A pilot study on diagnosing laryngopharyngeal reflux disease by pharyngeal pH probe monitoring

Larengofarengeal reflü hastalığının tanısında farengeal pH probu ile pilot bir çalışma

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Abstract

Objective: We aimed to evaluate (laryngopharyngeal reflux) LPR disease group and group with healthy volunteers and compare results obtained using Dx pH probe in the diagnosis of LPR disease.

Methods: Fifty-seven LPR patients with typical scores of reflux symptom index (RSI) and reflux finding scoring (RFS) system and 20 healthy volunteers without laryngopharyngeal symptoms and physical examination findings were included in the study after excluding other concomitant diseases. All patients were requested to complete RSI and RFS forms. Healthy volunteers, with RSI <13 and RFS <7 constituted the control group and LPR group consisted of patients with RSI >13 and RFS >7. Dx pH probes were applied to each group. Fisher's exact test, Shapiro-Wilk test, T test and Mann-Whitney test were used for statistical analysis. A p value <0.05 was considered to be significant.

Results: Between the two groups, there was no statistically significant difference in terms of age, sex and body mass index (BMI). Mean pHs were estimated as 6.97 in healthy volunteers and 6.27 in the LPR group (p<0.05). pH events were calculated separately for pHs <5.5 and <5.0. Besides, acid exposure times were estimated and compared in two groups. There was a significant statistical difference between two groups (p<0.05). In addition, pH events in the upright and supine position were calculated separately and intra- and intergroup comparisons were made. Any statistical significant difference was not detected in intragroup comparisons (p>0.05), despite a statistically significant intergroup difference (p<0.05).

Conclusion: Dx pH probe was found to be an alternative to other methods commonly used in the diagnosis of LPR. When compared with RSI and RFS scores, Dx pH probes provided consistent and accurate data. Dx pH probe application can be an alternative to frequently used diagnostic methods for LPR.

Key words: Laryngopharyngeal reflux, reflux symptom index, reflux finding score, pharyngeal pH probe.

Özet

Amaç: Çalışmamızda larengofarengeal reflü (LFR) hastalığı olan ve sağlıklı iki grup değerlendirilerek, Dx pH probunun LPR tanısında sonuçlarını karşılaştırmayı amaçladık.

Yöntem: Diğer hastalıklar ekarte edildikten sonra hem reflü semptom indeksi (RSİ) hem de reflü bulgu skoru (RBS) ile tipik skorlara sahip 57 LFR olgusu ile larengofarengeal yakınması ve fizik muayene bulguları olmayan 20 sağlıklı gönüllü çalışmaya alındı. Tüm olgulara RSİ ve RBS formları dolduruldu. RSİ <13 ve RBS <7 olanlar sağlıklı grubu oluştururken RSİ >13 ve RBS >7 olanlar LFR grubunu oluşturdu. İki gruba Dx pH probu takılarak veriler elde edildi. İstatistiksel değerlendirmede Fisher'in kesin olasılık testi, Shapiro-Wilk testi, T testi ve Mann-Whitney testi kullanıldı. p<0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: İki grup arasında yaş, cinsiyet ve vücut kitle indeksi bakımından istatistiksel fark saptanmadı. Sağlıklı gönüllülerde ortalama pH değeri 6.97 saptanırken hasta grupta 6.27 olarak hesaplandı (p<0.05). pH olayları, pH <5.5 ve pH <5.0 değerleri için ayrı ayrı hesaplandı; asit maruziyet süreleri de değerlendirilerek iki grup arasında karşılaştırıldığında istatistiksel olarak anlamlı fark saptandı (p<0.05). Ayrıca iki grubun pH olayları dik ve sırtüstü pozisyonlarda ayrı ayrı hesaplanarak hem kendi içlerinde hem de gruplar arasında karşılaştırma yapıldı. Kendi içlerindeki kıyaslamalarda istatistiksel olarak anlamlı fark saptanamadı (p>0.05), ancak iki grup arasında bu kıyaslamada istatistiksel olarak anlamlı fark saptandı (p<0.05).

Sonuç: Dx pH probu verileri RSİ ve RBS değerleri ile kıyaslandığında tutarlı ve doğru sonuçlar elde edilmiştir. Larengofarengeal reflü tanısında sık kullanılan diğer yöntemlere alternatif olabileceği görülmüştür.

Anahtar sözcükler: Larengofarengeal reflü, reflü semptom indeksi, reflü bulgu skoru, farengeal pH probu.

Gastroesophageal reflux (GER) is a spontaneous and effortless regurgitation of gastric contents into esophagus. However laryngopharyngeal reflux (LPR) is an atypical form of GER in which gastric contents severely regurgitate up to upper esophageal sphincter without retching or vomiting. Retrosternal burning sensation and regurgitation are

deomed

not observed in the majority of cases with LPR when compared with GER.[1-3]

Transnasal fiberoptic laryngeal examination, standard acid reflux test, dual-probe 24-hour pH monitorization, esophageal manometry, multi-channel intraluminal impedance test, Dx pH probe, Bravo pH probe and laryngeal sensitivity tests are preferred diagnostic test methods for LPR. Despite all of these diagnostic tests, a 100 % sensitive and specific single method leading to correct diagnosis is lacking.[4-7] Thanks to scoring system for symptomatic severity and endoscopic findings in LPR, difference between post-treatment state and baseline has become apparent. Belafsky et al.[2,3] formulated reflux finding scoring (RFS) system based on reflux symptom index (RSI) and fiberoptic laryngoscopic findings and conducted investigations on its applicability as a diagnostic tool in LPR.

Recently developed Ph measurement system (Dx pH) using minimally invasive oropharyngeal probe can evaluate refluxate material both in fluid and gaseous forms. Its easy applicability and more specific identification of pseudoreflux episodes are among advantages of Dx pH.[4-6] In our study we applied Dx pH probe for cases evaluated by RSI and RFS and aimed to share information related to its diagnostic efficacy in LPR and our clinical outcomes.

Materials and Methods

Fifty-seven LPR patients with typical scores of RSI and RFS but without any concomitant diseases who consulted to our outpatient clinics between November 2010 and October 2012 and also 20 healthy volunteers without any laryngopharyngeal symptoms and related physical examination findings were included in the study and body mass indexes (BMIs) of all participants were calculated.

Cases under treatment for the previous one month with the established diagnosis of LPR and/or GER, suspect cases with laryngeal malignancies, those with a history of laryngeal surgery or gastrointestinal system diseases are excluded from the study. All cases underwent routine examinations, then they were requested to respond to a RSI form which consisted of 9 items (Table 1). Endoscopic findings were scored and evaluated based on flexible fiberoptic examination results and a RFS form was completed (Table 2). In order to support our study with objective data, cases with RSI >13 and RFS >7 were considered as LPR patients and included in the study.

Before the procedure, oropharyngeal probe was calibrated in buffer solutions with pH 4 and 7 in accordance with the manufacturer's recommendations. Oropharyngeal

Table 1. Reflux symptom index (RSI).

Within the last month, how did the following problems affect you?	0: Not at all 5: Extremely					
Hoarseness or voice problems	0	1	2	3	4	5
Need for throat clearing						
Excess throat mucus or postnasal drip						
Difficulty swallowing food/liquids or pills						
Breathing difficulties or choking episodes						
Troublesome or annoying coughing						
Sensations of something sticking or a lump in your throat						
Heartburn, chest pain, indigestion or stomach acid coming up to mouth						

pH probe was inserted under direct vision and LED on its tip was engaged inside the cheek at the level of uvula. Recordings were retrieved for 24 hours and transferred into a computerized system. Data were analyzed and evaluated using Restecht Data Viewer program.

Table 2. Reflux finding score (RFS).

Pseudosulcus (infraglottic edema)	0: Absent 2: Present
Ventricular obliteration	0: Absent 2: Partial 4: Complete
Erythema/hyperemia	0: Absent 2: Arytenoids only 4: Diffuse
Vocal cord edema	0: Absent 1: Mild 2: Moderate 3: Severe 4: Polypoid
Diffuse laryngeal edema	0: Absent 1: Mild 2: Moderate 3: Severe 4: Obstructing
Posterior commissure hypertrophy	0: Absent 1: Mild 2: Moderate 3: Severe 4: Obstructing
Granuloma/granulation	0: Absent 2: Present
Thick endolaryngeal mucus	0: Absent 2: Present

Mean values of 24-hour pH recordings , total number of pH episodes, acid exposure times (the longest and total) related to the control and LPR groups measured by Dx pH probe were evaluated separately. Data of both groups were compared with each other and their statistical analyses were performed. To analyze relationship between reflux attacks in the upright and supine positions, intragroup analysis of the data related to individual pH events occurring in the upright and supine positions in both groups was performed and their statistical analysis was conducted.

Statistical Evaluation

All data obtained were entered into SPSS (Statistical Package for Social Sciences) Windows 15.0 program (SPSS Inc., Chicago, IL, USA). Numerical data were expressed as number of cases and percentages. Fisher's exact probability test was performed for categorical comparisons with appropriate corrections. For compatibility analysis of normality of distribution in continuous data Shapiro-Wilk tests were performed and data demonstrating normal distribution were assessed with parametric T test. Data with non-normal distribution non-parametric Mann-Whitney U test was used. The p values smaller than 0.05 were considered as statistically significant.

Results

Laryngopharyngeal reflux group consisted of total of 57 [12 (21%) men and 45 (79%) women] patients and the control group included 20 healthy volunteers [8 (40%) men and 12 (60%) women]. Mean ages of the control and the LPR groups were 44.8 (range: 22-71) years and 44.8 (range: 18-80) years, respectively. A statistically significant difference was not detected between both groups as for gender and age distribution (p>0.05) (Table 3).

Body mass indexes of the healthy volunteers ranged between 20-38 (median: 26.8) kg/m^2. Four cases were overweight (BMI>30 kg/m^2) and the corresponding BMIs for LPR group were 16.7-40.9 (median: 26.4) kg/m^2 and 13 cases were overweight. Any statistically significant difference was not found as for BMIs between both groups (p>0.05).

Reflux symptom indexes of the healthy volunteers and the LPR group changed between 1-10 (median: 4.0) and 13-39 (median: 20.0), respectively. A statistically significant difference was found between both groups as for RSI values (p<0.05) (Table 4).

Reflux finding scores of the healthy volunteers and the LPR group varied between 0-4 (median: 1.45) and 7-11

Table 3. Distribution of the study group according to gender of the participants.

	Male	Female	Total	p value
Healthy volunteers	8 (40%)	12 (60%)	20 (100%)	p>0.05
LPR group	12 (21%)	45 (79%)	57 (100%)	

(median: 8.28), respectively. A statistically significant difference was found between both groups regarding RFS values (p<0.05) (Table 4).

Median 24-hour pH values of the healthy volunteers and the LPR group were estimated as 6.7 (range: 6.09-7.64) and 6.27 (range: 5.6-6.88), respectively. A statistically significant difference was detected between median pH values of both groups (p<0.05) (Table 4).

In the group with healthy volunteers, any pH-events were not detected in 12 (60%) cases, while in 8 cases a total of 49 pH events were detected (median: 2.45; range: 1-13 pH events). In the LPR group, a total of 6094 (median: 106.91; range: 4-382 pH events) pH events were detected with a statistically significant difference between groups (p<0.05) (Table 4).

Ph events recorded in the supine and upright positions among healthy volunteers were analyzed separately and we found that 30 (61.2%) of 49 pH events had happened in the supine and 19 (38.8%) of them in the upright position. Intragroup comparisons of these data were evaluated and any statistically significant difference was not noted (p>0.05). However in the LPR group 3257 (53.45%) of 6094 pH events occurred in the supine and 2837 (46.55%) of them in the upright position. Intragroup comparisons of these data also could not reveal any statistically significant intragroup difference (p>0.05).

Total acid exposure time of all healthy volunteers was 1154 (median: 57.7) secs. When all cases in this group were analyzed individually, the longest acid exposure time was

Table 4. Statistical comparisons among mean RSI, RFS, pH values and the total number of pH events of both groups.

	Control group	LPR group	p value
RSI (mean)	4.0	20.0	p<0.05
RBS (mean)	1.45	8.28	p<0.05
pH	6.97	6.27	p<0.05
Total number of pH events	49	6094	p<0.05
Number of pH events	2.45	106.91	p<0.05
Total acid exposure time (mean)	57.7	6320.86	p<0.05

226 (median: 28.45) secs. In the LPR group, total acid exposure time was 360,289 secs (median: 6320.86) secs. All these cases in this group were analyzed individually and the longest exposure time was estimated as 895 (median: 647.23) secs. Averages of total acid exposure times of the healthy volunteers and the LPR group were 57.7 and 6320.86 secs, while the average of the longest exposure times of the corresponding groups were 28.45 and 647.23 secs, respectively with a statistically significant intergroup difference (p<0.05).

Discussion

Laryngopharyngeal reflux and GER occurs as a result of mucosal damage due to acid and pepsin exposure, however laryngeal mucosa is more responsive to acid and pepsin exposure relative to the esophageal mucosa.[8-11] Cellular damage occurs when acidity of the esophageal and laryngeal epithelium drop below pHs 4 and 5, respectively. Therefore, LPR symptoms might arise, before severity of acidic reflux is not sufficient to induce development of esophagitis.[12] Contrary to GER, complaints of heartburn and regurgitation are not frequently encountered in LPR.[13,14] Ossakow et al.[11] reported that patients with complaints of reflux had been either treated in the outpatient clinics of ENT (ear-nose and throat) (n=63) or gastroenterology (GE) (n=36). The authors also compared signs and symptoms of the cases and detected episodes of hoarseness in 100% of ENT cases (in none of GE patients), while the corresponding rates of heartburn in the ENT and GE groups were reported in 6 and 89% of the cases, respectively. In a different study, complaints of heartburn could not be demonstrated in more than 50% of cases with LPR. In LPR, pharyngeal and voice complaints are in the foreground. In a large series of patients with LPR, symptoms as dysphonia (71%), chronic coughing (51%), globus sensation and chronic throat cleaning (42%) have been reported.[8]

Various diagnostic criteria for LPR have been proposed. In a multi-centered study performed on 138 cases in ENT clinics of Turkey, LPR positivity was found to be 47% in 138 cases with normal physical examination (PE) findings and 62% in suspect reflux patients mostly with posterior laryngitis as assessed by 24-hour pH-monitoring tests.[15] The prevalent method used in the diagnosis and treatment of LPR is interrogation of LPR symptoms and signs which formulate diagnosis and treatment. Conservative or empirical treatment is among these methods and any standardization has not been established yet. Uncertainties still exist about indication for the initiation of LPR treatment, drug-dose selections, durations of treatment and monitorization

periods. Currently, practical algorithms of history taking and differential diagnosis to be used for the diagnosis of LPR are needed.[5,8,10,13,15]

In order to be able to evaluate LPR symptoms and their severity Belafsky et al.[3] described a reflux finding scoring (RFS) system which interrogated frequently encountered 8 symptoms of LPR. Scores of RFS ranges from 0 to 26 points. In their investigation of 40 cases with a diagnosis of LPR as assessed by 24-hour dual-probe pH monitorization tests, average pretreatment RFS score was found to be 11.5 pts, while the corresponding RFS scores at postoperative 2nd, 4th and 6th months were 9.3, 7.3 and 6.1 pts, respectively. In the control group with 40 participants without any past history of LPR, median RFS score was detected to be 5.2 (range: 3.6-6.8) pts and cases with scores of ≥7 were defined as LPR with a 95% predictive accuracy. In many studies performed, reproducible RFS system was used.[16-18] Oelschlager et al.[19] reported response rates to acid suppressive therapy as 83% in patients with RFSs above 7 pts and abnormal hypopharyngal pH monitorization findings and as 44% in asymptomatic cases and evaluated RFS and hypopharyngeal pH monitorization as complementary methods in the diagnosis of LPR. Despite different scoring systems, RFS is a reliable and developable method in the objective assessment of LPR. This scoring system provides a total reflux score which evaluates glottic and supraglottic anatomy in combination.[3,16-19]

In consideration of different symptomatic manifestations of GER and LPR, Belafsky et al.[2] developed a 9-item RSI which evaluates symptoms of LPR. With the intention to reveal sensitivity and validity of RSI, standard dual-probe pH monitorization procedures were applied on 25 cases to make a diagnosis of LPR. Subsequently, the patients completed RSI and voice handicap index (VHI) forms and the same forms were filled up by the same participants at posttreatment 6th months and average pre- and posttreatment RSI scores were compared (20.9 and 12.8 pts, respectively). In the same study, median RSI score in the asymptomatic control group was found to be 11.6 (range: 9.7-13.6) pts. Therefore, RSI values above 13 pts were regarded as abnormal findings. In many studies performed reproducible RSI scores were used.[16-18,20]

Even though RSI and RFS have been used as separate diagnostic criteria, in our study cases meeting the requirements of both criteria (LPR if RSI >13, and RFS >7 and healthy if RSI <13 and RFS <7) were included in the study. Besides RSI scores of both groups were compared and increases in the patient group were found to be statistically

significant (p<0.05). The same comparative assessments were done for RFS and increases in RFS values were regarded as statistically significant as is the case with RSI (p<0.05). This observation have demonstrated that both scoring systems can accurately and realiably discriminate between the LPR and the healthy control groups.

Cherry and Marguiles[21] and Malcomson[22] firstly described (1968) LPR which is one of the extraesophageal manifestations of GER and since then hundreds of investigations have been performed related to diagnosis and treatment of LPR. Dual-channel 24-hour esophageal monitorization technique has the highest diagnostic sensitivity and specificity for LPR. Diagnostic tools for GER including barium esophagography, esophagoscopy-guided biopsy, acid perfusion test (Bernstein) and radionuclide scanning tests cannot predict LPR. Sensitivity and specificity of 24-hour pH monitorization are nearly 90 and 98%, respectively and as a result this technique has been currently regarded as a gold standard due to its highest diagnostic accuracy for reflux in GERD, rather than LPR.[8,13,14] Reported diagnostic accuracy rates of 24-hour pH monitorization in determining laryngeal problems related to GER have ranged between 17.5 and 78.8 percent. Technological ultrastructure required for 24-hour pH monitorization, higher cost of the technique, procedure-related discomfort felt by the patient, potential problems in the placement of the probe, loss of mucosal contact, displacement of the probe, changes in pH due to oral intake, intermittent drying and wetting of the proximal probe are among the main culprits for the false predictive test results. Besides inability to obtain similar results in recurrent tests performed at different time intervals has been cited as disadvantages of this test.[8,10,14-16]

As an innovative diagnostic tool, Dx pH probe has been designed quite differently from conventional pH probes. Its teardrop-shaped sensor tip (conventional probes has a side-sensor) can function in the pharyngeal cavity without any risk of desiccation. Vapour condensation during expiration keeps the sensor humidified. Thus, false measurements due to drying up in the probe have been minimalized when compared with dual-channel pH monitorization. Hydrogen ion concentration measurement system encased in its electrode can evaluate refluxate material both in gaseous and liquid forms and also it can more reliably detect pseudoreflux events which cannot be discerned during dual-channel 24-hour pH monitorization studies. Thanks to this new technology, oropharyngeal pH values can be measured 2 times per second. Also it appears to be a superior technique

over 24-hour esophageal pH monitorization which can only measure pH at every 3-4 seconds. Placement of the probe can be observed with naked eye at the level of uvula which completely obviates the possibility of erroneous implantation of the probe. Although, debates about the exact positioning of 24-hour pH monitorization probe still continue, displacement of the probe after its implantation cannot be predicted beforehand which might lead to erroneous results. When data retrieved from Dx pH probe are transferred into a computerized system, any desired value can be determined as a baseline pH and relevant calculations can be performed.[3-6,17-20] In an investigation performed on 55 asymptomatic volunteers, Gloub et al.[5] reported parallelism between data obtained by Dx pH and standard dual-probe monitorization technique. In another study conducted in Emory University (Atlanta, 2007) Dx pH probe was compared to gold standard dual-probe 24-hour and detected mean pH measurements at the end of a 24-hour monitorization period (excl. meal and sleeping times) as 6.0 (standard dual-probe) and 7.0 (Dx pH probe). Dx pH probe successfully picked up 18 of 20 episodes of GER, while the remaining 2 episodes were detected by a standard probe. This phenomenon demonstrates that Dx pH probe provides reliable data related to LPR attacks.

Laryngeal mucosa is very vulnerable to acidic exposure and experimental studies have demonstrated that even one time exposure to acid refluxate can cause ulcerations in vocal cords.[21] However 24-hour pH monitorization is not sufficiently sensitive to detect these brief episodes of reflux. These observations can explain the reason for variable results obtained. In the literature various studies have proposed different criteria for the discrimination between physiologic and pathologic levels of LPR so as to decide for abnormal LPR at the laryngopharyngeal level. Some laboratories consider a single or two LPR attacks as pathologic and use their predetermined cut-off values for percentage of exposure times recorded under pH 4 conditions. In our study, a sudden and rapid deviation (0.5-2 secs) from the predetermined baseline pH was defined as a pH event. In the control group, 0.07% of the 24-hour monitorization, pH attacks were detected. This percentage indicates a statistically significant increase of 7.35% when compared with the patient group (p<0.05). Therefore in our study, normal cut-off values were predetermined and case studies were conducted in parallel with these outcomes. Using a multidisciplinary approach symptom scores, readings of reflux monitor and outcomes of empirical treatment are considered in combination so as to make the most appropriate approach to establish the diagnosis of LPR.

Another influential factor on the frequency of reflux is the potential gastric fluid regurgitation due to relaxation of the lower esophageal sphincter or increased intraabdominal pressure. Gastric contents, posture and gravitational forces are effective on this mechanism. As classical information, contrary to GER, in LPR, reflux events in the upright position are more numerous than those in the supine position. However in various studies contradictory outcomes have been reported. Ouatu-Lascar et al.[22] and Freidin et al.[23] reported higher number of reflux attacks in the upright position. Portale et al.[24] refuted existence of any correlation between reflux and supine or upright position. In our study, data obtained in upright and supine positions were recorded and evaluated separately without any statistically significant difference between these two groups as for number of pH events. In our study, acid exposure times were analyzed and differences between normal cases and patients were evaluated. In healthy cases, 24-hour monitorization test detected mean acid exposure time as 57.7 seconds. Even though some authors have reported that once daily exposure to acid reflux can induce ulceration in vocal cords, literature lacks sound information about the exact duration of the acid exposure which could induce mucosal damage.

As literature surveys reveal, RFS and RSI have been used separately for the diagnosis of LPR. Applicability and preferability in the diagnosis of LPR has been emphasized.[18,20] Still limited number of studies have applied monitorization with Dx pH probe to substantiate RFS and RSI findings for the establishment of LPR diagnosis. In our study, when clinical and physical examination, laryngeal endoscopy, together with application of RSI and RFS measurement tools before diagnosis and treatment of LPR were realized, pH measurements with Dx pH pharyngeal probe yielded significant diagnostic information favouring LPR.

Conclusion

This study has demonstrated that data obtained for LPR and the control groups by using RFS and RSI scoring systems suggest that monitorization with oropharyngeal probe can yield reliable diagnostic information leading to the diagnosis of LPR. Besides, thanks to this system, unnecessary drug use is avoided and an easily applicable diagnostic tool in the setting of outpatient clinics has been introduced. Improved patient compliance is its another advantage. In conclusion, addition of objective data to RSI and RFS test scores can ensure a better approach to diagnosis and treatment of LPR. In larger scale controlled

studies to be conducted in the future, this combined approach should be evaluated and relevant sensitivity and specificity studies should be performed.

Conflict of Interest: No conflicts declared.

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