GASTROESOPHAGEAL REFLUX DISEASE AND VOCAL DISTURBANCES

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ABSTRACT – *Context* - Gastroesophageal reflux disease is a chronic disease in which gastroduodenal contents reflux into the esophagus. The clinical picture of gastroesophageal reflux disease is usually composed by heartburn and regurgitation (typical manifestations). Atypical manifestations (vocal disturbances and asthma) may also be complaint. *Objective* – To analyse the clinical, endoscopic, manometric and pHmetric aspects of patients suffering from gastroesophageal reflux disease associated with vocal disturbances. *Methods* - Fifty patients with gastroesophageal reflux disease were studied, including 25 with vocal disturbances (group 1 – G1) and 25 without these symptoms (group 2 – G2). All patients were submitted to endoscopy, manometry and esophageal pHmetry (2 probes). The group 1 patients were submitted to videolaryngoscopy. *Results* - Endoscopic findings: non-erosive reflux disease was observed in 95% of G1 patients and 88% of G2. Videolaryngoscopy: vocal fold congestion, asymmetry, nodules and polyps were observed in G1 patients. Manometric findings: pressure in the lower esophageal sphincter (mm Hg): 11.6 ± 5.2 in G1 and 14.0 ± 6.2 in G2 ($P = 0.14$); pressure in the upper esophageal sphincter (mm Hg): 58.4 ± 15.9 in G1 and 69.5 ± 30.7 in the controls. pHmetric findings: De Meester index: 34.0 ± 20.9 in G1 and 15.4 ± 9.4 in G2 ($P<0.001$); number of reflux episodes in distal probe: 43.0 ± 20.4 in G1 and 26.4 ± 17.2 in G2 ($P = 0.003$); percentage of time with esophageal pH value lower than 4 units (distal sensor): 9.0% ± 6.4% in G1 and 3.4% ± 2.1% in G2 ($P<0.001$); number of reflux episodes in proximal probe: 7.5 ± 10.9 in G1 and 5.3 ± 5.7 in G2 ($P = 0.38$); percentage of time with esophageal pH values lower than 4 units (proximal probe): 1.2 ± 2.7 in G1 and 0.5 ± 0.7 in G2 ($P = 0.21$). *Conclusions* - 1) The clinical, endoscopic, and manometric findings observed in patients with vocal disturbance do not differ from those without these symptoms; 2) gastroesophageal reflux intensity is higher in patients with vocal disturbance; 3) patients without vocal disturbance can also present reflux episodes in the proximal probe.

HEADINGS - Gastroesophageal reflux. Voice disorders.

INTRODUCTION

In gastroesophageal reflux disease (GERD), a high prevalence digestive affliction, the gastroduodenal contents leak back into the esophagus and can reach beyond it, go through the upper esophageal sphincter (UES) and reach the aero-digestive airways[4, 20, 28]. Such an episode is called laryngopharyngeal reflux[9, 22].

The larynx, an important organ responsible for phonation, can be injured in this situation, resulting in a process called acid laryngitis, described by Cherry and Margulies[3] in 1968. The clinical manifestation is voice disorder[24] that affect life quality as they reduce the speaker's communicative effectiveness.

Besides GERD, other factors affect the voice considerably, with the most important being smoking, drinking, voice abuse, allergy, asthma, air conditioning and addiction to drugs, especially marijuana[18, 28, 32].

Two mechanisms have been mentioned in the etiopathogenesis of injured organs in the aero-digestive airways, most importantly the direct contact of refluxed material with the larynx[32].

According to Koufmann[13], laryngeal epithelium is 100 times more sensitive than the esophagus. Therefore, the reflux of small amounts of gastric secretion containing hydrochloric acid, pepsin and other digestive enzymes is sufficient to cause serious lesions in the larynx[23].

Another aspect to be considered is the fact that the larynx is practically defenseless given that its only defense mechanism is the UES. On the other hand, the esophagus has several defense mechanisms including peristalsis, the mucous barrier, bicarbonate production, and the LES[13].

The second mechanism that produces larynx inflammatory process is chemoreceptor stimulation resulting from refluxed material from the stomach, with vagal reflexes followed by coughing and throat clearing.

The prevalence of extra esophageal manifestations related to GERD is unknown. It is estimated that 4%

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to 10% of the patients that seek otorhinolaryngologic service show symptoms of this disease[12].

This paper aimed to analyze the clinical, endoscopic, manometric and pHmetric aspects of patients with GERD and vocal disturbances and to compare them with chronic refluxers without these symptoms.

METHODS

In this retrospective survey, 50 patients with GERD divided into groups of 25 each were studied. They had the following characteristics: Group 1 (G1): patients with typical symptoms of GERD and vocal disturbance (hoarseness, voice failure), being 3 men and 22 women, age varying from 24 to 68 years (average 46.8 ± 12.1 years). Group 2 (G2): 9 men and 16 women with GERD symptoms but without dysphonia (controls), mean age 39.1 ± 10.7 (extremes of 15 and 54 years).

Inclusion criteria: females or males, ranging in age from 15 to 70 years, suffering from GERD with or without dysphonia (G1 and G2, respectively).

Exclusion criteria: patients under 15 and above 70 years, pregnant women, alcoholics, smokers, and individuals with systemic diseases that affect esophageal motor activity.

After the agreement of the research project by the Ethical Committee on Research from our hospital (Of. n° 020/2010), the patients from both groups were submitted to endoscopic, manometric, and pHmetric esophagus exams to confirm GERD diagnostic.

Individuals with dysphonia were submitted to pharyngolaryngoscopy, carried out by an otorhinolaryngologist, responsible of the Voice Disturbances Ambulatory. Patients from G2 (controls) did not undergo this exam based on an instruction from the Ethics Committee.

- Endoscopy
  After a clinical evaluation, 10-hour fast, and oropharyngeal topical anesthetic with 10% xylocaine spray, the patients were submitted to high digestive endoscopy using Olympus flexible endoscopic video. The exam was performed with the patient in left lateral decubitus. Esophageal mucosa lesions were evaluated using Savary and Miller[25] classification.
- Esophageal manometry
  Esophageal manometry was performed using the usual technique of our laboratory[7] which included an 8-channel probe, physiographic process and continuous infusion device. Through the analysis of the graphic records the following parameters were evaluated: lower and upper sphincter resting pressure of the esophagus (LES, UES) and its peristalsis.
- Esophageal 24-hour pH study
  A pH catheter of two probes was passed transnasally into the previously anesthetized (xylocaine gel) patients after 24–hour fast and 1-week suspension of proton pump inhibitors. The patients were guided to avoid acid food and juices ingestion during the investigation. The distal probe was positioned 5 cm above LES, and

the proximal probe near the UES. The patient was examined at home for 24 hours[6, 12]. The following parameters were evaluated: number of reflux episodes and percentage of time in which the esophageal pH showed values below 4 units in the two probes and the De Meester index.
- Videolaryngoscopy
  The flexible device (Olympus) was introduced nasally into the patients after 12-hour fast and topic anesthesia with 10% xylocaine spray. The patient was seated. This exam permitted evaluation of vocal folds, pharynx, larynx and arytenoids (Figures 1, 2 and 3, Table 1).
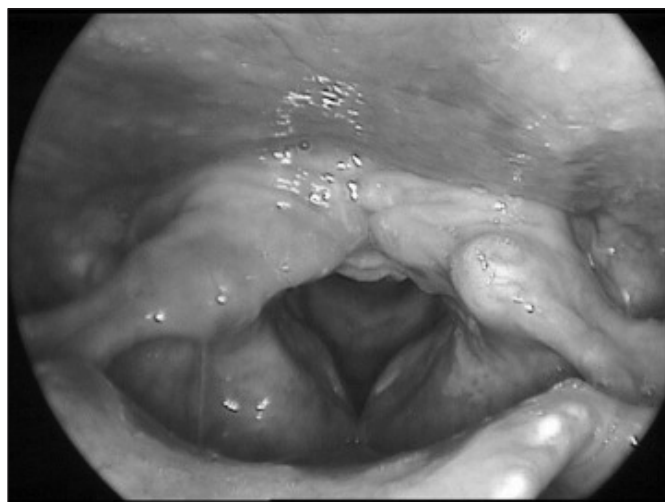- Statistical analysis

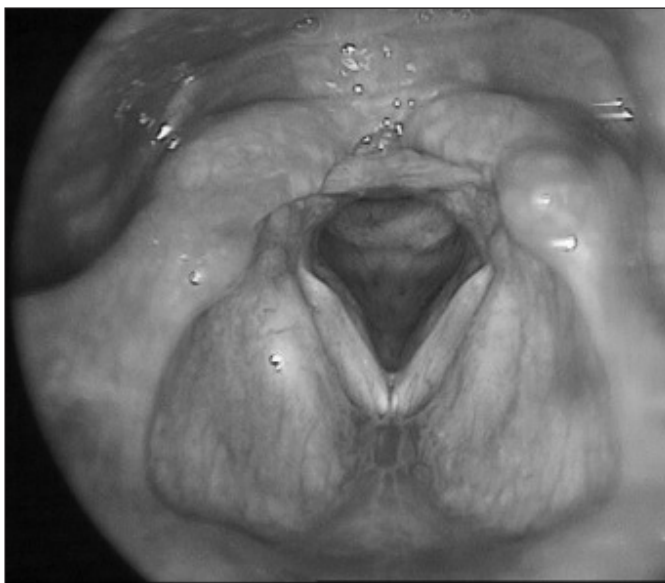FIGURE 1. Edema, packydermia and mucosal thickening of vocal folds and posterior glottis

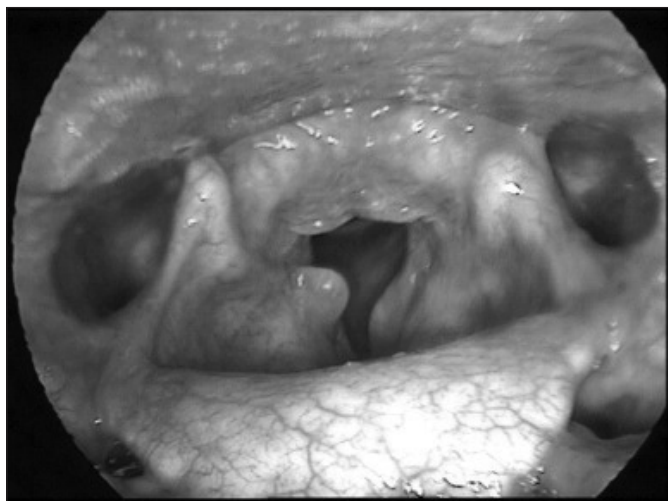
FIGURE 2. Edema in vocal fold, pachydermia inter-aritenoid

FIGURE 3. Polyp in right vocal fold; Reinke's edema in left vocal fold edema and pachydermia in posterior glottis

TABLE 1. Findings observed during pharyngolaryngoscopy

Findings	n
Edema / VF congestion	10
Pachydermia - arytenoid	6
Node in VF	5
Edema in arytenoids	4
Cyst in VF	2
Atrophy in VF	2
Polyp in VF	1
Asymmetry in VF	1

VF: vocal fold

To study the association between qualitative variables, the Chi-square test was used. Student t test was used for comparison of the quantitative variables. The significance level was 5%.

RESULTS

Hoarseness was the most frequently observed vocal disturbance among G1 patients and lasted between 6 months and 20 years (average 3.3 ± 1.6 years) followed by voice failure, referenced by 14 patients (average 1.6 ± 3.3 years). All G1 patients also reported pyrosis, with a mean duration of 9.1 ± 8.5 years. In the control group pyrosis lasted an average of 7.6 ± 6.8 years. The two groups did not differ significantly as to pyrosis duration ($P = 0.51$) (Table 2).

In relation to gender, there was a greater number of females in G1 than in G2 ($P = 0.047$) (Table 2).

High digestive endoscopy revealed similar findings in both groups. Non-erosive reflux (normal mucous relief) was observed in 95% of G1 patients and in 88% of G2 patients ($P = 0.53\%$). Hiatal hernia was diagnosed in 65% of the patients with vocal disturbance and in 60% of controls ($P = 0.77$). The hiatal hernia diagnostic was validated when epithelial transition (the Z line) was found 2 cm above the diaphragmatic crura[25]. The gastric retroversion maneuver showed cardiac orifice incompetence in 70% of G1 and in 60% of G2 patients, with no significant difference ($P = 0.54$).

The esophageal motor activity was studied in all the patients. The average pressure in the LES in individuals with dysphonia was of 11.6 ± 5.2 mm Hg, with no significant difference in relation to controls (14.0 ± 6.2 mm Hg; $P = 0.14$). A similar result was observed for UES with mean values of 58.4 ± 15.9 mm Hg for G1 and 69.5 ± 30.7 mm Hg for the controls. The esophageal body showed no motor

TABLE 2. Mean and standard deviation of the studied parameters in the two groups, for clinical, manometric and pHmetric findings

Parameter	Groups		P Value
	1	2	
Female	88%	64%	0.047
Age	46.8 ± 12.1	39.1 ± 10.7	0.02
Heartburn	9.1 ± 8.5	7.6 ± 6.8	0.51 NS
LES	11.6 ± 5.2	14.0 ± 6.2	0.14 NS
UES	58.4 ± 15.9	69.5 ± 30.7	0.11 NS
De Meester index	34.0 ± 20.9	15.4 ± 9.4	<0.001
Distal probe			
Number of reflux	43.0 ± 20.4	26.4 ± 17.2	<0.003
% time pH<4	9.0 ± 6.4	3.4 ± 2.1	<0.001
Proximal probe			
Number reflux	7.5 ± 10.9	5.3 ± 5.7	0.38 NS
% time pH<4	1.2 ± 2.7	0.5 ± 0.7	0.21 NS

LES = lower esophageal sphincter
UES = upper esophageal sphincter

disturbance in either group. The contraction amplitude in the distal third of the esophagus was 69.5 ± 25.7 mm Hg in voice disturbance patients and 70.0 ± 29.2 mm Hg ($P = 0.94$) in the controls (Table 2).

The prolonged esophageal pHmetry revealed that the De Meester index among dysphonia patients (34.0 ± 20.9) was higher than among controls (15.4 ± 9.4; $P<0.001$). A similar result was found concerning the number of acid reflux episodes in the distal probe, being 43.0 ± 20.4 in the individuals with dysphonia and 26.4 ± 17.2 in the controls ($P < 0.003$). The distal probe also showed that the percentage of time in which the esophageal pH values were lower than 4 units was greater among patients with dysphonia ($9.0\% \pm 6.4\%$) than among controls ($3.4\% \pm 2.1\%$), with significant difference ($P<0.001$). The proximal probe did not show significant differences. The number of reflux episodes in G1 patients was 7.5 ± 10.9 versus 5.3 ± 5.7 in the controls ($P = 0.38$). Time percentage with esophageal pH below 4 units was 1.2 ± 2.7 in G1 and 0.5 ± 0.7 in the controls ($P = 0.21$) (Table 2).

Videolaryngoscopy revealed alterations in the vocal folds in the majority of patients. The most common modifications were: congestion, atrophy, asymmetry, nodules, cysts, and polyps. Pachydermia and edema in arytenoids were other disturbances evaluated by this exam (Table 1; Figures 1, 2 and 3).

DISCUSSION

In this retrospective study the clinical, manometric and pHmetric aspects of the esophagus were evaluated in patients with GERD and dysphonia (G1) examined from January 2007 to December 2009. The findings were compared with the same parameters evaluated in chronic refluxers without voice disturbance (G2 – controls).

Group 1 patients were, at first, attended in the voice disturbance ward and then sent, as a routine practice, for gastroenterologic evaluation as they complained of pyrosis associated with hoarseness and voice failure.

Larynx direct exam showed lesions in the vocal folds (congestion, nodules, polyps) besides pakidermia and edema interarytenoideus, typical of reflux laryngitis[1, 21, 29].

Hicks et al.[8] carried out larynx endoscopic investigations of 105 normal volunteers and observed alterations on larynx in 86% of the casuistic. But, these authors did not exclude of the study, individuals using alcohol and tobacco, both factors that can cause lesions on larynx[18, 22, 32].

Female patients were more numerous among refluxers with dysphonia than in the control group ($P = 0.047$), as found by several authors[2, 14, 18, 30].

Patients with dysphonia were older (46.8 ± 12.1 years) than the controls (39.1 ± 10.7 years; $P = 0.02$), suggesting a longer time of aggression to larynx epithelium. However, statistical analysis showed no difference ($P = 0.51$) in relation to pyrosis duration between the two groups (9.1 ± 8.5 years and 7.6 ± 6.8 years).

Digestive endoscopy revealed that most of the patients with dysphonia (95%) did not present lesions in the esophageal epithelium (non-erosive reflux disease), corroborating other authors[13, 31]. Hiatal hernia, an important GERD pathogenic factor, was diagnosed in 65% of G1 patients and in 60% of G2 ($P = 0.77$), as also observed by Loffeld and Putten[16]. According to Koufman et al.[13], endoscopy is an excellent method to evaluate the esophagus. However, it is not the exam of choice for diagnosing laryngopharyngeal reflux. Our results are similar to findings of some other authors[14, 16].

Esophageal motor activity revealed that LES average pressure did not differ between patients with dysphonia and controls. These values were similar to the ones observed by Montenovo et al.[19] and Fouad et al.[5]. Somani et al.[27] reported a negative correlation between LES amplitude pressure and the esophagitis degree. According to these authors, non-erosive reflux disease individuals did not present hypotensive LES, as observed in the present study.

Knight et al.[11] studied 112 GERD patients with extra-esophageal manifestations. Hoarseness was the most prevalent as in the present casuistic. These authors reported esophageal dysmotility in 48% of patients with hoarseness. This finding differed from our casuistic in which the pressure amplitude in the distal third of the esophagus was 58.4 ± 15.9 mm Hg in dysphonic patients and none of them presented amplitude below 30 mm Hg in this esophageal segment (inefficient esophageal motility). This disagreement among findings might be related to exam methodology since the previous authors used a solid state pressure transducer, whereas we used a catheter with continuous infusion for the manometric study. In G2 patients, pressure amplitude in the esophageal distal third was of $70 + 29.2$ mm Hg, which does not differ from that of G1 ($P = 0.94$).

Pressure measurement in the UES did not differ from the one observed in the control group, with values similar to those published by Lemme et al.[15], who measured normal individuals. Given our expectation of finding lower indexes, it was surprising to find normal pressure values in individuals with hoarseness. In this situation, the refluxed content from the stomach would reach the larynx more easily, although no research shows this fact.

The results concerning the esophageal motor activity in the present study were similar to those of Shaker et al.[26] and Katz[10].

Pathologic gastroesophageal reflux was demonstrated by prolonged esophageal pHmetry in 88% of GERD patients with dysphonia, similar to levels found by other researchers[17, 31]. In the control group (without dysphonia), the exam positivity was 56%. In G1 patients, the De Meester index was higher than that observed in the control group ($P<0.001$). The number of reflux episodes and percentage of time with pH lower than four units in the distal probe, was higher in the group of dysphonic patients than among the chronic refluxers without voice disturbance ($P<0.003$ and $P<0.001$, respectively).

The seriousness of the gastroesophageal reflux explains the absence of clinical response when patients with dysphonia were submitted to the classic therapy with proton pump inhibitors. We observe that remission of symptoms occurs only after long-term treatment (8 weeks) administered twice a day.

No significant difference was observed between the groups as to pHmetric parameters recorded in the proximal probe ($P = 0.38$ for the number of reflux episodes and $P = 0.21$ for percentage of time with pH lower than 4 units). This result was not expected and no plausible explanation was found.

Of the 25 G1 patients studied, 10 actively use the voice because they are teachers. It is likely that GERD and voice abuse constituted a synergic cause, producing voice disturbance.

The conclusions of the present study are:
a) The clinical, endoscopic, and manometric findings observed in the patients with voice disturbance do not differ from those without these symptoms.
b) Gastroesophageal reflux is more serious in patients with dysphonia.
c) Patients without vocal disturbance can also present reflux episodes in the proximal probe.

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RESUMO – *Contexto* – A doença do refluxo gastroesofágico (DRGE) é uma doença crônica na qual o conteúdo gastroduodenal reflui para o esôfago. O quadro clínico da DRGE é usualmente referido como pirose e regurgitação (manifestações típicas). Manifestações atípicas (distúrbios da voz e asma) podem também ser referidas. *Objetivo* – Analisar os aspectos clínicos, endoscópicos, manométricos e pHmétricos de pacientes portadores da DRGE com distúrbios da voz. *Método* – Foram estudados 50 pacientes com a DRGE, sendo 25 com distúrbios da voz (grupo 1 – G1) e 25 sem estes sintomas (controles, grupo 2 – G2). Todos os pacientes foram submetidos a endoscopia, manometria e pHmetria esofágica (dois sensores). Os pacientes do G1 foram submetidos a videolaringoscopia. *Resultados* – Achados endoscópicos: DRGE não-erosiva foi observada em 95% dos pacientes de G1 e em 88% de G2. Videolaringoscopia: congestão das pregas vocais, assimetria, nódulos e pólipos foram diagnosticados nos pacientes do G1. Manometria esofágica: pressão no esfíncter inferior do esôfago (mm Hg): 11,6 ± 5,2 em G1 e 14,0 ± 6,2 em G2 ($P = 0,14$); pressão no esfíncter superior do esôfago (mm Hg): 58,4 ± 15,9 em G1 e 69,5 ± 30,7 nos controles. Achados pHmétricos: índice de DeMeester: 34,0 ± 20,9 em G1 e 15,4 ± 9,4 em G2 ($P<0,001$); número de episódios de refluxo no sensor distal: 43,0 ± 20,4 em G1 e 26, 4 ± 17,2 em G2 ($P<0,003$); percentagem do tempo com pH esofágico menor que 4 unidades (sensor distal): 9,0% ± 6,4% em G1 e 3,4% ± 2,1% em G2 ($P<0,001$); número de episódios de refluxo no sensor proximal: 7,5 ± 10,9 em G1 e 5,3 ± 5,7 em G2 ($P = 0,38$); percentagem de tempo com pH esofágico menor que quatro unidades (sensor proximal): 1,2% ± 2,7% em G1 e 0,5% ± 0,7% em G2 ($P = 0,210$). *Conclusões* – Os aspectos clínicos, endoscópicos e manométricos em pacientes com a DRGE e distúrbios da voz não diferem dos pacientes sem estes sintomas. A intensidade do refluxo gastroesofágico é maior nos pacientes com distúrbios da voz. Os pacientes sem distúrbios da voz podem também apresentar episódios de refluxo gastroesofágico no sensor proximal.

DESCRITORES – Refluxo gastroesofágico. Distúrbios da voz.

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