Reflux Laryngitis and Its Sequelae: The Diagnostic Role of Ambulatory 24-Hour pH Monitoring

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Summary: Ambulatory 24-h intraesophageal pH monitoring was performed in 32 patients with hoarseness, documented laryngeal pathologic findings or lesions, globus, and/or chronic cough. The laryngeal lesions included granulomas, stenoses, and carcinomas. Twenty-two (68.8%) of the patients had no symptoms specific for reflux. One-half of the patients underwent pH monitoring with a double probe, one probe being placed in the distal esophagus and the second being placed in the hypopharynx just behind the laryngeal inlet. Twenty-four (75%) of the patients had abnormal studies, i.e., significant reflux. Of those, 17 (70.8%) had upright reflux, 13 (54.2%) had supine nocturnal reflux, and 10 (41.7%) had both types. Seven of the 16 patients undergoing double-probe-type monitoring had reflux into the pharynx (43.8%). These data suggest that occult gastroesophageal reflux may be involved in the pathogenesis of many conditions commonly encountered in otolaryngologic practice. **Key Words:** Carcinoma of the larynx: etiology—pH monitoring—Occult gastrolaryngeal reflux—Reflux laryngitis—Subglottic stenosis: etiology.

Gastroesophageal reflux (GER) has long been implicated in the development of many otolaryngologic conditions (1–4). The clinical association of acid reflux with the development of laryngeal contact ulcers and granulomas has been well established, and the otolaryngologic literature contains many reports of successful empiric treatment of these conditions with antireflux therapy (4–8). The most characteristic "footprints" of GER are erythema, edema, and mucosal changes of the posterior larynx (9,10).

Gastric acid reflux has been associated with cases of subglottic stenosis (1,4,11), laryngeal carcinoma (1), globus (12–14), dysphagia (15,16), cricopharyngeal dysfunctional states (17,18), and even with chronic cough, asthma, pneumonia, and other chronic pulmonary conditions (19–23). Unfortunately, the protean manifestations of GER on the aerodigestive tract remain unsubstantiated, for the most part, since, until recently, no conclusive diagnostic test has been available (24,25). In a recent review of the problem of GER, Olson (1) concluded that, "There is fairly strong circumstantial evidence that refluxed stomach acid has a clinically definable effect upon the larynx."

Previously reported diagnostic techniques have all provided "circumstantial evidence" (26). At best, contrast esophagrams can detect the mucosal changes of esophagitis when it is present (26,27). Fluoroscopy can document reflux, but the significance of roentgenographic reflux is controversial. Such reflux has been shown in as few as 60% of severely symptomatic patients and in as many as 25% of asymptomatic patients. Thus, barium esophagography has both poor specificity and sensitivity, and its reliability is questionable (26). Finally, while the acid perfusion (Bernstein) test is a

reasonably sensitive indicator of esophagitis, it can only mimic pyrosis (heartburn) and globus, and cannot determine the degree of GER (26).

Three additional clinical observations (28) further add to the difficulty in making a diagnosis of GER-related conditions: (a) asymptomatic control subjects show some degree of reflux; (b) reflux is frequently intermittent; and (c) many patients, especially those with laryngeal manifestations of GER, do not have the gastrointestinal symptoms typically associated with GER.

The concept of continuous intraesophageal pH monitoring was first reported by Spencer in 1969 (29). Since then, it has undergone refinement as a result of advances in gastroenterologic research and technology (24,28,30), and has evolved into a sensitive and reliable method of evaluating GER. Unlike the previous diagnostic modalities, continuous pH monitoring measures the dynamic event of GER itself over an extended period of evaluation (24 h) (28).

The purpose of this paper is threefold: first, to present the results of 24-h pH monitoring in a group of 32 consecutive otolaryngologic patients with presumed GER; second, to propose clinical guidelines for the utilization of this new diagnostic tool; and third, to examine the potential role of GER in terms of the spectrum of its otolaryngologic manifestations.

MATERIALS AND METHODS

Thirty-two consecutive patients (seen from January through June, 1986) suspected of having GER due to their presenting otolaryngologic condition were referred to the section of gastroenterology for ambulatory 24-h pH monitoring. Twenty asymptomatic nonsmoking adults underwent single-probe ambulatory 24-h pH monitoring. Data from these normal subjects were compared to data from the study group.

The 14 females and 18 male patients in the study population ranged in age from 2 to 72 years (mean age 49.5 years, with a standard deviation of 17.0 years). There were two pediatric patients, both with subglottic stenosis.

Diagnoses included laryngeal carcinoma (n = 8), subglottic stenosis (n = 8), chronic dysphonia (n = 5), globus (n = 5), chronic cough (n = 4), and chronic sore throat (n = 2). The clinical criteria for inclusion in the pH monitoring study are shown in Table 1.

TABLE 1. *24-hour pH monitoring: clinical selection criteria by diagnostic subgroup*

Group I—Cancer of the larynx
(A) A strong history of GER symptoms
(B) Diffuse, red, widespread mucosal involvement with cancer in situ or microinvasive disease (with or without a history of reflux)
(C) Lesions of the posterior larynx, particularly those of the arytenoid and aryepiglottic fold (with or without history of reflux)
(D) Granulomas and/or stenosis following initial treatment (with or without a history of reflux)
(E) Squamous cell carcinoma of the larynx in nonsmokers (with or without a history of reflux)

Group II—Laryngeal stenosis
(A) A strong history of reflux symptoms, especially choking episodes at night and/or a chronic cough
(B) Persistent granulation tissue and/or massive edema following initial surgical management (even without a history of reflux)
(C) Treatment failures (without adequate explanation)
(D) Recurrent stenosis (over months or years) after apparent resolution

Group III—Chronic dysphonia (hoarseness)
(A) Erythema and edema of the posterior larynx
(B) Diffuse laryngeal erythema and edema with or without mucosal ulceration
(C) Laryngeal granulomas
(D) Bouts of hoarseness related to reflux history
(E) No other explanation for hoarseness

Group IV—Globus symptom
(A) Sensation of a lump in the throat related by history to GER
(B) Sensation of a lump in the throat and pharyngeal findings suggestive of GER
(C) Sensation of a lump in the throat without a demonstrable otolaryngologic abnormality, e.g., lingual tonsillitis, goiter, or mass lesion of the laryngopharynx (without a history of reflux)

Group V—Chronic cough
(A) Cough and a history of GER
(B) Choking episodes or nocturnal coughing
(C) Edema and erythema of the larynx suggestive of GER
(D) Complete negative work-up in other departments (pulmonary), normal chest x-rays, or a history of pneumonia

Group VI—Chronic sore throat
(A) Strong history of GER
(B) Laryngeal findings suggestive of GER
(C) Diffuse pharyngeal erythema without other medical explanation

History

The patients were asked a series of questions about esophageal symptoms, including heartburn, dysphagia, odynophagia, regurgitation, and eructation (sour burps). Confirmation or denial of tracheobronchial symptoms was also elicited, including chronic cough, choking episodes, asthma, and pneumonia. Each patient was questioned about laryngeal and pharyngeal symptoms: intermittent or chronic dysphonia, globus sensation, sore

throat, and throat tickle. A history of smoking was obtained as well as a history of voice usage and previous surgical or medical therapy for any disorder of the aerodigestive tract.

Presenting symptoms of the study group

Dysphonia, either intermittent or chronic, occurred in 21 (65.6%) patients (Tables 2 and 3). When the other throat symptoms were included, 27 (84.4%) patients had laryngeal or pharyngeal symptoms. Tracheobronchial symptoms were experienced by 14 (43.8%) patients, and gastrointestinal symptoms by 10 (31.3%) patients.

Manometric and pH studies

After an overnight fast, each patient underwent esophageal manometry in the gastroenterology laboratory with a low compliance pneumohydraulic fusion system, as previously described (31). Lower esophageal sphincter (LES) position and pressure were established using the slow pull-through technique. Sixteen (50%) of the patients underwent single-probe 24-h ambulatory pH monitoring by one of three systems that have been shown to give similar results: the Sandhill RMS, the Oxford Medilog 100, and the Delmar 706 (28). The Sandhill P-32 Konigsberg antimony pH probe and the Microelectrode MI-506 pH probe were used. The probe tip was passed transnasally and located manometrically 5 cm above the LES. The presence of gastric acid was documented by advancing the probe until pH readings were less than 2.5; the probe was then withdrawn to the monitoring position.

TABLE 2. *Frequency of presenting symptoms of 32 subjects by symptom subgroup*

Classification	No. of patients	Percent
Laryngeal/pharyngeal symptoms		
Chronic dysphonia	13	40.6
Intermittent dysphonia	8	25.0
Globus	8	25.0
Sore throat	5	15.6
Throat tickle	5	15.6
None	5	15.6
Tracheobronchial symptoms		
Chronic cough	11	34.4
Choking episodes	4	12.5
Asthma	2	6.3
Pneumonia	1	3.1
None	18	56.3
Gastrointestinal symptoms		
Regurgitation	8	25.0
Pyrosis (heartburn)	6	18.8
Dysphagia	4	12.5
None	22	68.8

Patients were instructed to abstain from all drugs for at least 24 h before and during the test. Patients were asked to abstain from smoking during the test, and to follow a diet consisting of foods with pH greater than 5; no carbonated beverages were allowed, and milk, coffee, and tea were restricted to meal times. Using an event marker, the patient recorded on the monitoring apparatus the meal times, bed and rising times, and any reflux, laryngeal, or respiratory symptoms that occurred.

A drop in pH to less than 4.0 was considered evidence of GER (28). The pH variables studied were those proposed by Johnson and DeMeester (30): the percentage of time when the esophageal pH was less than 4.0; the number of episodes per hour with pH less than 4.0 that lasted longer than 5 min; the number of episodes of GER per hour; and the longest duration of a GER episode. Values were calculated for total time, time in the supine position, and time in the upright position. All tracings were inspected by one author (G.J.W.) to confirm the computerized calculations and to ensure the quality of recording. The 24-h pH study was considered abnormal if the pH variables exceeded two standard deviations from the mean derived from asymptomatic normal subjects studied in our laboratory (28).

During the study period, we began to perform double-probe pH monitoring to evaluate the incidence of pharyngeal reflux. With double-probe monitoring, the positions of both the upper and lower esophageal sphincters were determined, and the second "pharyngeal probe" was piggy-backed onto the esophageal probe and positioned 2 cm above the upper esophageal sphincter (UES), just behind the laryngeal inlet (Fig. 1). For the patients with double-probe monitoring, we considered even a single pH drop below 4 recorded by the pharyngeal probe to be positive evidence for pharyngeal reflux. Sixteen patients underwent double-probe pH monitoring.

Other tests for gastroesophageal reflux disease

The acid perfusion (Bernstein) test, esophagoscopy, and/or barium esophagography had been performed on 24 of the 32 patients and the results were reviewed retrospectively. A positive Bernstein test result consisted of the reproduction of heartburn and chest pain when 0.1 N HCl was infused into the esophagus and the disappearance of those symptoms with infusion of normal saline. The endoscopic diagnosis of esophagitis was based on

TABLE 5. *Results of 24-h pH monitoring by diagnostic subgroup (abnormal studies—supine/upright/double probe/total)[a]*

Complaint/diagnosis	Abnormal study results			Total of group with abnormal studies
	Supine	Upright	Pharynx[b]	
Cancer of the larynx	2	4	2/5	6/8
Laryngeal stenosis	4	5	1/4	6/8
Chronic dysphonia	2	2	0/2	3/5
Globus symptom	2	3	1/2	3/5
Chronic cough	2	2	3/3	4/4
Chronic sore throat	1	1	0/0	2/2
Totals	13	17	7/16	24/32
Percent	40.6	53.1	43.6	75.0

[a] 10/24 (41.7%) of the patients with abnormal study results demonstrated *both* supine and upright abnormal reflux values.

[b] The numerator denotes the number of subjects with abnormal values; the denominator denotes the number of subjects in each group who underwent double-probe monitoring.

two still have tracheotomies, and those two patients are the remaining candidates for fundoplication. One is a 62-year-old woman with laryngotracheal stenosis secondary to GER and endotracheal intubation, and one a 44-year-old woman with subglottic stenosis, segmental tracheobronchial stenosis, and chronic pulmonary changes secondary to GER.

Case Examples

A 56-year-old woman (case 5) presented with a supraglottic carcinoma and underwent an endoscopic supraglottic laryngectomy with the CO_2 laser. Postoperatively, she had persistent granulation, erythema, and edema of the larynx; supraglottic stenosis developed and required tracheotomy and placement of a stent. Despite antireflux therapy, antibiotic therapy, and long-term stenting, her edema and granulation persisted. Following fundoplication, the stent was removed and the patient decannulated. She has been without evidence of recurrent carcinoma or stenosis for almost 1 year.

A 57-year-old woman (case 7) presented with airway obstruction characterized by diffuse laryngeal edema and erythema. She had undergone radiation for carcinoma of the larynx 2 years before. A careful search for recurrent carcinoma was made and none was found. She underwent a tracheotomy and treatment with antireflux therapy, but the appearance of her larynx did not improve. Subsequently, she underwent fundoplication and decannulation. At present her larynx appears normal.

A nonsmoking 52-year-old man (case 8) had per-

sistent and recurrent mucosal carcinoma, cinoma in situ, and microinvasive carcin diffuse erythema and ulceration involving the endolaryngeal surface extending into glottis. He underwent fundoplication, but later required laryngectomy for an aggre current lesion. (It is possible that this pati not have required laryngectomy had he u fundoplication earlier.)

Normal studies

There were eight patients with norma one of whom had a vocal cord granuloma these eight patients had clinical findings t GER-related diagnoses, and symptoms in resolved with medical antireflux therapy. maining three "probe-negative" patients, nosis of GER-related illness could not lished by either pH monitoring or a clinic therapy. Thus, misdiagnosis is likely, i were clinical "false positives," in whom probably not the underlying causative con

Barium esophagrams and other tests for GI and esophagitis

Twenty-four patients had double-contra swallow esophagrams. Sixteen (66.7%) h hernias, two (8.3%) demonstrated aspi barium, and four (16.7%) had esophagitis.

There was an association of hiatal he abnormal supine reflux values, and this fii statistically significant (p < 0.05).

Thirteen patients had Bernstein acid tests performed and only three patients (2:

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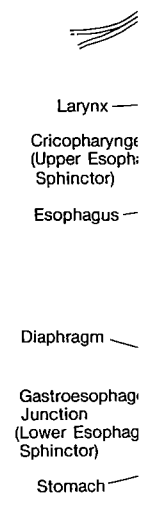
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RESULTS

Normative data

The 20 normal subjects experi
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and the data were similar to tho:
reported previously for normal st
The following results are for the
In our laboratory, 12 normal su
double-probe pH monitoring wit
pharyngeal reflux (33).

Laryngeal findings

Clinical examination of the lar
transnasal fiberoptic laryngoscor
crolaryngoscopy in selected cas
one-half of the 32 study patients l
thema; seven had diffuse erythei
posterior erythema. In addition,
ulceration, two had granulomas
plakia, eight had carcinoma, an
glottic stenosis.

Cigarette smoking

Of the 30 adults in the study p
were cigarette smokers. Of the e
carcinoma of the larynx, five w
three were nonsmokers.

pH monitoring

The monitored pH values (% t
the study population were abnoi
significantly from the control va
(Table 4). Every diagnostic subg
abnormal pH results (Table 5).

Overall, 24 (75.0%) of the subje
pH results. Seventeen (70.8%) o
demonstrated upright reflux, 13 (:
flux, and 10 (41.7%) reflux in both
the majority of the patients with
were either supine *or* upright refl
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reflux occurred during the day. :
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TABLE 6. *Subject profile, pH monitoring results, therapy*

No.	Age/sex	Selection criteria^a	24-h pH monitoring data (% time) Upright	Supine	Total	Pharynx^b	Rx^b	Outcome^b
Group I—Cancer of the larynx								
1	56/M	A	0.60	0.00	0.40	+	ART, S	R
2^c	46/M	B	1.00	1.00	1.00	−	S	R
3	44/F	D, E	6.90	0.00	4.70	ND	S, ART	R
4	62/F	C	5.68	0.00	4.44	−	S, ART	R
5	58/F	D	18.00	3.00	13.00	ND	ART, Fundo	R
6^c	69/M	E	3.00	0.00	2.00	−	ART, S	R
7	57/F	D	16.00	0.00	9.00	+	S, Fundo	R
8	52/M	B, E	7.57	19.30	12.92	ND	S, Fundo	R
Group II—Subglottic stenosis								
9^c	39/F	C	0.12	0.00	0.08	−	S	U
10	53/M	A	8.10	10.60	9.00	−	ART, S	I
11^c	68/F	D	0.00	0.20	0.08	−	S	R
12	30/F	A, D	1.01	11.00	6.82	ND	ART, S	I
13	2/M	C	13.50	16.60	15.40	ND	ART, S	R
14	44/F	A, B	9.05	0.04	5.93	ND	ART, S	U
15	62/F	C, D	32.30	0.00	9.80	+	ART, S	U
16	12/M	C	7.00	10.00	9.00	+	Fundo	R
Group III—Chronic dysphonia								
17^c	56/M	C	2.00	0.00	1.00	−	ART	R
18	56/M	C	3.60	8.10	5.24	ND	ART	R
19	56/M	A	17.50	0.00	10.00	−	ART	R
20^c	55/F	A	0.90	0.00	0.42	ND	ART	U
21	55/F	A, D	5.98	7.28	6.50	ND	Fundo	R
Group IV—Globus								
22^c	24/M	A	0.80	1.60	1.30	−	ART	R
23	59/M	C	7.00	27.00	12.00	+	ART	R
24	32/M	B	7.37	12.04	9.74	ND	ART	R
25	58/M	B	16.00	0.00	11.00	ND	ART	R
26^c	67/F	A	1.50	0.40	1.00	ND	ART	R
Group V—Chronic cough								
27	35/M	A, B, D	9.80	13.50	11.40	ND	ART	R
28	72/M	B	10.00	10.00	10.00	+	ART	R
29	70/M	B	3.00	1.00	2.00	+	ART	R
30	65/F	C	0.00	0.80	0.30	+	ART	R
Group VI—Chronic sore throat								
31	27/M	A, B, C	1.00	22.00	14.00	ND	ART	I
32	44/F	C	6.12	0.00	3.56	ND	ART	R

^a Refer to Table 1 for selection criteria in each group.
^b + = one episode of pH < 4.0 detected by pharyngeal probe; ART = antireflux thera
= not done; fundo = fundoplication; U = unimproved; and I = improved.
^c Patients with "normal" studies.

positive result. Manometry was normal in all 32 patients. Eight patients underwent esophagoscopy by a gastroenterologist (G.J.W.), and six were normal and two had esophageal erosions.

COMMENT

In this series of 32 patients, 24 had documented GER leading to "reflux laryngitis" or complications of gastric acid aspiration. At first, this seems to be a disparate group, but they actually share a

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establish a relationship between pharyngeal probe positivity and patient symptoms.

There was an association between the finding of diffuse laryngeal erythema and abnormal supine reflux (p < 0.001) and an association between supine reflux and the presence of a hiatal hernia (p < 0.05). Patients with these findings probably should be treated primarily for nocturnal supine reflux.

Our results indicate that cases of upright reflux were, however, more common. The incidence of upright reflux in this study is unprecedented when compared to the reported pH monitoring results of patients with typical GER (30,34). A partial explanation may be related to the nature of upright reflux, in that gastric acid in the upright patient may not stay in the esophagus long enough to produce heartburn or esophagitis. Another factor may be related to the low incidence of positivity to the Bernstein acid perfusion test: Less than one-quarter of the patients experienced heartburn during this test. Such patients may be constitutionally stoic and hence more prone to develop secondary sequelae without complaining of primary GER symptoms.

Ambulatory 24-h intraesophageal pH monitoring with or without the placement of a second pharyngeal probe is the first diagnostic test with a high degree of accuracy and specificity. During the study period, we began collecting double-probe pH data, and that technique is currently the standard for studying our adult patients. Ambulatory pH monitoring is simultaneously a powerful clinical tool and a powerful research tool; its limitations are discussed in the following section.

The limitations of pH monitoring

What is normal?

It is likely that GER is very common. Data collected from asymptomatic "normal" subjects suggest that this is the case (28). The current upper limits of normal are derived from normative data, yet some of the normal subjects may be GER patients in the preclinical phases of illness. Nevertheless, the range of normal that is currently accepted in the gastroenterology literature is derived from the limits set by the mean values plus two standard deviations.

All of the normative published data, to date, were obtained from single-probe pH monitoring studies (24,28,30). We have begun to examine asymptomatic normal subjects using the double-

probe system, and although pharyngeal reflux is uncommon in this group, it does occur (34). The question is, does a pH of less than 4 recorded in the hypopharynx prove pathological reflux, or is another standard needed?

Reflux is sometimes intermittent

In our series, five patients with clinically documented reflux findings had "normal" pH measurements, but all five responded to antireflux therapy.

As a case example, we are currently following a 46-year-old nonsmoking man who has had three small mucosal laryngeal carcinomas over a period of 8 years. Although he is aware that he has GER, particularly when he develops hoarseness (and a laryngeal lesion), he had had two negative ambulatory pH monitoring studies within the last 12 months. Recently, however, he developed hoarseness and returned for re-examination. This time the larynx was diffusely erythematous and repeat pH monitoring yielded 15% supine reflux in the esophageal probe with five positive pharyngeal episodes of acid pH during sleep. (This important case, another case of GER-induced laryngeal cancer, illustrates the occasional difficulty in making a diagnosis.)

Of the 32 patients in the study population, three patients probably did not have GER-related primary diagnoses. However, 29 of the patients either had positive pH studies (n = 24) or were clinically positive and responded to antireflux therapy despite having negative pH studies (n = 5). Therefore, the sensitivity of the pH probe in the study population was 24 of 29 (83%), and the false-negative rate with pH monitoring was therefore 5 of 29 (17%). Since the test is specific for GER, the rate of false-positive pH monitoring is probably nil. The clinical "false-negative" rate is unknown and is dependent upon the index of suspicion of the clinician; the false-positive rate of clinical diagnosis, i.e., misdiagnosis, in this series was 3 of 32 (9%).

Technical limitations of the pharyngeal pH probe

The relatively low yield of pharyngeal probe positivity is probably due to technical problems associated with the probe itself.

First, the probe is bipolar, such that it needs to be in contact with the pharyngeal mucosa to work properly. Unlike the esophagus, which at rest remains collapsed, the hypopharynx is relatively cavernous. Since the pharyngeal probe is piggy-backed

onto the esophageal probe, in many cases the probe may be suspended in the midhypopharynx.

Second, since the pharyngeal cavity is large and saliva production decreases at night, mucus may dry on the pharyngeal probe tip, rendering it non-functional.

Third, in some cases, acid aspiration, especially in upright refluxers with chronic cough, may be in the form of microdroplets that are not recorded by the probe.

Invasiveness of the test and patient acceptance

Patient aversion to tubes, hyperactive gag reflux, or simply an unwillingness to accept having a "tube" coming out of the nose for a 24-h period makes the test unacceptable to some patients. Patient aversion can be overcome with the majority of patients once; however, about one-half of the patients are unwilling to undergo repeat examinations. This detracts from the usefulness of the technique to provide follow-up data on the effectiveness of treatment and somewhat limits longitudinal studies of GER using the technique.

Alteration (betterment) of the subject's lifestyle during the test period (test bias)

During the pH monitoring period, subjects are asked to refrain from smoking, drinking coffee, tea, or milk except at meal times, and from taking nonessential medicines. These prohibitions are designed to standardize the test (28). Obviously, periodic and random consumption of any substance with pH of less than 4 would create false-positive readings. However, by interrupting such patterns of behavior, the test itself may temporarily improve the patient's condition and artificially improve his test performance, i.e., he may be less prone to reflux under test conditions than in his everyday existence.

Limited availability

pH monitoring is still limited to research centers and is not yet widely available. The expense of the equipment and manpower required may be prohibitive in some clinical settings.

Indications for ambulatory 24-h pH monitoring

We recommend the use of the patient selection criteria provided in the Materials and Methods section of this paper for diagnostic pH monitoring. Using these criteria, the yield has been excellent despite the variability in expression of GER

symptoms. Furthermore, the pH monitoring techniques identify the pattern of reflux (supine, upright, both) in each patient, allowing for more appropriate and individualized therapeutic intervention.

Carcinoma of the larynx

We have presented eight patients with carcinoma of the larynx in which GER may have played a significant role, and three of these patients were non-smokers in whom carcinoma was probably a direct result of GER. Of those three patients (cases 3, 6, and 8), two had positive studies, and the third patient (who continued to develop mucosal ulceration and erythroplakia of the larynx until antireflux therapy was instituted) had his study done after an extended period of antireflux therapy. (We presume that his study would have been abnormal had it been performed earlier.)

Of the eight patients with carcinoma of the larynx, six had abnormal studies and four were upright refluxers. Of the five patients studied with the double probe, two had abnormal pharyngeal studies.

GER must be considered as a potential causal factor in the development of carcinoma of the larynx. Richter (32) and Stanciu (35) have reported that cigarette smoking causes a marked reduction in LES pressure. Within 2 or 3 min of initiating cigarette smoking, the LES pressure drops to 50% of the resting potential.

In studying a series of patients with GER, 92% of the patients were smokers, and it was noted that episodes of GER in smokers occurred two-thirds of the time during the smoking of cigarettes (35). Tobacco and alcohol consumption as carcinogenic factors have been well established, and gastric acid is probably a third key variable.

All of the carcinomas were squamous cell carcinoma, a histologic tumor type that is rare in non-smokers, and thus probably lesions that were the result of GER. A future study of GER should include normal subjects, age- and sex-matched smokers, and age- and sex-matched patients with laryngeal carcinoma. We are currently performing pH monitoring on all patients with T_1 or T_2 carcinoma of the larynx and recommend that all "atypical cases" also be so studied.

Subglottic stenosis

Just as the cause of laryngeal carcinoma is multifactorial, so too is the cause of subglottic stenosis.

Injury to the intra-arytenoid region, most typically by an indwelling endotracheal tube, in concert with infection or other host factors resulting in perichondritis may lead to subsequent subglottic stenosis. GER, it appears, may also play a major role.

The eight cases of subglottic stenosis presented here represented the most recalcitrant, unresponsive, and difficult cases that we have seen in the last 5 years. Acid reflux was documented in six of the eight patients.

The highest incidence of acquired subglottic stenosis is reported in neonates (36). These infants are often premature, with birth weights of less than 1000 g, and they are intubated for weeks or months, often with tubes of 2.5- to 3.5-mm internal diameter. Also, they may require frequent reintubation. That the incidence of subglottic stenosis in this population is only 8% is remarkable (36). One possible explanation is that neonates do not produce much gastric acid; furthermore, they are usually intubated with uncuffed tubes.

The cuffed tubes used in older children and adults create a basin for the deposition of acid into the larynx. In critically ill intubated patients, intermittent reflux could lead to subglottic stenosis since the cuff of the endotracheal tube helps hold the acid within the larynx.

Little et al. (11), using a canine model of subglottic stenosis, demonstrated that gastric acid could produce severe subglottic stenosis. In that study, intracricoid mucosal lesions were created. Then, the subglottic region was swabbed with acid three times a week for several weeks. The animals developed severe stenosis, even though acid was actually in contact with the intracricoid surface for only a few seconds per week.

We have observed that the incidence of subglottic stenosis in our adult intensive care unit population has decreased dramatically in recent years. We believe that this is due to the use of smaller endotracheal tubes (with tube size selection being dependent upon the patient's sex and height) (37), and to the use of routine antistress ulcer regimens, so that stomach acid is neutralized around the clock in almost all of the intensive care unit patients.

It is highly likely that GER plays an important role in the development of subglottic stenosis. We recommend pH monitoring for all post-intubation subglottic stenosis cases and for other stenosis cases that are unresponsive to surgical correction.

Reflux laryngitis (chronic dysphonia)

Four of the five patients who were thought to have GER-related hoarseness improved with antireflux therapy. Clearly, granuloma patients, regardless of preexisting factors, such as intubation or voice abuse, should be considered as potential pH-monitoring subjects, particularly if there is a history of reflux and/or other associated findings. Laryngeal erythema, localized or diffuse, strongly suggests the possibility of reflux laryngitis; pH monitoring is usually diagnostic.

Globus

A sensation of a lump in the throat, globus, is uncommonly due to hysteria. A search for an offending lesion must be undertaken. At present, our work-up for a globus symptom includes a complete otolaryngologic evaluation, a barium swallow esophagram, and 24-hour pH monitoring.

GER-related globus may be secondary to actual reflux of acid into the larynx or may be due to distal esophagitis. Globus sensation secondary to inflammation of the lower esophagus could be mediated by way of the vagus in a manner similar to that of referred pain. In our experience, many patients with globus respond to antireflux therapy.

Chronic cough and other tracheobronchial symptoms

Our data indicate that upright refluxers are more prone to chronic cough and tracheobronchial symptoms than to gastrointestinal symptoms. Although our numbers were small, we found 100% pharyngeal positivity in this group (3 of 3), the highest incidence found. Certainly, the clinical appearance of the larynx can alert the clinician to the possibility of aspiration of gastric contents; however, the absence of such findings should not rule out GER altogether.

For example, a 35-year-old salesman (case 27), when calling on clients, would begin to cough until he vomited. He consulted 16 physicians before coming to our institution. His pH monitoring results were highly abnormal: He refluxed 9.8% of the time when upright and 13.5% of the time when supine. His symptoms resolved with antireflux therapy.

Patients with a chronic cough, choking episodes, asthma, and/or recurrent pneumonia who have had negative medical evaluations should undergo pH monitoring.

Chronic unexplained sore throat

While diffuse processes involving the pharynx are common, such conditions of a chronic nature are not. GER should be considered in such patients when other causes have been ruled out or when GER symptoms or findings are also present.

The magnitude of the GER problem in otolaryngologic practice

It has been reported that as many as 10% of Americans have daily heartburn and/or acid regurgitation, and as many as one-third have such symptoms at less frequent intervals (26). However, studies reported in the gastroenterology literature have primarily focused on esophagitis and its symptoms (26). In otolaryngology, GER-related disorders are infrequently reported and rarely studied, and, at present, there are no data available on the incidence of GER-related conditions in otolaryngologic practice.

During the study period reported here (January–June, 1986), the senior author, a laryngologist, saw approximately 320 different patients during 639 outpatient visits. Thirty-two of those patients had GER-related conditions; hence, the estimated incidence of such conditions in the author's practice was 10%.

Indeed, it is possible that 10% of otolaryngologic practice involves the recognition and treatment of GER-related disease. That alternative treatments (not antireflux therapy) are occasionally effective may be explained by the realization that some GER-related conditions are multifactorial. Furthermore, it seems likely that such conditions are currently being underdiagnosed; the addition of single- and double-probe pH monitoring to currently used diagnostic tools should facilitate more accurate diagnosis in the future.

In the gastroenterology literature, it is generally accepted that the rate of failure of aggressive medical antireflux therapy is 5% to 10% (26); the rate of failure of medical treatment in this series of otolaryngologic patients was 7 of 29 (24.1%). This finding may be spurious or it may reflect a more severe pattern of GER in otolaryngologic patients with GER disease.

Future directions in GER research

A new generation of pharyngeal probes needs to be developed. Unipolar probes with improvements in shape, method of stabilization, and resistance to tip drying will improve the yield in monitoring for pharyngolaryngeal reflux. There is clearly a need for the use of double- or multiple-probe monitoring studies in controlled populations. Furthermore, the optimal duration of antireflux therapy once a diagnosis of GER has been established is not known, although experienced clinicians recommend a duration of 6 to 12 months. There is a need for longitudinal studies of GER patients to develop a model of the "GER cycle" and to determine the most effective methods of treatment.

The causes of upright versus supine GER need to be understood to better facilitate appropriate therapy. The upright refluxer may be more difficult to treat than the supine refluxer, since treatment may require substantial modification of the patient's diet and lifestyle. The pathogenesis of GER is multifactorial and may be a function of diet, body habitus, stress, and a host of other factors; these may be elucidated with further research using the techniques of intraesophageal pH monitoring.

CONCLUSIONS

1. The otolaryngologist should maintain a high index of suspicion for GER as an etiologic factor in many otolaryngologic conditions. GER may play an important role in the development of carcinoma of the larynx, subglottic stenosis, chronic dysphonia, globus, chronic cough, and sore throat.

2. Otolaryngologic patients with GER infrequently complain of the gastrointestinal symptoms typically associated with GER.

3. Ambulatory 24-h pH monitoring is an accurate and specific diagnostic test for GER; however, the false-negative rate is about 15%. Clinical diagnosis is still invaluable in the diagnosis of GER-related conditions.

4. There is a high incidence of upright reflux in otolaryngologic patients, which may be why such patients present often first with complications rather than the symptoms of GER.

5. Practicing otolaryngologists should consider developing a working relationship with a gastroenterologist willing to study cooperatively patients with syndromes such as those presented here.

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