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The comparison of an empiric proton pump inhibitor trial *vs* 24-hour double-probe Ph monitoring in laryngopharyngeal reflux

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Abstract

Laryngopharyngeal reflux (LPR), which is defined as the backflow of gastric contents into the upper aerodigestive tract, is a relatively common disorder. However, its diagnosis still poses many problems. Twenty-four-hour double-probe pH monitoring is currently the diagnostic test of choice, but it has many disadvantages. Thus, an empiric trial of antireflux therapy has been suggested as an alternative method for diagnosis. The purpose of this article is to evaluate the validity of this alternative method in the management of LPR. The study group consisted of 36 patients with symptoms and physical findings suggesting LPR. The control subjects were 23 healthy adults. Twenty-four-hour double-probe pH monitoring was performed both in the study group and the control group, and the results were compared. In addition, the symptoms and physical findings in the study group was scored by the modified reflux symptom index (MRSI) and reflux finding score (RFS) at four intervals: before the start of therapy and at the second, fourth and sixth months of the therapy. The results of the 24-hour double-probe pH monitoring showed no significant difference between the study and the control groups ($p>0.05$). In the study group, the MRSI before the therapy was 13.6 ± 4.4. This index improved significantly to 4.3 ± 1.9 at the second month; to 1.5 ± 0.6 at the fourth month, and to 0.5 ± 0.2 at the sixth month of the therapy ($p<0.05$). The RFS before the start of the therapy was 14.8 ± 3.8; and it improved significantly to 7.7 ± 3.8 at the second month; to 4.5 ± 2.3 at the fourth month, and to 1.4 ± 0.9 at the sixth month of the therapy ($p<0.05$). The significant improvement in the MRSI and the RFS during the course of proton pump inhibitor therapy relates the patients' symptoms and physical findings to LPR. This implies the validity of the method, not only in the treatment of LPR, but in the diagnosis of this disorder, as well. Unfortunately, 24-hour double-probe pH monitoring has failed to differentiate LPR patients from healthy individuals.

Key words: Gastroesophageal Reflux; Laryngitis; Monitoring; Ambulatory; Proton Pump; Drug Therapy

Introduction

Gastroesophageal reflux (GER) is defined as the entry of the gastric contents into the oesophagus without associated belching or vomiting.[1] This pathology has been generally implicated in the pathogenesis of reflex oesophagitis, Barrett's oesophagus and oesophageal adenocarcinoma. Recently, laryngopharyngeal reflux (LPR) has been suggested as a term for the association of laryngeal disorders and GER.[2] LPR is the retrograde movement of gastric contents above the upper oesophageal sphincter into the larynx, pharynx and upper aerodigestive tract, causing pharyngeal and/or laryngeal symptoms.

While the prevalence of reflux-related otolaryngologic symptoms and findings in otolaryngology practice has been estimated as four to 10 per cent,[3,4] the prevalence of reflux in patients with voice disorders may be as high as 50 per cent.[5] The clinical presence of LPR is most commonly characterized by laryngeal symptoms, such as hoarseness, vocal fatigue, chronic and intermittent cough, excessive throat clearing. Additionally, pharyngeal symptoms, such as globus, mild dysphagia and sore throat, may coexist. The presence of laryngopharyngeal complaints without a history of obvious pharyngeal or laryngeal disease leads to a suspicion of LPR.[6]

The laryngeal findings of LPR include mucosal oedema and erythema of the posterior glottis, vocal fold oedema, ventricular obliteration, mucosal hypertrophy, granuloma/granulation tissue, subglottic oedema and excessive endolaryngeal mucus.[7–9] These findings in a patient with above-mentioned

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TABLE I
MODIFIED REFLUX SYMPTOM INDEX (MRSI)

'Within the last month, how did the following problems affect you?'	0 = no problem 3 = severe problem			
1. Hoarseness or a problem with your voice	0	1	2	3
2. Clearing your throat	0	1	2	3
3. Excess throat mucus or postnasal drip	0	1	2	3
4. Difficulty in swallowing food, liquids or pills	0	1	2	3
5. Coughing after you ate or after lying down	0	1	2	3
6. Breathing difficulties or choking episodes	0	1	2	3
7. Troublesome or annoying cough	0	1	2	3
8. Sensation of something sticking in the throat	0	1	2	3
9. Heartburn, chest pain, indigestion or stomach acid coming up	0	1	2	3

laryngopharyngeal symptoms provide clues for the diagnosis of LPR. However, it should be kept in mind that the laryngeal findings are not always associated with symptom severity.[7]

Although not without limitations, reflux of gastric contents into the laryngopharynx is best demonstrated by the 24-hour double-probe pH monitoring.[10,11] Because of the technical disadvantages of the probe located in the pharynx and the intermittent nature of LPR, 24-hour double-probe pH monitoring may not document acid reflux in all patients.[12] In addition, there is a lack of consensus on the interpretation of the test results. Therefore, an empiric trial of antireflux therapy has been proposed as an alternative diagnostic tool. This approach provides both diagnostic and therapeutic advantages and, has sensitivity and specificity that are comparable to the 24-hour double-probe pH monitoring.[13]

The purpose of this investigation was to evaluate the validity of an empiric trial of proton pump inhibitor (PPI) therapy in the diagnosis of LPR, and to compare its efficacy to that of 24-hour double-probe pH monitoring.

Materials and methods

A group of 36 patients with laryngopharyngeal complaints and physical findings suggesting LPR formed the study group. Twenty-three adults without a known history of laryngopharyngeal disease or complaint, and with normal laryngopharyngeal physical findings were enrolled as the control group.

Recordings of 24-hour double-probe pH monitoring were obtained from the study group and the control group before the initiation of medical therapy. The test was performed by using a disposable antimony pH catheter with two internal reference sensors, Zinetics 24 (Medtronic, Minneapolis, USA). The use of medications that would relax the upper oesophageal sphincter or stimulate the secretion of gastric contents were stopped one week before the procedure. Gaseous, acidic, spicy or hot food and drinks were not allowed during the 24-hour recordings. Before the procedure, the pH probes were calibrated using pH 7.0 and pH 1.0 buffer solutions. The catheter was placed transnasally under the direct vision of flexible endoscopy. The proximal probe was positioned in the hypopharynx, 0.5 cm below the arytenoids. All patients were instructed to keep a detailed diary of oral intake. Data were recorded on a battery-powered Digitrapper pH 400 (Medtronic, Minneapolis, USA). On completion of the recordings, the data were downloaded into the computerized system for analysis using PC Polygram® software (Medtronic, Minneapolis, USA). The percentage of time, in which the pH was less than 4.0 in the distal probe, was calculated separately in three situations: an upright position, a supine position and the total test period. The results were compared to the mean $\pm$ 2SD of the control group and, in addition, to the normal limits of the literature, ranging as follows: upright 2.8–12.12 per cent; supine 0.60–3.67 per cent; total 1.90–8.30 per cent.[10,11,14–20] Even a single reflux event in the proximal probe was considered as abnormal.[10] The study group and the control group were compared by the Mann-Whitney-U test. The evaluation of the patients in the study group with regard to the normal limits of the literature was statistically analysed by the two-tailed Fisher's exact test.

A modified reflux symptom index (MRSI) was used for the documentation of symptom severity at each visit of the patient (Table I). MRSI is the modification of the reflux symptom index of the Center for Voice Disorders of Wake Forest University, Winston-Salem, NC, USA.[7] A complete

TABLE II
REFLUX FINDING SCORE (RFS)[8]

Subglottic oedema	2 if present			
Ventricular obliteration	2 if partial			4 if complete
Erythema/hyperemia	2 if arytenoids only			4 if diffuse
Vocal fold oedema	1 mild	2 moderate	3 severe	4 polypoid
Diffuse laryngeal oedema	1 mild	2 moderate	3 severe	4 obstructing
Posterior commissure hypertrophy	1 mild	2 moderate	3 severe	4 obstructing
Granuloma/granulation	2 if present			
Thick endolaryngeal mucus	2 if present			

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TABLE III
TWENTY-FOUR HOUR DOUBLE-PROBE PH MONITORING RESULTS OF THE STUDY GROUP AND THE CONTROL GROUP. NO SIGNIFICANT DIFFERENCE WAS NOTED BETWEEN TWO GROUPS (P>0.05)

Proximal probe	Study group (n = 36)	Control group (n = 32)
Percentage of time pH<4.0 (total time)	0.4 ± 0.1	0.3 ± 0.2
Percentage of time pH<4.0 (upright)	0.6 ± 0.9	0.6 ± 0.7
Percentage of time pH<4.0 (supine)	0.2 ± 0.3	0.1 ± 0.1
Distal probe		
Percentage of time pH<4.0 (total time)	4.1 ± 3.9	3.7 ± 2.7
Percentage of time pH<4.0 (upright)	4.3 ± 4.3	4.5 ± 4.7
Percentage of time pH<4.0 (supine)	3.4 ± 1.6	2.6 ± 1.8

head and neck examination together with videolaryngoscopy was also performed at each visit of the patient. The physical findings were scored according to the reflux finding score (RFS)[8] as shown in Table II.

Regardless of the results of 24-hour double-probe pH monitoring, each patient of the study group was given a reflux diet and behaviour modification, and an empiric trial of PPI (lansoprozole, 30 mg b.i.d.) therapy of two months. After the second month, the therapy was maintained with lansoprozole, 15 mg, for an additional four months. Patients were evaluated for two month intervals to assess improvement of symptoms and physical findings based on MRSI and RFS. The paired-samples *t*-test was used to compare the scores of each visit.

Results

The study group included 13 men and 23 women. The ages ranged from 19 to 71 (mean = 39). The control group consisted of 14 men and nine women. The ages ranged from 19 to 51 (mean = 31).

The mean ± 2 standard deviation (SD) of results obtained from proximal and distal probes during the 24-hour double-probe pH monitoring in both groups are shown in Table III. The comparison of the percentage of time, in which pH was less than 4.0, revealed no significant difference between the two groups ($p>0.05$). When the results of each patient of the study group and of each individual of the control group were compared with regard to the range of normal limits presented in the literature, the distributions of normal and abnormal members in both groups were not significantly different according to the two-tailed Fisher's exact test (Table IV) ($p>0.05$).

The values of MRSI and RFS are given in Table V. The mean MRSI improved significantly from 13.6 ± 4.4 to 4.3 ± 1.9 within the first two months, and decreased more profoundly to 0.5 ± 0.2 at the end of the sixth month of the therapy ($p<0.05$). During the course of the therapy; 68.1 per cent, 63.7 per cent and 68.1 per cent of reductions in MRSI were noted at the second, fourth, and sixth months, respectively. Similarly, RFS showed significant improvement from 14.8 ± 3.8 to 7.7 ± 3.8 at the end of the second month of the therapy, and finally, to 1.4 ± 0.9 at the end of the maintenance therapy ($p<0.05$). The reductions of RFS at the second, fourth and sixth months were 47.8 per cent, 41 per cent and 67.6 per cent, respectively. The reduction was more pronounced at the end of the sixth month.

Discussion

Twenty-four-hour double-probe pH monitoring is accepted as the most sensitive and the most specific diagnostic tool currently available in LPR, because it demonstrates the presence of pharyngeal and oesophageal acid exposure. Unfortunately, 24-hour double-probe pH monitoring is not a perfect test and controversies exist. There is no consensus on the normal limits for 24-hour double-probe pH monitoring in the literature. The percentage of time, in which pH is less than 4.0 in the distal probe, is regarded as the most useful discriminator between physiological and pathologic reflux.[21] However, the normal values presented in the literature for this criteria vary widely, ranging between 2.8–12.12 per cent in the upright position, 0.60–3.67 per cent in the supine position and 1.90–8.30 per cent for the total test period.[10,11,14–20] The normal values in the present study were within the limits of the literature: 9.2 per cent in the upright position, 4.4 per cent in the supine position, 6.4 per cent for the total test period.

Even a single reflux event in the proximal probe is considered indicative of LPR.[10] However, it has been noted that pharyngeal reflux occurs in normal healthy controls with a prevalence of 16–21 per cent.[22,23] Likewise, in the present study, the test results of the LPR patients did not reveal any significant difference, neither when compared to the mean ± 2SD of the control group, nor when compared to the normal limits presented in the literature.

TABLE IV
EVALUATION OF THE STUDY GROUP AND THE CONTROL GROUP WITH REGARD TO THE NORMAL PH MONITORING VALUES PRESENTED IN THE LITERATURE. NO SIGNIFICANT DIFFERENCE NOTED IN THE DISTRIBUTION OF NORMALS AND ABNORMALS BETWEEN TWO GROUPS (P>0.05)

Probe	Cases	Study group	Control group
Distal	Normal	24	16
	Abnormal	12	7
Proximal	Normal	6	4
	Abnormal	30	19
Distal and Proximal	Normal	5	4
	Abnormal	31	19

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TABLE V
THE MEAN ± 2SD VALUE OF MODIFIED REFLUX SYMPTOM INDICES AND REFLUX FINDING SCORES OF THE STUDY GROUP AT ENTRY AND AT EACH VISIT

	Entry	2nd month	4th month	6th month
Modified reflux symptom index	13.6 ± 4.4	4.3 ± 1.9	1.5 ± 0.6	0.5 ± 0.2
Reflux finding score	14.8 ± 3.8	7.7 ± 3.8	4.5 ± 2.3	1.4 ± 0.9

Probe placement is another controversy for 24-hour double-probe pH monitoring. Loss of mucosal contact, probe displacement, pH changes caused by oral intake, intermittent drying and moistening of the proximal probe are the problems blamed for spurious test results.[12] The presence of the proximal probe in the posterior pharynx has been speculated to precipitate acid reflux secondary to irritation, possibly resulting in false-positive results.[13] The tendency for false-negative tests has been given as high as 20–50 per cent.[24] Thus, a negative test result may not exclude the diagnosis of LPR, whereas a positive test only confirms the co-existence of reflux with the symptoms. However, this does not assure a cause-and-effect relationship. This relationship can only be proved with confidence, when the symptoms or the signs related to LPR markedly improve or resolve with medical or surgical therapy.[25]

The empiric trial of antireflux therapy with medications, such as H_2-receptor blockers and PPIs, has been shown to be effective.[9,26–32] In these studies, the response to the empiric antireflux therapy ranged between 50–100 per cent. The probability of diagnosing LPR based on the criterion of 'outcome/decision' for the 24-hour double-probe pH monitoring and the empiric trial of antireflux therapy are comparable: 80 per cent *vs* 85 per cent, respectively.[33] In the present study, a significant improvement in symptoms has been noted at the end of the second month of the therapy. The reduction in symptom scores was 68.1 per cent, indicating the presence of a relationship between the symptoms and the pharyngeal reflux. This finding is in correlation with the literature.[7,13,33]

The duration of the empiric trial of antireflux therapy is proposed as two months.[13,33] On the other hand, it has been noted that the physical findings of LPR improve more slowly and continue to get better throughout, at least, six months of the therapy.[2,7] Similarly, in the present study, reflux finding scores improved significantly and gradually during the course of the antireflux therapy. The most pronounced reduction in reflux finding scores was at the sixth month, with a final mean score of 1.4 ± 0.9 indicating a complete resolution of physical findings. Even though the treatment of LPR improve the symptoms in a period of two months, the mucosal damage recovers by approximately six months. Thus, cessation of the therapy based on improvement of symptoms alone may be premature.[7]

In conclusion, the empiric trial of PPI is an alternative for the 24-hour double-probe pH monitoring for the diagnosis of LPR. It provides reliable information about the relationship between the pharyngeal reflux and the laryngopharyngeal symptoms and physical findings. The improvement in symptoms by two months confirms the presence of this relationship. However, this improvement should not be regarded as the cure. The medical therapy should be maintained for at least four more months. This period might allow the complete resolution of mucosal injury secondary to the pharyngeal reflux.

References

1 Bain WM, Harrington JW, Thomas LE, Schaefer SD. Head and neck manifestations of gastroesophageal reflux. *Laryngoscope* 1983;**93**:175–9
2 Koufman J, Sataloff RT, Toohill R. Laryngopharyngeal reflux: consensus conference report. *J Voice* 1996;**10**:215–6
3 Koufman JA, Wiener GJ, Wu WC, Castell DO. Reflux laryngitis and its sequela: the diagnostic role of ambulatory 24-hour monitoring. *J Voice* 1988;**2**:78–9
4 Toohill RJ, Mushtaq E, Lehman RH. Otolaryngologic manifestations of gastroesophageal reflux. In: Sacristan T, Alvarez-Vincent JJ, Bartual J, eds. *Proceedings of XIV World Congress of Otolaryngology, Head and Neck Surgery*. Amsterdam: Kugler-Ghedini Publications, 1990,3005–9
5 Kofman JA, Amin MR, Panetti M. The prevalence of reflux in 113 consecutive patients with laryngeal and voice disorders. *Otolaryngol Head Neck Surg* 2000;**123**:385–8
6 Shay SS, Abreu SH, Tsuchida A. Scintigraphy in gastroesophageal reflux disease: a comparison to endoscopy, LESp, and 24-h pH score, as well as to simultaneous pH monitoring. *Am J Gastroenterol* 1992;**87**:1094–101
7 Belafsky PC, Postma GN, Koufman JA. Laryngopharyngeal reflux symptoms improve before changes in physical findings. *Laryngoscope* 2001;**111**:979–81
8 Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). *Laryngoscope* 2001;**111**:1313–7
9 Shaw GY, Searl JP. Laryngeal manifestations of gastroesophageal reflux before and after treatment with omeprazole. *South Med J* 1997;**90**:1115–22
10 Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of the laryngeal injury. *Laryngoscope* 1991;**101**(suppl 53):1–64
11 Mattioli S, Pilotti V, Spangaro M, Grigioni WF, Zannoli R, Felice V, *et al*. Reliability of 24-hour home esophageal pH monitoring in diagnosis of gastroesophageal reflux. *Dig Dis Sci* 1989;**34**:71–8
12 Ulualp SO, Toohill RJ. Laryngopharyngeal reflux. State of the art diagnosis and treatment. *Otolaryngol Clin North Am* 2000;**33**:785–802
13 Wong RK, Hanson DG, Waring PJ, Shaw G. ENT manifestations of gastroesophageal reflux. *Am J Gastroenterol* 2000;**95**(suppl 8):S15–22
14 Bianchi Porro G, Pace F. Comparison of three methods of intraesophageal pH recordings in the diagnosis of gastroesophageal reflux. *Scand J Gastroenterol* 1988;**23**:743
15 Boesby S. Gastro-esophageal acid reflux and sphincter pressure in normal human subjects. *Scand J Gastroenterol* 1975;**10**:731–6
16 Fink SM, McCallum RW. The role of prolonged pH monitoring in the diagnosis of gastroesophageal reflux. *Am Med Assoc* 1984;**252**:1160–4

17 Johnson LF, DeMeester TR. Twenty-four-hour pH monitoring of the distal esophagus: a quantitative measure of gastroesophageal reflux. *Am J Gastroenterol* 1974;**62**:325–32
18 Pujol A, Grande L, Ros E, Pera C. Utility of inpatient 24-hour intraesophageal pH monitoring in diagnosis of gastroesophageal reflux. *Dig Dis Sci* 1988;**33**:1134–40
19 Smout AJ, Breedijk M, van der Zouw C, Akkermans LM. Physiological gastroesophageal reflux and esophageal motor activity studies with a new system for 24-hour recording and automated analysis. *Dig Dis Sci* 1989;**34**:372–8
20 Wiener GJ, Koufman JA, Wu WC, Cooper JB, Richter JE, Castell DO. Chronic hoarseness secondary to gastroesophageal reflux disease: documentation with 24-hour ambulatory pH monitoring. *Am J Gastroenterol* 1989;**84**:1503–8
21 Kahrilas PJ, Quigley EMM. Clinical esophageal pH monitoring: a technical review for practice guideline development. *Gastroenterology* 1996;**110**:1982–96
22 Shaker R, Milbrath M, Ren J, Toohill R, Hogan WJ, Li Q, *et al*. Esophagopharyngeal distribution of refluxed gastric acid in patients with reflux laryngitis. *Gastroenterology* 1995;**109**:1575–82
23 Ulualp SO, Toohill R, Hoffmann RC, Arndorfer RC, Shaker R. Revelations about 24-hr ambulatory pharyngeal pH monitoring. *Gastroenterology* 1998;**1290**:A315
24 Vaezi MF, Schroeder PL, Richter JE. Reproducibility of proximal pH parameters in 24-hour ambulatory esophageal pH monitoring. *Am J Gastroenterol* 1997;**92**:825–9
25 Richter JE. Extraesophageal presentations of gastroesophageal reflux disease: an overview. *Am J Gastroenterol* 2000;**95**(suppl 8):S1–3
26 Hanson DG, Kamel PL, Kahrilas PJ. Outcomes of antireflux therapy for the treatment of chronic laryngitis. *Ann Otol Rhinol Laryngol* 1995;**104**:550–5
27 Jaspersen D, Weber R, Hammar CH, Draf W. Effect of omeprazole on the course of associated esophagitis and laryngitis. *J Gastroenterol* 1996;**31**:765–7
28 Kamel PL, Hanson D, Kahrilas PJ. Omeprazole for the treatment of posterior laryngitis. *Am J Med* 1994;**96**:321–6
29 McNally PR, Maydonovitch CL, Prosek RA, Collette RP, Wong RK. Evaluation of gastroesophageal reflux disease as a cause of idiopathic hoarseness. *Dig Dis Sci* 1989;**34**:1900–4
30 Metz DC, Childs ML, Ruiz C, Weinstein GS. Pilot study of the omeprazole test for reflux laryngitis. *Otolaryngol Head Neck Surg* 1997;**116**:41–6
31 Waring JP, Lacayo L, Hunter J, Katz E, Suwak P. Chronic cough and hoarseness in patients with severe gastroesophageal reflux disease. Diagnosis and response to therapy. *Dig Dis Sci* 1995;**40**:1093–7
32 Wo JM, Grist WJ, Gussack G, Delgaudio JM, Waring JP. Empiric trial of high-dose omeprazole in patients with posterior laryngitis. A prospective study. *Am J Gastroenterol* 1997;**92**:2160–5
33 Gerson LB, Robbins AS, Garber A, Hornberger J, Triadafilopoulos G. A cost-effectiveness analysis of prescribing strategies in the management of gastroesophageal reflux disease. *Am J Gastroenterol* 2000;**95**:395–407

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