Dual-probe pH monitoring for the assessment of gastroesophageal reflux in the course of chronic hoarseness in children

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The purpose of our study was to assess gastroesophageal reflux (GER) by dual-probe pH monitoring in children suffering from chronic hoarseness for more than six months.

Seventeen children (aged between 2 and 12 years, 10 boys and 7 girls) were enrolled. All children underwent a laryngoscopy and a 24-hour dual-probe pH monitoring. At both sensor, distal and proximal esophageal, a pathological GER was defined as the presence of episodes of acid reflux with pH<4 during a fraction of the total recording time greater than 5.2 percent. The computer considered the child was supine when asleep and upright when awake.

Laryngoscopy revealed interarytenoid erythema and/or edema with vocal cord nodules or granulomas in 13 cases (76.4%), isolated vocal nodules or granulomas in three cases (17.6%) and a normal appearance in one case (5.8%).

At both sensors, the majority of refluxes occurred when the child was upright, as analyzed by the percentage of time the intra-esophageal pH was below four (% time pH<4), number of refluxes, reflux episodes/hour and longest reflux episode, $p<0.05$ between upright and supine for each parameter. The median total % time pH<4 on the proximal and distal probes was respectively 1.62 percent (95% CI 1.50-3.79) and 11.49 percent (95% CI 8.81-27.17), $p<0.0003$.

Among the 17 hoarse children, a pathological GER was observed in 12 (70.5%) at the distal sensor and in three (17.5%) at both sensors.

Among the 16 hoarse children with abnormal findings on laryngoscopy, two (12.5%) had diagnosed pathological GER at the proximal and 11 (68.7%) at the distal sensor. The only child with normal findings on laryngoscopy exhibited a pathological GER at both sensors.

Our results suggest that chronic hoarseness is associated with a pathological GER. The majority of these documented refluxes ocurred when the child was awake.

Key words: hoarseness, dysphonia, gastroesophageal reflux, pH monitoring, child.

Hoarseness is a common complaint in both adults and children. The voice becomes hoarse and has diminished ability to change volume and pitch. It occurs when laryngeal function or anatomy is altered in such a way that proper apposition of the vocal cords for normal speech production is prevented. In children, the importance of "voice change" has not been stressed in the literature. However, Cohen et al.[1] highlighted that in children there is a tendency to postpone the examination merited by a hoarse voice, probably because of the rarity of malignancy in the child's larynx. Laryngeal structural anomalies, infection, inflammation and trauma, as well as neurogenic vocal cord dysfunction, can all result in hoarseness in children[2].

In adults, gastroesophageal reflux (GER) has been increasingly implicated as a cause of chronic laryngeal symptoms such as cough, sore throat, persistent throat clearing, globus sensation and hoarseness[3-5]. The incidence of hoarseness in association with GER ranges from 55 to 79 percent[5-7].

Limited data has been published on this subject in children. Pathogenic reflux in children has recently been associated with acute laryngitis, recurrent croup, stridor, obstructive sleep apnea, laryngospasm and cough[8]. To our knowledge, no correlation has been suggested between GER and hoarseness in this age group.

The purpose of our study was to assess GER by dual-probe pH monitoring in children suffering from chronic hoarseness.

Material and Methods

Between January 1995 and December 1996, 17 children (aged between 2 and 12 years, 10 boys and 7 girls) suffering from chronic hoarseness for more than six months were enrolled in the study. None of them were known to have classical symptoms of GER: emesis, dysphagia, rumination, belching, choking, gagging, failure to thrive, heartburn, indigestion, sour taste in mouth, and nocturnal dyspnea or cough. None were receiving any drugs which might affect gastrointestinal motility or gastric acid production.

All the children enrolled underwent a laryngoscopy and a clinical evaluation performed by the same Pediatric Otolaryngologist. All were then referred to the Pediatric Gastroenterology Department for 24-hour dual-probe pH monitoring. We used a "Digitrapper" recording device (Synectics, Stockholm, Sweden) and medical dual-channel pH catheter with two antimony pH sensors, model 91-9011, 2.1 mm diameter, 175 cm length (Ingold, Urdorf, Switzerland). The probe was introduced nasally. The distal sensor was placed at the level of the lower esophagus, 3 cm above the lower esophageal sphincter (LES), with the Strobel formula, length from nares to LES (cm): 5+0.25 height[9]. The proximal sensor, upper esophageal, was positioned either 10 or 15 cm above the distal sensor depending on the child's height. The position of both probe tips were checked radiographically. The system was calibrated before each recording. The probes registered every four seconds on each channel for between 18 and 24 hours.

Recording equipment was put in a rucksack on the child's back. The children received no food by mouth for two to three hours before the investigation and then ate a normal diet.

The parents recorded the child's actions such as eating and sleeping. The computer considered the child was supine when asleep and upright when awake. Each procedure was carried out by the same member of the staff. The pH monitoring tracings were analyzed by the same Pediatric Gastroenterologist to confirm the computerized calculations and to insure the quality of the recording.

The data from the "Digitrapper" were loaded into a computer and analyzed using an Esophagram program (Esophagram Software Package: Gastrosoft Inc., Chicago, IL). Computer analysis of the stored data was used to calculate at both levels, distal and proximal, the different parameters while the child was upright, supine and in total. The following parameters were: the percentage of time the intra-esophageal pH was below four (% time $pH<4$), the total number of refluxes, the number of reflux episodes per hour (reflux episodes/hr), the number of episodes longer than five minutes and the longest reflux episode.

At the distal sensor, a pathological GER was defined as the presence of episodes of acid reflux with $pH<4$ during a fraction of the total recording time greater than 5.2 percent[10]. Since there is no literature data concerning the acidic exposure of proximal sensor, we retained the same pathological criteria for pathological GER at the proximal sensor as for the distal one, thus probably underestimating the phenomenon. In addition, an upper esophageal reflux episode was considered secondary to GER only if associated with a lower esophageal reflux episode.

Calculation of median and 95% confidence interval (CI) of all quantitative parameters were done using the State View System. The data were non-parametrically distributed and were statistically analyzed using the non-parametric tests of Wilcoxon and Mann-Whitney ($p<0.05$).

Results

Fiberoptic laryngoscopy revealed interarytenoid erythema and/or edema with vocal cord nodules or granulomas in 13 cases (76.4%). Isolated vocal nodules or granulomas without interarytenoid erythema were observed in three cases (17.6%) and a normal laryngoscopy was found in one case (5.8%) (Table I).

At both sensors, the majority of refluxes occurred when the child was upright, as analyzed by % time $pH<4$, number of refluxes episodes/hr and longest reflux episode, $p<0.05$ between upright and supine for each parameter (Tables I and II). The median total % time $pH<4$ on the proximal

and distal probes was respectively 1.62 percent (95% CI 1.50-3.79) and 11.49 percent (95% CI 8.81-27.17), p<0.0003 (Table I).

Among the 16 hoarse children with abnormal findings on laryngoscopy, two (12.5%) had a pathological GER at the proximal and 11

Table I. Laryngoscopy and 24-hour pH Monitoring Findings for 17 Dysphonic Children

				Inferior probe			Superior probe		
Patients	Age (years)	Sex	Laryngoscopy	% time pH<4 total	pH<4 upright	pH<4 supine	% time pH<4 total	pH<4 upright	pH<4 supine
GER negative									
1	2	F	VCN	0.18	0.8	0	0.09	0.2	0
2	7	M	IEE+VCN	2.7	5.17	0.16	1.62	3.19	0
3	9	M	IEE+VCN	2.94	3.9	2.06	1.23	2.54	0
4	8	M	IEE+VCN	3.37	6.67	0.14	1.03	2.07	0
5	6	F	IEE	5.17	9.5	0.46	1.48	2.84	0
GER positive									
6	3	M	IEE	62.65	58.18	65.04	5.71	6.06	5.53
7	11	F	IEE+VCN	43.18	60.97	17.14	1.85	1.42	2.35
8	12	F	VCN	40.21	31.82	50.59	5.08	5.21	4.92
9	9	M	IEE+VCN	29.89	22.52	37.5	0.94	1.51	0.35
10	12	F	IEE	28.02	58.21	2.81	5.02	5	5.04
11	12	M	VCN	25.55	43.13	1.85	5.91	9.89	0.56
12	11	M	IEE	19.86	11.03	28.23	3.06	5.87	0.34
13	6	M	NL	13.8	21.49	3.58	7.18	4.72	10.41
14	8	M	IEE	11.49	19.13	0.94	0.4	0.68	0
15	10	F	IEE	6.38	13.39	0.66	0.8	1.77	0
16	7	F	IEE	5.22	8.67	1.46	2.02	1.94	2.11
17	5	M	IEE+VCN	5.27	8.99	0	1.59	2.71	0

GER: Gastroesophageal reflux. NL: Normal. IEE: Interarytenoid erythema and/or edema. VCN: Vocal cord nodules or granulomas.

Table II. Overall pH Monitoring Results for 17 Children

pH variables	Inferior probe median (95% CI)	Superior probe median (95% CI)
Total % time pH<4	11.49 (8.81-27.17)*	1.62 (1.50-3.79)
Upright % time pH<4	13.39 (12.05-33.06)*	2.71 (2.12-4.65)#
Supine % time pH<4	1.85 (2.01-22.9)*	0.34 (0.35-3.38)
Total number of refluxes	170 (108.6-335.02)*	24 (16.10-52.5)
Number of upright refluxes	154 (96.5-223.5)*#	20 (12.19-46.8)#
Number of supine refluxes	13 (6.9-130.5)*	1 (0.31-9.21)
Total reflux episodes/hr	8.6 (5.2-16.3)*	1.06 (0.73-2.60)
Upright reflux episodes/hr	14.8 (9.1-24.8)*#	1.82 (1.09-4.69)#
Supine reflux episodes/hr	1.11 (0.76-13.16)*	0.1 (0.02-0.92)
Longest reflux (min)	19 (16.60-39.98)*	7 (5.65-14.46)
Longest reflux while upright (min)	11 (10.87-30.86)*	6 (4.52-8.06)
Longest reflux while supine (min)	4 (2.51-22.89)	1 (1.14-11.4)

* Inferior probe vs superior probe, p<0.05 with Mann-Whitney test.
# Upright position vs supine position, p<0.05 with Wilcoxon test.

Among the 17 hoarse children, a pathological GER, according to the definition depicted in Methods, was observed in 12 (70.5%) at the distal sensor and in three (17.5%) at both sensors. The number of episodes greater than five minutes on the proximal and distal probes was respectively, one (95% CI 0.69-2.36) and two (95% CI 2.89-11.69), non-significant.

(68.7%) at the distal sensor. The only child with normal laryngoscopic exhibited a pathological GER at both sensors (Table I).

Discussion

Gastroesophageal reflux was first suggested as an etiological factor in laryngeal disease by Cherry and Margulies[11], who reported three

patients with contact ulceration of the larynx and significant GER on barium studies. Their theory was supported experimentally by the formation of granuloma at the site of daily application of gastric acid to vocal cords in two 2 dogs for six weeks[12].

Classically, GER is divided into uncomplicated, complicated and extraesophageal forms. Children with laryngeal symptoms fall into the latter extraesophageal group. The notion of silent GER is not a new one[13]. The data from our study help to emphasize that laryngeal symptoms with characteristic laryngeal lesions, particularly chronic hoarseness, may be secondary to occult GER. Classical symptoms of GER were found in 20 to 50 percent of patients with head and neck manifestations[4]. Thus, many otolaryngology patients have a pattern of GER disease that is distinctly different from the pattern seen in gastroenterology patients with esophagitis[4]. In patients attending ear-nose-throat disease clinics, GER is often occult, with a relative lack of esophagitis and its symptoms, making diagnosis of GER occasionally difficult.

There are two theories by which GER may cause laryngeal symptoms. The first is the "vagally mediated reflex" theory where the stimulus is acid in the lower esophagus and the response is chronic repetitive throat clearing and cough which would eventually lead to laryngeal lesions[5]. This neural mechanism is difficult to prove and there remains limited evidence for this theory. The second is the "direct acid injury" theory in which the refluxate must tranverse through the upper esophageal sphincter (UES). It was believed that pharyngeal pH monitoring might help to clarify this theory but unfortunately technical difficulties, such as intermittent drying out of the probe leading to pseudo-reflux, complicated matters[5]. However, the duration of acid refluxate contact with mucosa plays a key role in determining the degree of mucosal injury. As well as acid, refluxate contains pepsin, trypsin, bile and other gastroduodenal enzymes, all of which may damage laryngeal mucosa[14].

Unfortunately, there is surprisingly little data on laryngeal symptoms related to GER in either adults or children attending digestive clinics. In adults, two reports state that laryngeal symptoms occur in between six to 25 percent[15]. In children, a recent study has shown that GER was found in the presence of laryngeal symptoms: 61 percent laryngomalacia, 58 percent stridor, 56 percent laryngitis, 25 percent laryngeal papillomatosis and only 14 percent dysphonia[16]. However, we have already reported a pharyngeal acid reflux in a series of eight children with recurrent acute laryngitis who underwent two-channel pH monitoring for 24 hours[17]. That study suggests the role of GER in recurrent laryngitis in children[17]. We have also recently reported in three different series of children, using only distal probe 24-hour pH monitoring, that from 59 to 64 percent of those children suffering from chronic dysphonia had pathological GER[18-20].

Children in our study were selected for pH monitoring on the basis of their hoarseness and signs of "posteior acid laryngitis". These classical laryngeal changes are highly suggestive, but not pathognomonic, of GER. However, the posterior larynx is the area most often affected, probably due to positional and gravitational effects[3,21]. The causal relationship of these lesions with acid exposure is supported by canine studies in which similar lesions were reproduced by intermittent applications of gastric acid to the vocal cords or subglottic area, but not by applications of normal saline or saliva[12,22]. In the only known reported association between GER and hoarseness in children, Putman and Orenstein[23] described an eight-year-old girl who presented with hoarseness, night-time cough and gastrointestinal bleeding. No laryngoscopy was performed but pH monitoring disclosed a pH below 4 for nine percent of the total recording time. Postprandial reflux was greatly increased. Most of the refluxes occurred while she was supine[23].

In this study, the classical criteria for a pathological GER were retained at the distal sensor[10]. Since there is no literature data concerning the acidic exposure of proximal sensors, we retained the same criteria for pathological GER at the proximal sensor as for the distal one, thus probably underestimating the phenomenon at the proximal one. In addition, an upper esophageal reflux episode was considered secondary to GER only if associated with a lower esophageal reflux episode. In our study a pathological GER was found in 70.5 percent of cases at the distal probe and in only 17.5 percent of cases at the proximal one. Although the proximal probe has excellent specificity (91%) it has poorer sensitivity and

reproducibility (55%) for identifying abnormal amounts of proximal esophageal acid reflux[24]. Therefore, a negative test result does not exclude proximal reflux with microaspiration as a cause of atypical reflux symptoms[24].

In hoarse children without symptoms of GER, esophageal acid exposure time was much greater when the child was awake, the majority of refluxes were of short duration and their frequency was high. The reason for this is not known. It may be that these patients are repetitive air swallowers (aerophagics), a hypothesis currently under investigation[6]. The short duration and paucity of supine reflux may explain the low frequency of endoscopic esophagitis. This is supported by Katz[6] who studied 10 adults with hoarseness and GER, seven of whom had abnormal hypopharyngeal reflux predominantly in the upright position, of short duration and high frequency. These patients had no esophageal symptoms. Furthermore, Wiener et al.[5] studied 33 adults with hoarseness and signs of posterior laryngitis. GER, more than three times greater than the upper limit of the normal, was shown in 78.8 percent of patients. This GER was worse in the upright position but of long duration. Less than half of these patients had typical symptoms of GER. Of special interest is the fact that the severity of the GER noted in those patients was not proportional to the incidence of traditional symptoms of esophagitis (heartburn and chest pain). The fact that patients with reflux laryngitis had GER predominantly in the upright position may help to explain this disparity[5]. All these articles claim that the upright pattern of reflux seems to differentiate patients with hoarseness and GER from symptomatic patients with esophagitis. Why the characteristics of esophagitis are absent in these patients is not clear, but it may relate to the predominance of upright reflux, as opposed to supine GER. Koufman[4] explained this by the fact that clearance of refluxate is dependent on normal gastric motility and that esophageal dysmotility is uncommon in patients with otolaryngeal symptoms.

On the other hand, patients with both severe esophagitis and hoarseness apear to have a different pattern of reflux, being predominantly nocturnal supine refluxers[7,25]. In young infants, Vandenplas et al.[26] found that the acidity of long duration reflux episodes (the area under pH 4) is a determining factor in the prediction of esophagitis.

In our study, chronic hoarseness was associated with a pathological GER in 17.5 percent of cases at the proximal probe and in 70.5 percent of cases at the distal one. The pH traces highlighted that the majority of these documented refluxes were of short duration and occurred when the child was awake. Laryngoscopy is an essential investigation in the chronically hoarse child: it shows erythema, edema, nodules and granulomas, which are often attributed to vocal cord abuse. In these circumtances, GER should be considered, and 24-hour pH monitoring is indicated to determine appropriate treatment.

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