Original Article

A Prospective, Randomized, Placebo-controlled, Double-Blind Study of Rabeprazole for Therapeutic Trial in Chronic Idiopathic Laryngitis

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ABSTRACT

Background: Gastroesophageal reflux disease and laryngitis are common diseases in Thai population. Since now, we found that acid reflux was one of the most common causes of laryngitis. The term laryngophayngeal reflux (LPR) is used to describe esophageal acid reflux into laryngeal and pharyngeal areas. Twenty-four-hour pH monitoring seems to be the best modality to establish LPR, although some caution should be concerned in the interpretation of these results. Treatment of patient with suspected "reflux laryngitis" with antireflux medications has been shown to be effective. Although limited double-blind, controlled study recently showed equivocal result in improvement among patients treated with PPIs versus placebo.

Patients and Methods: This is a prospective, randomized, placebo-controlled, double-blind study to evaluate effect of rabeprazole for therapeutic trial in chronic idiopathic laryngitis. Symptoms and laryngeal finding were assessed prior to and 12 weeks after randomization to rabeprazole or placebo group.

Results: Thirty patients had qualified for the study. In all cases, ambulatory, 24-hour, double probe pH monitoring and video laryngoscopy were done. All enrolled patients completed the study. There were 4 males and 11 females in both rabeprazole group and placebo group. The most common symptoms were globus sensation (86.7%), excess throat mucous (80%), heartburn or regurgitation (70%). The mean reflux symptom index (RSI) at the initial pretreatment visit was 11.4 and the mean RSI at the completion of the 12-week treatment period was 5.3. The mean RSI difference between pre and post treatment was 6.1 ± 3.7. When determined clinical response, the improvement of symptom score more than 60% from pretreatment, there was no statistically significance between rabeprazole and placebo group. ($p = 0.143$) In subgroup of positive pH monitoring, RSI significantly decreased in rabeprazole group when compare to placebo. While in pH negative subgroup, rabeprazole improved symptom score without statistically significances when compared with placebo. ($p > 0.05$) In general, symptom scores improved over time for patients in both groups. There were no statistical differences between rabeprazole and placebo groups for symptoms improvement at 4 and 8 weeks therapy. All patients underwent video laryngoscopy at pretreatment period. Only 22 had undergone video laryngoscopy at the end of treatment. There was no differences in pretreatment and % improvement of RFS at the end of study between rabeprazole (7.4 ± 2.8) and placebo group. (7.6 ± 2.6) ($p = 0.84$) In subgroup of previous medication used, rabeprazole can improve RSI symptoms 81.78%. There was no adverse reaction demonstrated in both groups.

Conclusions: Rabeprazole improves clinical symptoms and laryngeal signs in LPR patients with positive 24-hour pH monitoring results. 24-hour pH monitoring is helpful in identification of patients likely to response to antireflux therapy.

Key words : Rebeprazole, chronic, laryngitis

[Thai J Gastroenterol 2005; 6(1): 28-36]

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BACKGROUND

Gastroesophageal reflux disease (GERD) is believed to be associated with a variety of laryngeal conditions and symptoms, of which reflux laryngitis is perhaps the most common. Initial presentation may be the symptoms of hoarseness, globus sensation, sore throat, chronic throat clearing, excessive throat secretion and chronic cough.

The term laryngophayngeal reflux (LPR) is used to describe esophageal acid reflux into laryngeal and pharyngeal areas. Although the actual prevalence of ENT-associated disorders related to GERD is still unknown, it is estimated that 4-10% of patients presenting to an otolaryngology office have symptoms and findings associated with GERD[1]. Laryngeal signs of arytenoids redness or edema are highly suggestive of reflux laryngitis. However, some argue that no laryngeal signs need to be present to make the diagnosis of reflux laryngitis. Since now, the most effective method to diagnose LPR is not clear. Dual-channel pH monitoring is presently the most accepted method to document reflux laryngitis. Similar to empiric treatment of patients with reflux laryngitis that has been shown to be effective.

There are two schools of thought concerning how gastric acid causes laryngeal pathology. The first implicates a direct acid-peptic injury to the larynx and surrounding tissue via esophago-pharyngeal reflux[2-7]. To implicate acid induced laryngeal damage, the gastric content must reflux proximally from the distal and proximal esophagus and through the upper esophageal sphincter (EUS) into the laryngeal area. Based on canine and rabbit models in which acid and pepsin is applied to laryngeal mucosa, only minute amounts of acid exposure can cause significant laryngeal injury. Because laryngeal mucosa is not continually coated by saliva, the gastric content cannot be neutralized or washed out. Also, because the laryngeal mucosa is not normally exposed to acid and pepsin, intrinsic cellular mechanisms to protect against chemical injury may not be present. The second hypothesis suggests that acid in the distal esophagus stimulates vagally mediated reflexes resulting in chronic throat clearing and coughing, which eventually leads to laryngeal lesions and symptoms[8-11]. A combination of these mechanisms could perhaps be present in the same patient.

Given that reflux laryngitis probably results from direct exposure of the larynx and hypopharynx to acid and pepsin, some authors have studied pharyngeal acid reflux. LPR has been well documented to occur in those with suspected reflux laryngitis[12-14], however, LPR also occurs in normal healthy controls with a prevalence of 16-21%[12].

Several previous studies, have documented a low prevalence of heartburn and endoscopic esophagitis in reflux laryngitis patients[14-18]. The explanation of this findings is still unclear. The prevalence of abnormal acid reflux by 24-hour pH monitoring in patients with suspected reflux laryngitis ranges from 17.5% to 70%[13-14,18-20]. This variability probably associated with patient heterogeneity and to methodology concerning whether the pH probe is placed in the hypopharynx, distal or proximal esophagus.

Pharyngeal pH monitoring seems to be the best modality to establish LPR, although some caution should be concerned in the interpretation of these results. For example, hypopharyngeal reflux has been documented in normal healthy controls. Some authors postulate that the presence of the probe in the posterior pharynx may actually precipitate acid reflux secondary to irritation, resulting in false-positive results[21]. Likewise, some kinds of foods, such as citric acid-containing beverages and carbonated soft drink, are associated with false-positive results. During pharyngeal pH monitoring, loss of mucosa contact between the pH probe and the cavernous posterior pharynx may occur, with subsequent abnormal pH recording resulting in "pseudoreflux". The pathophysiology of the pH pattern is most likely an artifact resulting from the probe either drying up or moving away from the pharyngeal mucosa. Along with the fact that LPR and gastroesophageal reflux are intermittent phenomena, reliance on the results of pharyngeal probe monitoring has the potential to decrease the diagnostic yield when evaluating patients with suspected reflux laryngitis[22-30].

Treatment of patient with suspected "reflux laryngitis" with antireflux medications has been shown to be effective. Although limited double-blind, controlled study recently showed equivocal result in improvement among patients treated with PPIs versus placebo. Most studies are not comparable because of differences in patient selection, research methodology, and outcome parameters studied, as well as in pharmacological agents and regimen used[14,16,24-29].

There is only few data about LPR or extraesophageal reflux in Thai patients. In which Thai culture

always uses citrus fruit or spicy ingredients for cooking. So, we had initiated this research to identify this group of Thai patients.

PATIENTS AND METHODS

Patients were recruited through the Gastroenterology and Otolaryngology departments at King Chulalongkorn Memorial hospital. Patients were required to have one or more of the following symptoms for at least three months: hoarseness, throat pain, throat clearing, globus sensation or dry throat and ENT examination consistent with reflux laryngitis. Patients were excluded if they had viral or bacterial laryngitis, laryngeal carcinoma, or a strong history of seasonal allergies.

Patients completed a questionnaire, which asked for daily symptom severity and frequency and underwent dual probes 24-hour pH monitoring and video laryngoscopy with the data was recorded and evaluated at the end of the study.

All patients were randomly assigned to the treatment group or the control group. The treatment group was given 40 mg rabeprazole (Eisai) twice a day for 3 months. The control group received a placebo pill (twice daily for 3 months) which looks identical to the rabeprazole capsule. All patients were instructed not to make behavioral modifications known to improve or worsen gastroesophageal reflux, thereby controlling for this variable. Patients were called every two weeks to ensure that none were developing significant worse laryngitis or esophagitis.

All patients were seen at 1, 2 and 3 month to repeat the symptoms questionnaire and video laryngoscopy. At the completion of the study, patients were asked for the global symptom improvement.

pH Monitoring

Acid suppression therapy was stopped at least 7 days prior to initial testing. A 24-hour dual-channel pH probe was then placed. All pH probes had an 15-cm spacing between the two pH sensors. Esophageal manometry was done to confirm that the lower sensor was located 5 cm above the lower esophageal sphincter. Data (symptoms and pH values) were analyzed by a software program that reported events and calculated acid exposure times. A drop in the pH of the upper esophageal sensor was considered a pharyngeal reflux episode if it went below pH 4. These criteria are based on normative data previously published[25,50]. All tracings were individually reviewed, rather than relying on the computer interpretation, to determine pharyngeal acid reflux episodes.

Symptom Scores

Symptom scores were recorded by visual analog scale and transformed into 0-5 scores for evaluate reflux symptom index (RSI). Severity was indicated by the subject on a vertical, nongraduated line. These verity mark placed by the patient was measured and given a value between 0 and 5.

A composite laryngeal symptom score was calculated by adding the scores of the following nine symptoms: hoarseness, postprandial or annoying cough, excessive throat mucous and clearing of throat, sensations of something sticking in throat or a clearing of throat, difficulty swallowing, heartburn, chest pain, indigestion or stomach acid coming up and breathing difficulties or choking episodes. This composite score is meant to enhance the power of the data and has been used by others.

Laryngoscopy

Video Laryngoscopy were performed with a flexible endoscopy and topical anesthetic by one of two laryngologists. The description of the findings was categorized for the purpose of this report into Reflux Finding Scores (RFS). Video laryngoscopy recordings from the four sessions of each patient (initially, 1 month, 2 month and 3 month) were reevaluated by two experienced laryngologists to determine RFS.

Statistical Analysis

After a treatment period of 12 weeks, the RSI was readministered. All data were coded and recorded into Statistical Program for Social Sciences (SPSS) 11.5. The chi-square test and independent t-test were utilized to evaluate statistical differences between categorical and continuous data, respectively. Significance was accepted at $p < 0.05$.

RESULTS

Thirty patients had qualified for the study. In all cases, ambulatory, 24-hour, double probe pH monitoring and video laryngoscopy were done. All enrolled patients completed the study. There was no adverse reaction to rabeprazole. There were 4 males and 11

females in both rabeprazole group and placebo group. The mean age between the two groups was not significantly different. (Table 1)

The most common chief complaint was globus sensation (66.7%). One patient in each group smoked or had history of frequent alcohol drinking. There was no patient with history of asthma or allergic reaction was included. The mean quality of life effect was 48%. Common aggravating factors included fatty and spicy meal. Mean body mass index (BMI) was 22.7 ± 3.6 kg./m^2. There was statistically significant in BMI between both groups. Mean BMI in rabeprazole group was 21.3 ± 3.6 kg./m^2., while in control group was 24.0 ± 3.3 kg./m^2. (p = 0.041)

Study patients were given the RSI at the initial visit, and they were followed every 2 weeks until the end of the study. The most common symptoms were globus sensation (86.7%), excess throat mucous (80%) and heartburn or regurgitation (70%). In this study, we rarely found the patient with cough problem. There were 33.3% with coughing after meal or lying down and 3.3% with troublesome or annoying cough. (Table 2)

A direct comparison showed a nonsignificant trend of rabeprazole reducing the individual symptom score more than placebo. (Table 3)

The mean RSI of patients at the initial pretreatment visit was 11.4 (± 5.2), and at the completion of the 12-week treatment period was 5.3 (± 5.3). The mean RSI difference between pre and post treatment was 6.1 (± 3.7).

The mean pretreatment RSI was 10.6 (± 5.2) in rabeprazole group and 12.1 (± 5.1) in placebo group. There were no statistically differences in pretreatment RSI between both groups (p = 0.439).

24-hour pH Monitoring

Of the 30 patients, 21 (70%) had a positive 24-hour pH testing characterized by increased acid reflux values in the distal or proximal esophagus. Twelve of the 21 patients were found to have increased acid reflux both distally and proximally. Only 3 patients were found to have distal acid reflux, whereas 6 had only distal acid reflux. Nine patients had no acid reflux in both upper and lower pH study.

Twenty-four-hour pH monitoring results were not

Table 1 Subject demographics and reflux data

Data	N (%)	Rabeprazole	Placebo	p
Mean age (year)	44.7 ± 13.5	44.8 ± 11.6	44.63 ± 15.2	0.975
Body mass index (mean ± SD Kg/m^2)	22.7 ± 3.6	21.3 ± 3.6	23.99 ± 3.3	0.041
Sex				
Male	8 (26.7%)	4	4	
Female	22 (73.3%)	11	11	
Chief complaint				
Globus sensation	20 (66.7%)	8	12	0.30
Sore throat	4 (13.3%)	3	1	0.22
Burning sensation in throat	4 (13.3%)	1	3	0.22
Hoarseness	1 (3.3%)	1	0	
Dryness of throat	1 (3.3%)	1	0	
Smoking	2 (6.7%)	1	1	
No smoking	28 (93.3%)	14	14	
Alcohol drinking	2 (6.7%)	1	14	
No alcohol drink	28 (93.3%)	1	14	
Aggravating factors				
Fatty meal	10 (33.3%)	3	7	
Citrus meal	4 (13.3%)	2	2	
Spicy meal	10 (33.3%)	5	5	
Coffee and tea	2 (6.7%)	1	1	

Table 2 Symptoms according to the reflux symptom index (RSI) before treatment

Symptoms	Present	Absent	Mean Score ± SD
Hoarseness or a problem with voice	14 (46.7%)	16 (53.3%)	2.9 ± 1.2
Coughing after meal or lying down	10 (33.3%)	20 (66.7%)	2.0 ± 1.1
Troublesome or annoying cough	1 (3.3%)	29 (96.7%)	3.0
Excessive throat mucous or postnasal drip	24 (80.0%)	6 (20.0%)	2.8 ± 1.2
Clearing of throat	20 (66.7%)	10 (33.3%)	2.8 ± 1.1
Sensations of something sticking in throat or a lump in throat	26 (86.7%)	4 (13.3%)	3.1 ± 1.0
Difficulty swallowing foods, liquids, or pills	7 (23.2%)	23 (76.8%)	1.9 ± 0.7
Heartburn, chest pain, indigestion or stomach acid coming up	21 (70.0%)	9 (30.0%)	2.9 ± 1.3
Breathing difficulties or choking episodes	0	30 (100.0%)	0

Table 3 The Reflux Symptom Index Improvement after 12 weeks Treatment

Symptoms	Group	N	% Improvement		p
			Mean	SD	
Hoarseness or a problem with voice	Rabeprazole	7	64.3	47.6	0.916
	Placebo	7	66.7	34.4	
Coughing after meal or lying down	Rabeprazole	2	100	0	0.242
	Placebo	8	50	53.5	
Troublesome or annoying cough	Rabeprazole	0	0		
	Placebo	1			
Excessive throat mucous or postnasal drip	Rabeprazole	11	54.6	36.8	0.425
	Placebo	13	42.8	33.8	
Clearing of throat	Rabeprazole	8	68.8	43.8	0.093
	Placebo	12	39.6	30.0	
Sensations of something sticking in throat or a lump in throat	Rabeprazole	13	59.6	36.8	0.705
	Placebo	13	53.9	39.9	
Difficulty swallowing foods, liquids, or pills	Rabeprazole	4	75.0	50.0	0.135
	Placebo	3	16.7	28.9	
Heartburn, chest pain, in digestion or stomach acid coming up	Rabeprazole	8	76.0	34.3	0.398
	Placebo	13	61.5	39.0	
Breathing difficulties or choking episodes	Rabeprazole	0	0	0	
	Placebo	0	0	0	

statistically different between rabeprazole and placebo group in term of % time of acid exposure. (Table 4) Of the 18 positive upper pH monitor, the time of acid exposure in supine position were longer than in upright position (10.6% VS 5.2%)

There were no statistically different between sex in % time of acid reflux from 24-hour pH monitor results. We used % time of pH <4 more than 4% of total pH record time to define positive lower pH monitor and 1% to define positive upper pH monitor. When evaluated 24-hour pH results as positive and negative results, it's still no statistically significant between both sex. (Table 5 and 6)

Symptom Response

When considered clinical response, the improve-

Table 4 Pretreatment 24-pH monitoring in both Rabeprazole and Placebo group

pH Probe Position	% Time of Acid Exposure (Mean ± SD)		p
	Rabeprazole	Placebo	
Upper	5.6 ± 7.6	4.1 ± 4.6	0.49
Lower	7.4 ± 9.0	9.0 ± 20.0	0.79
Upper supine	7.2 ± 11.8	5.7 ± 8.0	0.68
Upper upright	3.8 ± 4.6	2.8 ± 3.6	0.54
Lower supine	5.6 ± 8.8	7.4 ± 20.5	0.76
Lower upright	8.3 ± 9.8	10.2 ± 19.9	0.75

Table 5 Time of Acid Reflux in Male and Female Patients

pH Probe Position	% Time of Acid Reflux (Mean ± SD)		p
	Rabeprazole	Placebo	
Upper	4.3 ± 5.0	5.0 ± 6.6	0.809
Lower	14.9 ± 27.9	5.8 ± 7.3	0.162
Upper supine	3.6 ± 5.9	7.4 ± 10.8	0.356
Upper upright	4.6 ± 4.7	2.8 ± 3.8	0.291
Lower supine	12.0 ± 28.8	4.6 ± 7.4	0.264
Lower upright	16.0 ± 27.9	6.9 ± 7.8	0.167

Table 6 24-hour pH Monitoring Results in Male and Female Patients

pH Probe Position	Patients				p
	Male		Female		
	Positive	Negative	Positive	Negative	
Upper	4	4	14	8	0.500
Lower	4	4	11	11	1.000
Upper supine	3	5	12	10	0.409
Upper upright	5	3	12	10	0.697
Lower supine	2	6	8	14	0.559
Lower upright	5	3	12	10	0.697

ment of symptom score more than 60% from pretreatment period, 9 of 15 patients in rabeprazole group had improvement in RSI. Similar findings were noted in placebo group, that 5 of 15 patients had RSI improvement. There was no statistically significance was demonstrated between both group. ($p = 0.143$)

In subgroup of positive pH monitoring, RSI demonstrated a statistically significant improvement when patients were given rabeprazole rather than placebo. Rabeprazole was better than placebo at reducing RSI in nearly all position except positive pH in supine position. While in pH negative subgroup, rabeprazole improved symptom score without statistically significance when compare with placebo. ($p > 0.05$) (Table 7)

In general, symptom scores improved over time for patients in both groups. There were no statistical differences between rabeprazole and placebo groups for symptoms improvement at 4 and 8 weeks therapy.

The eight male patients were assigned in both group equally. Two of 4 rabeprazole group had symp-

Table 7 12-week Treatment Results Subgroup by pH monitoring

24-hour pH monitor Results	N	Patients				p
		Rabeprazole		Placebo		
		Improve	Not improve	Improve	Not improve	
Upper pH positive (All)	18	6	2	2	8	0.020
Upper pH positive (Supine)	15	4	2	2	7	0.085
Upper pH positive (Upright)	17	7	1	2	7	0.007
Lower pH positive (All)	15	6	1	2	6	0.019
Lower pH positive (Supine)	10	4	1	1	4	0.058
Lower pH positive (Upright)	17	6	2	1	8	0.008
Upper pH negative (All)	12	3	3	4	2	0.558
Upper pH negative (Supine)	15	5	4	3	3	0.833
Upper pH negative (Upright)	13	2	5	3	3	0.429
Lower pH negative (All)	15	3	4	4	4	0.782
Lower pH negative (Supine)	20	5	5	4	6	0.653
Lower pH negative (Upright)	13	3	4	4	2	0.391
Any 24-hour pH monitor Results	30	9	6	5	10	0.143

tom scores improvement at 12 weeks. While 1 of 4 placebo group had symptom scores improvement at the same time. There was no statistically differences between both groups. (p = 0.465)

Seven of 10 female in rabeprazole group had symptom scores improvement at 12 weeks. Five of 12 in placebo group had symptom scores improvement at the same time. However, Rabeprazole was not significantly better than placebo in reducing RSI. (p = 0.184)

Twelve of 30 patients had both upper and lower acid reflux documented on the pretreatment study. There was only pH probes positive in both upper and lower pH probes subgroup that demonstrated statistically significance between treatment and placebo group.

Laryngoscopy

All patients underwent video laryngoscopy at pretreatment period. Only 22 patients had undergone video laryngoscopy at the end of treatment. The main reason of incomplete ENT examination was transportation problems. RFS analysis was based on 22 patient data.

Mean of pretreatment RFS was 7.2 (± 2.9 SD) in female and 8.4 (± 3.6 SD) in male patient. Sex showed a nonsignificant trend of improvement in the rabeprazole and placebo groups. (p = 0.304)

There was no differences in pretreatment RFS between rabeprazole (7.4 ± 2.8) and placebo group (7.6 ± 2.6). (p = 0.84) At the end of study, % improvement was not statistically different between rabeprazole and placebo group.

There was no statistically difference between rabeprazole and placebo group for pretreatment RFS and % improvement of RFS at the end of treatment.

Drug used before and between Study

In general practice, we found that there was a lot of medicine for reflux disease and laryngitis treatment. In our study, 1 patients had received antacids before study period. The history of H2-receptor antagonists and prokinetic usage were found in 4 (13.3%) and 1 patients (3.3%), respectively.

Four patients had received 20 mg./day omeprazole. All of them had stopped medication for at least 3 months before study period. The reason that previous treatment discontinued was ineffective control of LPR symptoms.

In subgroup of previous medication used patients, rabeprazole can improve both RSI symptoms (81.8% ± 14.7) and RFS (7 ± 2.2)

Drug Safety and Adverse Reaction

There was no adverse reaction demonstrated in both rabeprazole or placebo groups. Drug compliance was monitored by pill count with adherent rate more than 95%. At the end of treatment, patients in

rabeprazole group was asked for overall improvement. 12 of 14 (85.7%) rabeprazole group thought that rabeprazole was effective drug for laryngopharyngeal reflux treatment.

DISCUSSION

Although treatment options for gastroesophageal reflux disease are readily available, the challenge in managing patients with respiratory symptoms caused by GERD is in establishing the diagnosis. Early attempts in identifying these patients showed that the causal relationship between reflux and respiratory symptoms could be determined in a large number of patients by measurement of proximal esophageal acid exposure. Other experts have proposed the use of an empiric antireflux therapy as a tool for establishing the diagnosis. The patients who responded to the treatment were thought to have acid reflux.

A placebo effect in clinical trials is a well-documented phenomenon and is more likely to occur when the disease is dominated by subjective rather than objective findings. For example, clinical trials in the treatment of reflux esophagitis have found that 24-34% of the therapeutic response could be ascribed to placebo response. The diagnosis of reflux laryngitis is based in large part on subjective symptoms (lump in throat, excessive phlegm, etc.) Therefore, it is not surprising that the treatment of reflux laryngitis is prone to the placebo effect.

The purpose of this study was to determine the efficacy of gastric acid suppression in reflux laryngitis using a placebo-controlled, randomized, double-blind study design. All patients was followed until the end of the study. There was some problems about transportation and appointment, so only 22 patients was completed laryngoscopic examination at the end of study.

A direct comparison showed a nonsignificant trend of rabeprazole reducing the individual symptom score more than placebo. It is possible because the patient in each symptom group is too small to define statistical differences.

In subgroup of positive pH monitoring, RSI demonstrated a statistically significant improvement when patients were given rabeprazole rather than placebo. We found that rabeprazole was better than placebo at reducing RSI in nearly all position. In positive pH, supine position subgroup, the RSI improvement also preferred to rabeprazole group but the number might be too small to identify statistical significance.

While in pH negative subgroup, rabeprazole improved symptom score without statistically significance when compare with placebo. It could be explained in a few reasons. First, this group of patients did not have acid reflux problem. It might be other gastric contents, like pepsin or bile reflux that we can not measure in clinical practice. Second, as previously described, it might be little amount of acid that was less than 1 or 4% of exposure time cut point but there was also some mucosal injury coexist in individual patient. We documented the initial RSI response to therapy over 12-week period, whereas the short term response that was accessed at 4 and 8 weeks demonstrated no statistical differences.

This study found that laryngoscopic appearance improved equally in both the rabeprazole and placebo arms over the course of 3-month study. However, some authors have shown that the physical findings of reflux laryngitis may take six or more months to reverse. Belafskyfound that a 19% reduction in physical findings was noted at 2 months, a 37% reduction was noted at 4 months, and a 47% reduction was noted at more than 6-month study period[30] . Therefore, the 3- month follow-up period of this study may not have been long enough to observe any changes in the laryngoscopic findings.

We recognize that our study has some limitation. First, the small number of randomized patients may have obscured the identification of demographic or physiological characteristics of patients with acid-related laryngitis. Second, reflux symptom index is subjective tools. So, it still depends on investigators and patients relationship.

In summary, we conclude that rabeprazole improves clinical symptoms and decreases reflux finding sore in patients with posterior laryngitis related to GERD. 24-hour pH monitoring is helpful in the identification of patients likely to response to antireflux therapy.

The study used high-dose rabeprazole to ensure complete gastric acid suppression. Despite using a high dose of rabeprazole in this study, we recommend 40 mg rabeprazole twice a day as a starting dose for the treatment of reflux laryngitis.

Furthermore, the issue of initially performing esophageal testing versus empiric medical therapy is still now controversy with limited data in Thailand.

Esophageal manometry and 24-hr pH monitoring usually costs 2,000 Baht and 2,500 Baht per patient, respectively. While the cost of rabeprazole is around 3,960 Baht per 3-month. We are not sure whether we have to invest 4,500 Baht for prediction of treatment response or not. Cost effective study should be done to answer this question.

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