Laryngeal and voice disorders in patients with gastroesophageal symptoms. Correlation with pH-monitoring[1]

Alterações laríngeas e vocais em pacientes com sintomas de refluxo gastroesofágico. Correlação com exame de phmetria

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ABSTRACT

PURPOSE: To investigate laryngeal and voice disorders in patients with gastroesophageal symptoms and their correlation with pH-monitoring.

METHODS: A prospective study was carried out in patients attended at the Voice Disorder Outpatient Clinics of Botucatu Medical School in a five-year period and had vocal and gastroesophagic symptoms. Patients underwent videolaryngoscopy, auditory-perceptual vocal analyses, computerized acoustic vocal analysis and dual probe pH-monitoring for 24 hours.

RESULTS: Fifty-seven patients were included (aged between 21 and 65 years; 45 women and 12 men), 18 had normal (31.6%) and 39 had abnormal pH-monitoring results (68.4%). Videolaryngoscopy recorded several laryngeal lesions for both patients with normal and abnormal pH-monitoring, but mostly for the latter group, highlighting posterior pachyderma. Auditory-perceptual vocal assessments identified vocal changes of several intensities for both groups but especially for patients with abnormal pH-monitoring results. All acoustic parameters, except f0, were abnormal for both groups, compared to the control population.

CONCLUSION: Acoustic and perceptual vocal changes and laryngeal lesions were recorded for both patients with normal pH-monitoring results and patients with abnormal pH-monitoring results, evidencing the importance of clinical history and videolaryngoscopic findings for diagnosing acid laryngitis.

Key words: Gastroesophageal Reflux. Dysphonia. Larynx. Voice.

RESUMO

OBJETIVO: Investigar as alterações laríngeas e vocais em pacientes com sintomas de refluxo gastroesofágico e correlacioná-las com o exame de phmetria.

MÉTODOS: Estudo prospectivo que incluiu os pacientes atendidos nos ambulatórios de Distúrbios da Voz da Faculdade de Medicina de Botucatu no período de cinco anos com sintomas vocais e gastroesofágicos. Os pacientes foram submetidos à videolaringoscopia, às análises vocais perceptivo-auditivas, a analise vocal acústica computadorizada e ao exame de pHmetria de dois canais com monitorização durante 24 horas.

RESULTADOS: Foram incluídos 57 pacientes (entre 21 a 65 anos; 45 mulheres e 12 homens). Desses, 18 apresentavam pHmetria normal (31,6%) e 39 alterada (68,4%). As videolaringoscopias registraram diversas lesões laríngeas tanto nos pacientes com pHmetria normal como alterada, sendo mais relevantes neste último grupo, destacando-se a paquidermia posterior. As avaliações vocais perceptivo-auditivas identificaram alterações vocais de diversas intensidades em ambos os grupos, mais importantes nos pacientes com pHmetria alterada. Todos os parâmetros acústicos, exceto Fo, mostraram-se alterados em ambos os grupos, quando comparados aos controles.
CONCLUSÕES: Alterações vocais perceptivas e acústicas, e lesões laríngeas foram registradas tanto nos pacientes com phmetria normal como alterada, sinalizando para a importância da historia clínica e dos achados videolaringoscópicos no diagnóstico das laringites ácidas.
Descritores: Refluxo Gastroesofágico. Disfonia. Laringe. Voz.

Introduction

Gastroesophageal reflux affects 20 to 40% of the population, leading to highly frequent otolaryngological symptoms such as postnasal and pharyngeal secretion, hoarseness, dysphagia, nocturnal laryngospasm, otalgia, chronic cough, sensation of a "ball" in the throat and bronchopneumonia[1-3]. Voice disorders have been emphasized for their presence among 50% patients with gastroesophageal reflux symptoms[3].

During videolaryngoscopy, the most important changes for acid laryngitis have been: erythema and pachyderma in posterior glottis, edema and hyperemia of vocal folds, vocal nodules, pseudosulcus, cyst, polyp, hyperplasia of postcricoid mucosa, contact ulcer, erythema and/or edema of tracheobronchial tree segments, granuloma in posterior glottis and larynx secretion[4]. Some authors have also recorded functional disorders, in which the phonatory dynamics is compromised by acid reflux, including mucus propulsion retardation, aperiodic muco-undulatory movement, signs of muscular tension with hypercontraction of ventricular folds, irregular vibration of the mucosa of vocal folds and glottal closure. Such alterations peak with impaired vocal quality and justify the dysphonia shown by these patient[5].

Several changes in the vocal characteristics can be diagnosed during speech assessments, sometimes early by means of auditory-perceptual and computerized acoustic analyses. The benefits of these analyses have been proved for GERD patients with vocal symptoms. Ross *et al.*[5] recorded increased musculoskeletal tension, abrupt vocal attack and varied degrees of dysphonia in auditory-perceptual analyses. As to acoustic measures, those authors did not notice changes in the fundamental frequency (f0) but found higher shimmer values, justifiable by the possible presence of laryngeal lesions like laryngeal edema, pseudosulcus and nodule. These lesions change the mass and the tension of vocal folds, influencing their vibration pattern and time, important prerequisites to control vocal intensity.

The laryngeal mucosa is known to be more sensitive to acid reflux than the esophageal mucosa since the esophagus has its own peristalsis, epithelium covered by a layer of keratin and is permanently bathed with secretions rich in bicarbonate, which give the mucosa higher protection[6]. The larynx, devoid of such protective agents, becomes more vulnerable to lesions, usually diagnosed even for patients with normal endoscopic and pH-monitoring results.

The pH-monitoring is considered the gold standard test for diagnosing the acid reflux disease[1,7]. It employs a dual probe, one of them positioned in the hypopharynx and the other one in the esophagus. Records are considered pathological when pH values are inferior to 4 at a frequency higher than 0.1% of the total measures performed during 24 hours[7]. However, some patients who are dysphonic and have relevant gastroesophageal symptoms have shown pH-monitoring results within normal patterns, raising doubts about the specificity of this test for diagnosing acid laryngitis.

The aim of this study was to analyze videolaryngoscopic changes, vocal characteristics and their correlation with pH-monitoring results in dysphonic patients with gastroesophageal symptoms.

Methods

This prospective study included patients who were attended at the Voice Disorder Outpatient Clinics of Botucatu Medical School between 2006 and 2011 and had permanent dysphonia associated with gastroesophageal symptoms at a frequency equal or superior to twice a week including heartburn, burning sensation, acid reflux, epigastric pain and satiation. All patients filled the study protocol containing detailed questions about their voice. Then, they underwent videolaryngoscopy by means of a multifunctional system with image capturing (model Eco X-30-TFT/USB, Germany), attached to a 70º rigid

telescope, 8 mm (Asap, Germany), and stroboscopic light source (Atmos, Germany), with image record in a DVD. They were also subjected to auditory-perceptual vocal analyses using GRBASI scale and computerized acoustics (Multi-speech 3700, MDVP, Kaypentax, USA) by skilled speech therapists. Acoustic measures were obtained from the sustained emission of vowel /a/ at basal frequency and intensity during three seconds. The analyzed acoustic parameters were: fundamental frequency (f0), jitter, PPQ, shimmer, APQ, SPI and NHR. Results were compared to those of patients without vocal or gastroesophageal symptoms and with adequate vocal quality according to auditory-perceptual analysis. The study was approved by the Human Research Ethics Committee of Botucatu Medical School (protocol 493/08),

Finally, patients underwent dual-channel pH-monitoring during 24 hours. They were instructed to suppress, one week prior to the test, antacid medicines and proton-pump inhibitors, as well as acid food and juice during the investigation. To introduce the dual conductor of the pH-monitoring probe (model AL-2, Alacer Biomédica, Brazil), patients received topic anesthesia with gel xylocaine in the nasal cavity. The upper probe was kept in the hypopharynx region, at 25 cm from the lower esophageal sphincter (LES), while the lower probe was kept at five cm above the former. pH-monitoring was kept for 24 hours, recording the number of reflux episodes and the percentage of times pH was inferior to 4, according to DeMeester score[7]. Results were classified as normal when the recorded values were inferior to 14.7 associated with absence of reflux at the proximal sensor.

Excluded from the study were carriers of neurologic, autoimmune, respiratory or endocrine diseases that might compromise laryngeal mucosae or vocal quality, as well as patients with history of prolonged tracheal intubation or laryngeal microsurgery.

Statistical analysis

For the results of videolaryngoscopic test, acoustic and perceptual-auditory vocal analysis and pH-monitoring, Student's t test was employed, considering 5% significance level.

Results

The study population totaled 57 adult patients aged between 21 and 65 years (average of 43 years) and included 45 women (78.9%) and 12 men (21.1%). pH-monitoring was normal for 18 (31.6%) and abnormal for 39 (68.4%) of those patients. Tabagism was reported by 15 patients (n-2, normal pH-monitoring group; n-13, abnormal pH-monitoring group).

Vocal abuse was identified for 33 patients (57.8%; n-12, normal pH-monitoring group; n-21, abnormal pH-monitoring group). Investigation relative to the profession of these patients detected some classes of professionals with high phonatory demand, which are shown in Figure 1, highlighting the largest number of teachers which corresponded to 13 patients (n-7, normal pH-monitoring group; n-6, abnormal pH-monitoring). Among the remaining professions are: sellers (n-8), traders (n-8), secretaries (n-3) and a pastor (n-1).

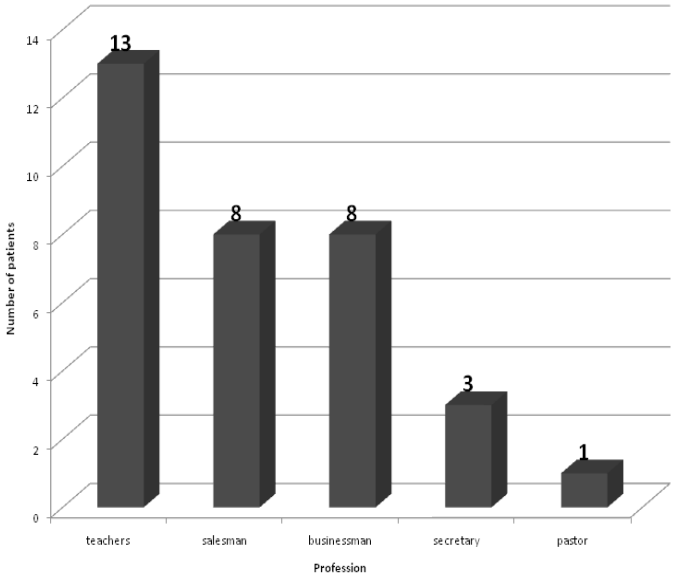

FIGURE 1 - Profession of patients with vocal abuse.

Videolaryngoscopy indicated several laryngeal lesions for both patients with normal pH-monitoring results and patients with abnormal pH-monitoring results, as shown in Table 1, with emphasis on pachyderma in posterior commissure. More than one change was detected in the videolaryngoscopic test for some patients of both groups. Patients with abnormal pH-monitoring results had a larger number of lesions; however, in 31% cases patients with normal pH-monitoring results reported gastroesophageal symptoms and had laryngeal lesions identified by videolaryngoscopy. Some of the major laryngeal lesions diagnosed for such patients are illustrated in Figures 2 to 4.

TABLE 1 - Correlation between videolaryngoscopic findings and pH-monitoring.

Videolaryngoscopic findings	Normal pH-monitoring N (%)	Abnormal pH-monitoring N (%)	p value
Posterior pachyderma	11 (19.30)	14 (24.56)	0.075
Absence of lesions	0 (0.00)	4 (7.01)	0.18
Reinke's edema	0 (0.00)	4 (7.01)	0.18
Polyps	2 (3.50)	3 (5.26)	0.67
Nodules	2 (3.50)	3 (5.26)	0.67
Edema /hyperemia	1 (1.76)	3 (5.26)	0.77
Pseudosulcus	1 (1.76)	2 (3.50)	0.94
Posterior granuloma	1 (1.76)	1(1.76)	0.57
Leukoplasia	0 (0.00)	1(1.76)	0.49
Leukoplasia + edema	0 (0.00)	1(1.76)	0.49
Pachyderma + edema	0 (0.00)	1(1.76)	0.49
Pachyderma + nodules	0 (0.00)	1(1.76)	0.49
Pachyderma + cyst	0(0.00)	1(1.76)	0.49
Total	**18 (31.58)**	**39 (68.42)**	

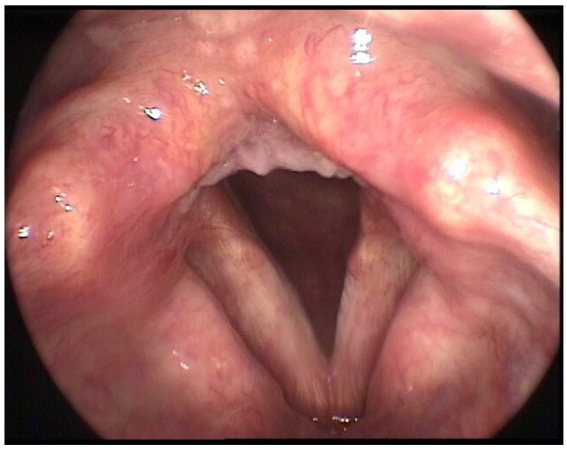

FIGURE 2 - Posterior pachyderma (arrow).

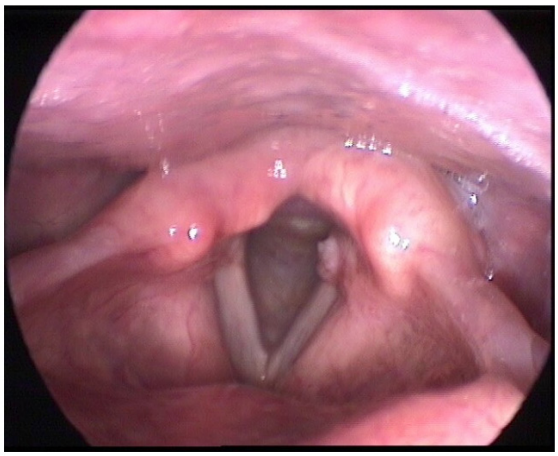

FIGURE 3 - Granuloma in left vocal fold (arrow).

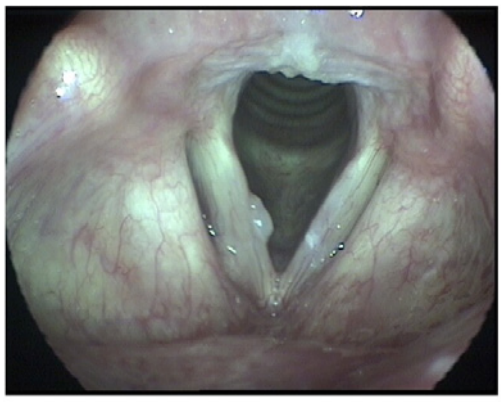

FIGURE 4 - Polyp in right vocal fold (arrow) and posterior packyderma.

According to the results of auditory-perceptual vocal tests shown in Table 2, which also include pH-monitoring results and videolaryngoscopic findings, the highest GRBASI scores were recorded for patients with abnormal pH-monitoring results, the largest number of whom had scores 1 and 2 (G2, p-0.04), corresponding to carriers of laryngeal lesions such as Reinke's

edema, polyp and posterior pachyderma, in addition to associated lesions.

TABLE 2 - Correlation among GRBASI scores, videolaryngoscopic findings and pH-monitoring.

pH-monitoring X GRBASI score	Normal pH-monitoring				Abnormal pH-monitoring			
Videolaryngoscopic findings	G0	G1	G2*	G3	G0	G1	G2*	G3
Absence of lesions	0	0	0	0	2	1	1	0
Posterior pachyderma	0	8	3	1	0	7	6	1
Nodules	0	2	0	0	0	2	1	0
Polyps	0	1	1	0	0	0	2	1
Reinke's edema	0	0	0	0	0	1	2	1
Leukoplasia	0	0	0	0	0	1	0	0
Pseudosulcus	0	1	0	0	0	0	1	1
Posterior granuloma	0	0	1	0	0	0	1	0
Edema /hyperemia	0	0	0	0	0	1	2	0
Pachyderma + edema	0	0	0	0	0	1	0	0
Leukoplasia + edema	0	0	0	0	1	0	0	0
Pachyderma + nodules	0	0	0	0	1	0	0	0
Pachyderma + cyst	0	0	0	0	1	0	0	0
Total	**0**	**12**	**5**	**1**	**5**	**14**	**16**	**4**
***p - 0.04**								

The acoustic parameters of dysphonic patients with normal pH-monitoring results and abnormal pH-monitoring results, respectively, were compared to those of the control population of both sexes, as shown in Tables 3 and 4. Both patients with normal pH-monitoring results and patients with abnormal pH-monitoring results had acoustic parameter values far from the standard values, especially for jitter, shimmer, PPQ, APQ and SPI.

TABLE 3 - Correlation between mean and standard deviation (SD) of acoustic parameters for patients with normal pH-monitoring results and controls of both sexes.

Acoustic parameters	Normal pH-monitoring Male	Controls Male	p value	Normal pH-monitoring Female	Controls Female	p value
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
f0	134.8 ±41.276	129±32.224	0.77	198.0±30.094	210.7±28.1	0.008
% jitter	2.163 ±1.512	0.563±0.266	0.002	2.304 ±1.603	0.678±0.469	<0.001
% PPQ	1.265 ±0.894	0.326±0.137	0.002	1.429 ±1.118	0.392±0.273	<0.001
% shimmer	5.105±4.136	2.379±0.967	0.041	4.866 ±4.29	2.203±0.841	0.005
APQ	3.558 ±2.791	1.831±0.696	0.045	3.575 ±3.232	1.555±0.546	0.004
NHR	0.189 ±0.094	0.128±0.021	0.039	0.164 ±0.123	0.114±0.018	0.064
SPI	31.725±18.094	13.960±5.701	0.005	19.329 ±16.082	8.050±3.861	0.002

TABLE 4 - Correlation between mean and standard deviation (SD) of acoustic parameters for patients with abnormal pH-monitoring results and controls of both sexes.

Acoustic parameters	Abnormal pH-monitoring	Controls	p value	Abnormal pH-monitoring	Controls	p value
	Male			Female		
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
f0	134 ±25.192	129±32.224	0.72	188.4 ±36.377	210.7±28.1	0.014
% jitter	2.456 ±1.825	0.563±0.266	0.002	2.176 ±1.373	0.678±0.469	<0.001
% PPQ	1.497 ±1.173	0.326±0.137	0.003	1.284 ±0.890	0.392±0.273	<0.001
% shimmer	6.995 ±5.181	2.379±0.967	0.007	4.696 ±3.033	2.203±0.841	<0.001
APQ	4.916 ±3.304	1.831±0.696	0.006	3.374 ±2.278	1.555±0.546	<0.001
NHR	0.195 ±0.0944	0.128±0.021	0.025	0.149 ±0.056	0.114±0.018	0.007
SPI	19.223 ±10.079	13.960±5.701	0.14	19.353 ±14.752	8.050±3.861	<0.001

According to the comparison of acoustic parameters between patients with normal pH-monitoring results and those with abnormal pH-monitoring results, shown in Table 5, none of the assessed parameters showed statistical difference between the study groups.

TABLE 5 - Mean and standard deviation (SD) among acoustic parameters for patients with abnormal and patients with normal pH-monitoring results.

Acoustic parameters	Abnormal pH-monitoring			Normal pH-monitoring		
	Mean ± SD Male	Mean ± SD Female	p value	Mean ± SD Male	Mean ± SD Female	p value
f0	134 ±52.036	189 ±36.792	<0.001	140 ±45.595	198 ±30.094	0.002
% jitter	2.456 ±2.012	2.166 ±1.394	0.65	2.163 ±1.512	2.304 ±1.603	0.87
% PPQ	1.497 ±1.301	1.284 ±0.904	0.60	1.265 ±0.894	1.429 ±1.118	0.77
% shimmer	6.995 ±5.324	4.696 ±3.083	0.12	5.105±4.136	4.866 ±4.29	0.92
APQ	4.916 ±3.672	3.387 ±2.314	0.14	3.558 ±2.791	3.575 ±3.232	0.99
NHR	0.167 ±0.115	0.149 ±0.056	0.09	0.189 ±0.094	0.164 ±0.123	0.69
SPI	19.223 ±10.201	19.398 ±14.993	0.98	31.725±18.094	19.329 ±16.082	0.17

Discussion

Gastroesophageal reflux disease affects approximately 10 to 15% of the population and deserves attention since it evolves with esophageal and extraesophageal symptoms. The latter include otolaryngological symptoms, as well as chronic cough, globus sensation in the throat, secretion in the pharynx, gagging, dysphagia, laryngospasm and dysphonia[1-3,4,8].

The diagnosis of gastroesophageal reflux disease (GERD) requires highly detailed clinical history while complimentary tests, commonly requested, include upper gastrointestinal endoscopy, electromanometry and 24-hour dual channel pH-monitoring. The latter has been highlighted by most authors, among the remaining tests, due to its accuracy for diagnosis[1,7]; others, however, have stated that not even this test is decisive for GERD diagnosis, usually requiring therapeutic test for proving[9]. There are several arguments such as the position of probes installed in pH-monitoring, since the closer the pharyngeal probe is to the upper esophagic sphincter, the larger is the number of acidity cases. For patients with otolaryngological and gastroesophageal symptoms and with videolaryngoscopic changes characteristic of laryngeal reflux, the diagnosis of acid laryngitis leaves few doubts, even for those with normal pH-monitoring results, as noted for 30% of the patients in this study.

The main videolaryngoscopic findings for patients with acid laryngitis are hyperemia of vocal folds, edema, hyperplasia of lymphoid tissues in the base of the tongue, erosions of mucosae, granulomas, leukoplasia, epithelial thickness, polyps, nodules, and others[4,8-10]. A large number of these lesions were recorded in the present study, highlighting pachyderma of posterior glottis (Figures 2 and 3). For some patients, more than one laryngeal lesion was diagnosed, almost always associated with pachyderma (Figure 4). This lesion is a frequent endoscopic finding for patients with gastroesophageal symptoms and seems to correspond to the site first exposed to acid reflux. For some patients, pachyderma precedes the emergence of other laryngeal lesions.

We believe that some lesions detected in acid laryngitis must be carefully interpreted since they can be identified even in patients without gastroesophageal symptoms. However, the close relationship between laryngeal lesion and acid reflux was previously demonstrated by some experimental studies in which the laryngeal mucosa of animals received direct irrigation of hydrochloric acid and histologically showed marked changes in its coverage[11].

Another point to be considered is that several laryngeal lesions diagnosed for patients with reflux may worsen with the exposure to other aggressor agents such as tabagism, inhaling pollutants, recurrent rhinitis and vocal abuse. For chronic smokers, Reinke's edema and leukoplasia are frequently diagnosed, keeping a direct relationship with the smoking habit. A large number of these patients, however, also have inappropriate feeding habits such as excessive ingestion of caffeine and alcoholic beverages, which further stimulate episodes of gastroesophageal reflux, closing thus a vicious circle.

Of the patients with abnormal pH-monitoring results in this study, four did not have laryngeal lesions although they were dysphonic. These findings reinforce the importance of a multidisciplinary approach in vocal analyses. Thus, vocal assessments may identify functional phonatory deviations which precede the emergence of mucosal lesions. The auditory-perceptual vocal analysis in this study identified vocal deviations of varied degrees, for both patients with abnormal pH-monitoring results and patients with normal pH-monitoring results, although it was less relevant for the latter.

Results of acoustic vocal analyses for both patients with normal pH-monitoring results and patients with abnormal pH-monitoring results are summarized in Tables 3, 4 and 5. Most acoustic parameters assessed for both groups were abnormal compared to those of the control group, especially for women. The comparison of acoustic measures for patients with normal or abnormal pH-monitoring results, shown in Table 5, indicated that the values behaved very similarly for both groups, without statistical difference. Oguz *et al.*[12] carried out acoustic vocal analysis for 48 patients with symptoms of gastroesophageal reflux (25 with abnormal pH-monitoring results – named objective, and 23 with normal pH-monitoring results, named symptomatic) and compared these data with values obtained for a control group composed of 64 volunteers. Those authors observed significant changes in the acoustic parameters of frequency disorder measures for both patients with abnormal pH-monitoring results and patients with normal pH-monitoring results, compared to controls, corroborating the results of the present study. High acoustic measures were also recorded by Pribuisiene *et al.*[13] for 108 patients with diagnosis of GERD and 90 controls, highlighting for men, respectively, percentage of jitter (0.25±0.13 versus 0.18±0.04) and percentage of shimmer (2.39±1.31 versus 1.57±0.59). For women, the comparative values of such parameters were, respectively: percentage of jitter (0.36±0.44 versus 0.18±0.05) and percentage of shimmer (2.19±0.99 versus 1.47±0.44). The values of f0 were similar to those for patients of the control group of both sexes. Those same authors also found important vocal changes in the auditory-perceptual analyses for patients with GERD. For Selby

et al.[14], treatment with proton-pump inhibitors for at least eight weeks may enhance vocal improvement, as observed for 44% of their patients.

Conclusion

Acoustic and perceptual vocal changes and laryngeal lesions were recorded for both patients with normal pH-monitoring results and patients with abnormal pH-monitoring results, evidencing the importance of clinical history and videolaryngoscopic findings for diagnosing acid laryngitis.

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