GASTROESOPHAGEAL REFLUX DISEASE AND VOCAL DISTURBANCES

Maria Aparecida Coelho de Arruda HENRY1, Regina Helena Garcia MARTINS2, Mauro Masson LERCO3, Lídia Raquel CARVALHO3 and Vânia Cristina LAMÔNICA-GARCIA4

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-erose 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 without vocal disturbance can also present reflux episodes in the proximal probe. 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 in 1968. The clinical manifestation is voice disorder 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.

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. According to Koufmann, 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.

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.

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%...
to 10% of the patients that seek otorhinolaryngologic service show symptoms of this disease\cite{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\cite{25} classification.

**Esophageal manometry**

Esophageal manometry was performed using the usual technique of our laboratory\cite{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\cite{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**
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\(^{(29)}\). 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

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TABLE 1. Findings observed during pharyngolaryngoscopy

<table>
<thead>
<tr>
<th>Findings</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema /VF congestion</td>
<td>10</td>
</tr>
<tr>
<td>Pachydermia - arytenoid</td>
<td>6</td>
</tr>
<tr>
<td>Node in VF</td>
<td>5</td>
</tr>
<tr>
<td>Edema in arytenoids</td>
<td>4</td>
</tr>
<tr>
<td>Cyst in VF</td>
<td>2</td>
</tr>
<tr>
<td>Atrophy in VF</td>
<td>2</td>
</tr>
<tr>
<td>Polyp in VF</td>
<td>1</td>
</tr>
<tr>
<td>Asymmetry in VF</td>
<td>1</td>
</tr>
</tbody>
</table>

VF: vocal fold

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

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

LES = lower esophageal sphincter
UES = upper esophageal sphincter

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FIGURE 3. Polyp in right vocal fold; Reinke’s edema in left vocal fold edema and pachydermia in posterior glottis
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% ± 6.4%) than among controls (3.4% ± 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 with hoarseness. In this situation, the refluxed content from the stomach would reach the larynx more easily, although 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 published by 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. 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% ± 6.4%) than among controls (3.4% ± 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).

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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.


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 piorre e regurgitação (manifestações típicas). Manifestações atípicas (distúrbios da voz e asma) podem também ser referidas. Objetivo – Analisar os aspectos clínicos, endoscopicos, manométricos e pHmetricos 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 endoscopicos: DRGE não-erosiva foi observada em 95% dos pacientes do 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 pHmetricos: 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 do 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, endoscopicos 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.

REFERENCES


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