; gustation test; histamine H2 receptor antagonist; proton pump inhibitor; taste disturbance
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Introduction

Gastroesophageal reflux disease (GERD) is a common problem with classic esophageal symptoms such as heartburn and acid regurgitation. The number of reported extra-esophageal disorders associated with GERD is also increasing. For example, laryngopharyngeal reflux (LPR) is induced by acid reflux and is characterized by chronic hoarseness, sore throat, need of throat clearing, and chronic cough (Ylitalo et al. 2001). It has been shown that sour or bitter taste sensation is one of the symptoms caused by LPR and GERD (McConaghy and Oza 2013). If the gastric acid reaches the tongue, it causes a sour or bitter taste in the mouth. However, gustatory dysfunction caused by LPR and GERD was not well known. In 2017, Kabadi et al. (2017) documented the presence of taste disturbances among patients with GERD using a questionnaire; namely, 40% of patients with GERD and 52.2% of patients with both GERD and gastroparesis complained of taste changes. For those GERD patients who noticed taste changes, 20% reported sweet and bitter taste changes, 40% reported changes in saltiness, and 50% in sourness. Altundag et al. (2016) also showed taste disturbances among LPR patients as diagnosed with reflux finding score (RFS) and reflux symptom index (RSI). They performed gustation tests using four basic taste test strips assessing for sweetness, saltiness, sourness, and bitterness, and reported that bitter taste scores were significantly disturbed in a group of LPR patients when compared to a control group. It was also shown that no disturbances were found in sweet, salty, and

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sour taste scores.

It has been reported that proton pump inhibitor (PPI) could ameliorate symptoms, such as heartburn, belching, and hoarseness, caused by GERD and LPR (El-Serag et al. 2001; Noordzij et al. 2001; Tokashiki et al. 2002; DelGaudio and Waring 2003; Park et al. 2005; Shin et al. 2012). It was also shown that sour-taste sensation in the mouth that persisted for 10 years was decreased and disappeared after PPI therapy (Mantani et al. 2005). Additionally, histamine H2 receptor antagonist (H2 blocker) is useful for the control of symptoms caused by acid reflux (Wada et al. 2005). Both PPI and H2 blocker could inhibit acid reflux through reduction of intragastric acid (Miner et al. 2003; Rohss et al. 2004; Topaloglu et al. 2004; Bersenas et al. 2005; Shimatani et al. 2007; Tolbert et al. 2011). However, to the best of our knowledge, there have been no studies investigating the effects of PPI or a H2 blocker on taste cells and hypogeusia among patients with LPR. Therefore, in this study, we assessed the effects of PPI and a H2 blocker on taste disturbances associated with LPR.

Methods

Reflux symptom index (RSI) and reflux findings score (RFS)

All subjects were asked to complete the questionnaire of RSI, a classification of symptoms of LPR, proposed by Belafsky et al. (2002). It is a self-administered test for the assessment of 9 symptoms: 1. Hoarseness or a problem with your voice; 2. Clearing your throat; 3. Excess throat mucus or postnasal drip; 4. Difficulty swallowing food, liquids, or pills; 5. Coughing after you ate or after lying down; 6. Breathing difficulties or choking episodes; 7. Troublesome or annoying cough; 8. Sensation of something sticking in your throat or a lump in your throat; and 9. Heartburn, chest pain, indigestion, or stomach acid coming up. The score for each individual symptom ranges from 0 (no problem) to 5 (severe problem), and patients selected one of five scores. A maximum total score of RSI was 45. Translated (Japanese) version of the RSI was used in this study. RSI greater than 13 was considered to be abnormal, as previously reported (Belafsky et al. 2002; de Bortoli et al. 2012). An otolaryngologist, who is blinded to the RSI, also performed videolaryngoscopic examinations. RFS, eight item severity scale, was proposed by Belafsky et al. (2001), and RFS was calculated with videolaryngoscopic findings (Table 1). RFS greater than 7 was considered to be abnormal as previously reported (Belafsky et al. 2001; de Bortoli et al. 2012).

Subjects and study design

This is a randomized active-controlled study. Patients who visited the otorhinolaryngology department of the University Hospital with symptoms of LPR were asked whether they have taste disturbance or not. The inclusion criteria for the patients were as follows: existence of LPR symptoms, diagnosis of LPR with both of RSI and RFS, and existence of symptoms of taste dysfunction. Patients were recruited from 2015 to 2016. The exclusion criteria were a history of smoking; olfactory dysfunction; systemic diseases (e.g., diabetes and collagen diseases); cancer; surgery of the oral cavity, throat, larynx, esophagus, stomach, intestine, trachea, and lung; age under 20 or over 60 years; pregnancy; any disease of the oral cavity; any infection; radiation therapy to the head and neck; any drug that affect this study; any issue which affect this study; or refusal of consent. All patients received esomeprazole (20 mg) once a day, a PPI used in the treatment of acid-related diseases, or famotidine (20 mg) once a day, a histamine H2 receptor antagonist (H2 blocker), for 8 weeks. Health insurance and patients covered the expense of drug in this study. Although we could prescribe esomeprazole, omeprazole, lansoprazole, and rabeprazole as PPIs in our hospital, it has been reported that

Table 1. Eight items and severity scores of reflux finding score (RFS).

Reflux Finding		Score
Subglottic edema	absent	0
	present	2
Ventricular	partial	2
	complete	4
Erythema/hyperemia	arytenoids only	2
	diffuse	4
Vocal fold edema	mild	1
	moderate	2
	severe	3
	polypoid	4
Diffuse laryngeal edema	mild	1
	moderate	2
	severe	3
	obstructing	4
Posterior commissure hypertrophy	mild	1
	moderate	2
	severe	3
	obstructing	4
Granuloma/granulation tissue	absent	0
	present	2
Thick endolaryngeal mucus	absent	0
	present	2

esomeprazole provides more effective intragastric acid control compared with omeprazole, lansoprazole, or rabeprazole (Miner et al. 2003; Rohss et al. 2004). Thus, esomeprazole was selected in the present study. Likewise, famotidine was used as a H2 blocker, because famotidine was superior to ranitidine and cimetidine in inhibition of gastric acid secretion and treatment of GERD (Langtry et al. 1989; Wesdorp 1992; Bersenas et al. 2005; Ozer et al. 2012).

This study was approved by Nagoya City University Ethics Committee and was performed in accordance with the Declaration of Helsinki. We have obtained written informed consent from each participant.

Randomization

Eligible 40 participants were randomly assigned to one of the two groups (treatment with esomeprazole, a PPI or famotidine, a H2 blocker). Permuted block randomization in a 1:1 ratio (block size of 20) was employed for treatment allocation. The random sequence was generated using the Excel software at center. Only the staff at the center had access to the allocation sequence.

Visual analogue scale (VAS)

Symptoms of taste disturbance were assessed before and 8 weeks after therapy using a 10-cm visual VAS that ranged from "no disturbance" to "as bad as it could be."

Taste testing procedure

Gustatory function was evaluated using filter-paper discs (Sanwa Chemical Laboratory, Nagoya, Japan), a test commonly used in Japan (Tomita et al. 1986; Ogawa et al. 2017; Tsuji et al. 2018). The recognition thresholds for four basic tastes (sweet, salty, sour, and bitter) were assessed using sucrose, sodium chloride, tartaric acid, and quinine hydrochloride before and 8 weeks after treatment with a PPI or H2 blocker. There were 5 concentrations for each taste; '1' was the lowest concentration and '5' was the highest: (sucrose; 8.8, 74, 292, 584, and 2,336 mM), (sodium chloride; 51.4, 214, 856, 1,710, and 3,420 mM), (tartaric acid; 1.3, 13.3, 133, 266, and 532 mM), and (quinine hydrochloride; 0.025, 0.5, 2.5, 12.5, and 100 mM). The paper disc (5-mm diameter) for each taste was placed 2 cm lateral to the midline tongue (chorda tympani nerve area) or on the lateral borders of the circumvallate papilla (glossopharyngeal nerve area). The taste test was performed starting from the lowest concentration '1,' moving up to the highest concentration '5.' When the taste at the highest concentration '5' was not recognized, a score of 6 was assigned as previously reported (Ogawa et al. 2017; Tsuji et al. 2018). The lowest concentration at which patients correctly recognized the quality of taste was defined as recognition threshold as previously reported (Tomita et al. 1986; Ogawa et al. 2017; Tsuji et al. 2018). We measured both of right and left thresholds, and the mean of both thresholds was used as the outcome. The tester who performed taste testing was blinded to the treatment. Before introducing the next taste, the subject's mouth was rinsed with distilled water to avoid the effect of the previous taste.

Data analysis

Data are expressed as mean ± standard error of the mean (SEM). A statistical comparison of results between groups was performed using the chi-squared test for sex and Mann-Whitney test for age. Wilcoxon signed-rank test was used for comparison of results of VAS score, taste test, RSI, and RFS before and after treatment. Mann-Whitney test was also used for comparison of results of VAS score, taste test, RSI, and RFS between H2-blocker group and PPI group. A probability of $p < 0.05$ was considered an acceptable level of significance.

Results

Patients

Forty Japanese patients with LPR were included in this study. Twenty patients (9 women and 11 men; mean age 50.0 ± 1.7 years, range 26-59 years) received a PPI, while 20 patients (11 women and 9 men, mean age 47.1 ± 1.8 year, range 29-59 years) received a H2 blocker. There were no significant differences in age and sex between the two groups. Moreover, there were no significant differences in serum levels of zinc between PPI group (72.8 ± 1.2 μg/dL, range 67-87 μg/dL) and H2-blocker group (73.6 ± 1.3 μg/dL, range 66-88 μg/dL).

VAS score

The VAS scores of taste disturbance symptoms were recorded 4 and 8 weeks after therapy with a PPI or H2 blocker as well as before therapy (Table 2). The VAS scores at 4 and 8 weeks after PPI treatment were significantly lower than the VAS score before treatment (VAS score at 4 weeks after treatment $p < 0.05$, and VAS score at 8 weeks after treatment $p < 0.01$). The VAS score at 8 weeks after PPI treatment was also significantly lower than that at 4 weeks after treatment ($p < 0.01$). By contrast, H2-blocker treatment did not significantly change the VAS scores. Although there were no significant differences

Table 2. Visual analogue scale (VAS) of taste disturbance symptoms before and after treatment with H2 blocker or PPI.

	Before H2-blocker treatment	Four weeks after H2-blocker treatment	Eight weeks after H2-blocker treatment	Before PPI treatment	Four weeks after PPI treatment	Eight weeks after PPI treatment
VAS	7.28 ± 0.29	6.83 ± 0.20	6.59 ± 0.33	6.85 ± 0.42	6.28 ± 0.31♦	5.56 ± 0.30*♦♦¶¶

H2 blocker, histamine H2 receptor antagonist; PPI, proton pump inhibitor.
*$p < 0.05$ versus eight weeks after H2-blocker treatment.
♦$p < 0.05$ versus before PPI.
♦♦$p < 0.01$ versus before PPI.
¶¶$p < 0.01$ versus four weeks after PPI.

between H2-blocker group and PPI group before treatment, the VAS score 8 at weeks after PPI treatment was significantly lower than that at 8 weeks after H2-blocker treatment ($p < 0.05$).

Gustation tests in the chorda tympani nerve area

The gustation tests were performed for both groups before and 8 weeks after therapy. Table 3 shows the recognition thresholds for each taste in the anterior tongue (chorda tympani nerve area). There was no significant difference in the threshold of each of four tastes before treatment between H2-blocker and PPI groups. Moreover, there were no significant changes in the thresholds of the four basic tastes after H2-blocker treatment. By contrast, PPI treatment resulted in a significant decrease in the threshold for bitter taste ($p < 0.01$), whereas there were no significant changes in the thresholds for sweet, salty, or sour taste. Thus, the threshold of bitter taste after PPI treatment was significantly lower than that after H2-blocker treatment ($p < 0.05$).

Gustation tests in the glossopharyngeal nerve area

The recognition thresholds for each taste in the posterior tongue region (glossopharyngeal nerve area) are shown in Table 4. Before treatment, there was no significant difference noted in the threshold for each of the four tastes between the two groups. In H2-blocker group, the threshold only for bitter taste was significantly improved ($p < 0.01$), although sweet, salty, and sour tastes showed no significant changes. By contrast, the thresholds for salty, sour, and bitter were significantly decreased after PPI treatment ($p < 0.01$ for salty, $p < 0.001$ for sour and bitter), with no significant differences noted for sweet taste. Moreover, the thresholds for salty, sour, and bitter in PPI group were significantly lower than those in H2-blocker group ($p < 0.05$ for sour and bitter, $p < 0.001$ for salty). These results indicate that PPI therapy is more effective in improving the perception of salty, sour, and bitter, compared with H2 blocker.

RSI and RFS

All 40 subjects completed the questionnaire of RSI before and after treatment. Before treatment, there were no significant differences noted in RSI between patients received a H2 blocker and PPI. RSI score after treatment with a H2 blocker was significantly lower than that before treatment (Table 5, $p < 0.01$), and PPI treatment significantly decreased RSI ($p < 0.001$). Importantly, RSI in patients received a PPI were significantly lower than that in

Table 3. Recognition threshold in chorda tympani nerve area before and 8 weeks after treatment with H2 blocker or PPI.

	Before H2-blocker treatment	After H2-blocker treatment	Before PPI treatment	After PPI treatment
Sweet	3.40 ± 0.13	3.35 ± 0.18	3.35 ± 0.17	3.30 ± 0.18
Salty	3.10 ± 0.16	3.05 ± 0.23	3.15 ± 0.11	2.90 ± 0.22
Sour	3.15 ± 0.15	3.10 ± 0.16	3.10 ± 0.16	2.80 ± 0.16
Bitter	3.30 ± 0.16	3.25 ± 0.16	3.30 ± 0.15	2.75 ± 0.16*◆◆

H2 blocker, histamine H2 receptor antagonist; PPI, proton pump inhibitor.
*$p < 0.05$ versus after H2 blocker.
◆◆$p < 0.01$ versus before treatment.

Table 4. Recognition thresholds in glossopharyngeal nerve area before and 8 weeks after treatment with H2 blocker or PPI.

	Before H2-blocker treatment	After H2-blocker treatment	Before PPI treatment	After PPI treatment
Sweet	3.85 ± 0.17	3.65 ± 0.22	3.65 ± 0.13	3.45 ± 0.20
Salty	3.80 ± 0.19	3.80 ± 0.16	3.50 ± 0.14	3.00 ± 0.13***◆◆
Sour	3.70 ± 0.19	3.65 ± 0.21	3.70 ± 0.15	3.10 ± 0.14*◆◆◆
Bitter	4.20 ± 0.09	3.65 ± 0.11◆◆	4.05 ± 0.09	3.20 ± 0.17*◆◆◆

H2 blocker, histamine H2 receptor antagonist; PPI, proton pump inhibitor.
*$p < 0.05$ versus after H2 blocker.
***$p < 0.001$ versus after H2 blocker.
◆◆$p < 0.01$ versus before treatment.
◆◆◆$p < 0.001$ versus before treatment.

Table 5. Reflux symptom index (RSI) and reflux findings score (RFS) before and 8 weeks after treatment with H2 blocker or PPI.

	Before H2-blocker treatment	After H2-blocker treatment	Before PPI treatment	After PPI treatment
RSI	26.5 ± 1.7	21.9 ± 1.4$^{♦♦}$	23.6 ± 1.6	14.9 ± 1.5$^{**♦♦♦}$
RFS	14.0 ± 0.7	12.8 ± 0.6$^{♦}$	13.5 ± 0.8	9.2 ± 0.7$^{***♦♦}$

H2 blocker, histamine H2 receptor antagonist; PPI, proton pump inhibitor.
**p < 0.01 versus after H2 blocker.
***p < 0.001 versus after H2 blocker.
♦p < 0.05 versus before treatment.
♦♦p < 0.01 versus before treatment.
♦♦♦p < 0.001 versus before treatment.

patients received a H2 blocker ($p < 0.01$).

RFS was calculated with videolaryngoscopic findings before and after treatment. No significant differences of RFS before treatment were found between H2-blocker and PPI groups. After H2-blocker treatment, RFS was significantly decreased compared with the value before treatment (Table 5, $p < 0.05$). Likewise, RFS was significantly decreased after PPI treatment ($p < 0.01$). Importantly, RFS after treatment in PPI group was significantly lower than that in H2-blocker group ($p < 0.001$).

Discussion

It has been reported that PPI therapy can ameliorate various symptoms, such as heartburn, belching, chest pain, regurgitation, hoarseness, throat clearing, excess throat mucus, postnasal drip, difficulty swallowing, cough, breathing difficulties, and globus sensation (Noordzij et al. 2001; Tokashiki et al. 2002; Shin et al. 2012). However, the effects of PPIs on taste disturbances have not been reported. It is important to examine the effect of PPIs on taste function, because taste disturbances have negative effects on health and the quality of life of patients and should not be ignored.

In this study, PPI therapy decreased the VAS scores for taste disturbances, indicating that PPI therapy improves the subjective perception of taste. In addition, PPI therapy diminished taste disturbances in both the chorda tympani nerve area and the glossopharyngeal nerve area among patients with LPR. These results suggest that taste disturbances can be treated with PPIs. Thus, physicians should pay attention and consider PPI therapy for the control of taste disturbances among patients with LPR.

Altundag et al. (2016) showed that bitter taste was significantly damaged in Turkish patients with LPR, whereas sweet, salty, and sour tastes were not impaired. In the present study, we showed that the perception salty, sour, or bitter was improved after PPI therapy. Such a difference could be due to a variety of factors. We examined taste functions in the anterior tongue (chorda tympani nerve area) and posterior tongue (glossopharyngeal nerve area) separately, although Altundag et al. (2016) did not separately analyze the taste functions in these areas. In addition, Altundag's group included patients with no complaint of LPR (RFS < 11 and RSI < 13) as the control (Altundag et al. 2016).

DelGaudio and Waring (2003) showed that only eight out of 30 (27%) patients showed improvement in their GERD symptom scores 4 weeks after PPI treatment, while 19 out of 30 (63%) patients showed significant improvement 8 weeks after PPI treatment, indicating that prolonged use of PPIs resulted in improved symptom scores. In the present study, we therefore compared the taste symptoms and functions before and 8 weeks after treatment to assess the effect of therapy on taste disturbances. However, taste tests were not performed 4 weeks after treatment due to the financial reason; namely, the expenses of tests were covered by patients and health insurance.

In this study, sweet taste was not improved 8 weeks after treatment with a PPI or H2 blocker. However, there is a possibility that sweet taste is improved more than 8 weeks after therapy with a PPI or H2 blocker. Further studies are necessary to solve this question.

Taste disturbances in patients with GERD and LPR have recently been reported (Altundag et al. 2016; Kabadi et al. 2017); yet, the mechanism of taste disturbances caused by GERD and LPR is unknown. However, one possible explanation is the injury of the tongue caused by gastric acid and pepsin. Gastric juice and pepsin can cause injury to the esophagus (Bardhan et al. 2012). Southwood et al. (2015) showed that pepsin could be detected in the sinus lavages of patients with chronic rhinosinusitis, and that pepsin induced mitochondrial damage of human nasal epithelial cells in vitro. Rats exposed to pepsin/HCl had a dysfunction in their eustachian tubes (Heavner et al. 2001). Bulmer et al. (2010) reported that laryngeal mucosa was damaged at pH 2.0 with pepsin. Adams et al. (2000) documented that acid and acid/pepsin mixtures promote carcinogenesis in the cheek pouch of hamsters. Microscopic studies by Ohrui et al. (1997) revealed that separation of the

intercellular space and cell detachment from culture vessels occurred after exposure to gastric juices. It has been considered that gastric juices and pepsin are refluxed up to the oral cavity, as pepsin has been detected in the saliva of patients with GERD (Birtic et al. 2012; Saritas Yuksel et al. 2012; Na et al. 2016). Pepsin is most active around pH 2, and its activity is declined as acidity is reduced (−45% at pH 4.5, −40% at pH 5.0, fell to −10% at pH 6.0) (Bardhan et al. 2012). Campos and Sancho (2003) reported that pepsin has a native-like conformation at the pH 4.0-6.5, although it is catalytically inactive. Pepsin stored at pH 7.0 was inactive but stable, and −80% of its activity was recovered when it was returned at pH 3.0 (Bardhan et al. 2012). Taking these into consideration, PPI therapy may improve taste disturbances by reducing the pH of the refluxate.

DelGaudio and Waring (2003) showed that 13 out of 17 (76%) responders had worsening GERD symptoms within 1 month after PPI therapy was stopped. Considering this, taste disturbances may relapse after suspension of PPI therapy, even if taste disturbances improved during therapy.

There is a possibility that esomeprazole induces side effects such as dermatitis, headache, and diarrhea (Shukla et al. 2010; Pipaliya et al. 2016). To our knowledge, there have been no papers which show the effect of esomeprazole on taste receptor cells and side effects of taste disturbance and dry mouth caused by esomeprazole. However, Teare et al. (1995) showed that omeprazole reduced salivary flow in some patients. Markitziu and Aframian (1996) also showed a case in which dysgeusia and reduction of salivary flow were seen after omeprazole therapy. Considering these, there is a possibility that esomeprazole induces side effect of dry mouth and taste disturbance, since esomeprazole is the S-isomer of omeprazole.

We could not compare PPI with placebo in this study, because we had no financial support. Health insurance and patients covered the expense of drug in this study, and we needed active control which satisfies subjects included in this study. Additionally, H2 blocker can inhibit intragastric acid. We therefore selected a H2 blocker as a control.

It has been reported that omeprazole provides superior gastric acid suppression to famotidine (Topaloglu et al. 2004; Tolbert et al. 2011). Esomeprazole also provides more effective intragastric acid control than omeprazole (Miner et al. 2003; Rohss et al. 2004). Thus, esomeprazole is superior to famotidine in inhibition of gastric acid. Moreover, Ng et al. (2012) reported that esomeprazole is superior to famotidine in preventing upper gastrointestinal complications. This study showed that esomeprazole had stronger ability than famotidine to ameliorate hypogeusia. Although the mechanism is unclear, one possibility is that esomeprazole has superior potency than famotidine in inhibition of gastric acid secretion and GERD.

In this study, we have shown that treatment with a H2 blocker can improve RSI and RFS. In this context, famotidine has suppressive effects on intragastric acidity (Bersenas et al. 2005; Shimatani et al. 2007). Famotidine also had the best short-term therapeutic effect among adults with GERD, compared with other H2 blockers: ranitidine, cimetidine, and nizatidine (Zhao et al. 2016). In addition, RSI and RFS after PPI treatment was significantly lower than those after H2-blocker treatment, suggesting that PPI is superior to a H2 blocker in improving RSI and RFS.

H2-blocker therapy significantly improved bitter taste in posterior tongue. However, three tastes of salty, sour, and bitter in posterior tongue after PPI treatment were significantly better than those after H2-blocker treatment. There was also significant difference of bitter taste in the anterior tongue between H2-blocker group and PPI group after treatment. These suggest that PPI is superior to H2 blocker in the improvement of taste disturbance.

To the best of our knowledge, this is the first study to show that PPI has the ability to ameliorate hypogeusia among patients with LPR. The treatment with a PPI improved perception of bitter taste in the anterior tongue (chorda tympani nerve area) and also salty, sour, and bitter tastes in the posterior tongue (glossopharyngeal nerve area) among patients with LPR. It is conceivable that the reduction in acid secretion caused by PPI is responsible for the improvement of taste disturbance.

Conflict of Interest

The authors declare no conflict of interest.

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