

Chronic Cough and Hoarseness in Patients with Severe Gastroesophageal Reflux Disease

Diagnosis and Response to Therapy

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Gastroesophageal reflux may be responsible for atypical symptoms such as chronic cough and hoarseness. Our aim was to evaluate and treat patients with severe gastroesophageal reflux and chronic cough or hoarseness with intensive antireflux therapy. Twenty-seven patients with typical heartburn symptoms in addition to significant cough or hoarseness were treated with aggressive antireflux therapy. We recorded the response of each symptom to the antireflux therapy. Two patients were lost to follow-up. Twenty of the 25 (80%) patients showed some improvement in cough or hoarseness, nine (36%) had no atypical symptoms at follow-up. The response of heartburn to therapy was strongly predictive of successful therapy for the atypical symptoms. Cough and hoarseness improved in only two of the five patients with residual heartburn symptoms compared to 18 of 20 patients with no heartburn ($P < 0.04$). Only patients with no heartburn symptoms at follow-up had complete resolution of atypical symptoms. There were no important differences on ambulatory pH monitoring between partial and complete responders. Improvement in atypical reflux symptoms, such as chronic cough and hoarseness, is common with aggressive antireflux therapy. There are no findings on ambulatory esophageal pH monitoring that uniquely identify patients who are likely to respond to antireflux therapy.

KEY WORDS: gastroesophageal reflux; antireflux therapy; chronic cough; hoarseness.

Gastroesophageal reflux (GER) may be responsible for unexplained extraesophageal symptoms, such as chest pain, asthma, chronic cough, or hoarseness (1). GER, documented by ambulatory esophageal pH monitoring, is common in patients with chest pain (2-5). However, antireflux therapy eliminates chest

pain in some, but not all, such patients (6-8). GER is also common in patients with asthma (9). Antireflux therapy meets with modest success in controlling asthma symptoms (10, 11). The limited improvement in these atypical symptoms may be due to the fact that chest pain and asthma have many causes. In an individual patient, an association may be proven only by improvement in any given symptom with antireflux therapy.

GER occurs with variable frequency in patients with unexplained cough or hoarseness (12-15). Some small studies suggest that proximal esophageal acid exposure may identify patients with these symptoms

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(16, 17). Antireflux therapy improves cough and hoarseness symptoms in some, but not all, such patients (12, 14, 18). Again, the response to antireflux therapy may be the best and only way to prove an association. The aim of this study was to evaluate the response to antireflux therapy and the reflux patterns in patients with unexplained cough or hoarseness.

MATERIALS AND METHODS

From October 1992 to December 1993, we evaluated and treated 27 patients (6 men, 21 women) seen in a combined gastroenterology/surgery clinic with complaints of severe heartburn, who also had significant cough or hoarseness. All patients were asked about the presence and severity of typical and atypical reflux symptoms. The symptoms (chest pain, heartburn, cough, hoarseness, and asthma) were scored by the patient from 0 (none) to 4 (severe). Scores greater than 2 were considered clinically important. Nineteen patients (9 men, 10 women), who had heartburn, but no atypical symptoms served as a control group.

The patients underwent dual-channel ambulatory esophageal pH monitoring while taking no antireflux therapy. For the 24-hr esophageal pH study, a probe was passed nasally such that an antimony pH electrode was placed 5 and 20 cm above the manometrically determined lower esophageal sphincter. The results were recorded and processed by the Gastrosoft esophageal Software Package, version 5.50C2 (Synectics Medical, Inc., Irving, Texas). The patients were asked to consume three meals during the study period. A reflux episode was defined as beginning when the pH dropped below 4.0 and ending when the pH rose above 5.0. We recorded the number of reflux episodes and reflux time for the distal and proximal esophagus, overall, and in both the upright and supine position.

The 27 patients received aggressive antireflux therapy consisting of omeprazole 20–40 mg daily (six patients), or antireflux surgery (21 patients). The Nissen fundoplication was the procedure of choice, but a Toupet or Belsey-Mark IV fundoplication was performed if there was evidence of impaired esophageal clearance (18). All but three operations were performed laparoscopically. We recorded the response of each symptom to the antireflux therapy after one to six months (mean 3.2 months). Comparisons of pH parameters between different groups and subgroups were made with the Mann-Whitney test for nonparametric measurements. Comparisons of response to therapy were made with the Fisher's exact test.

RESULTS

Nine patients had cough as the predominant atypical symptom, four had predominantly hoarseness, while 14 had both. Two patients were lost to follow-up. Twenty of the remaining 25 (80%) patients showed some improvement in cough or hoarseness, nine (36%) had no atypical symptoms at follow-up.

The antireflux therapy was effective as the typical symptoms of GER improved in 22 of the 25 patients.

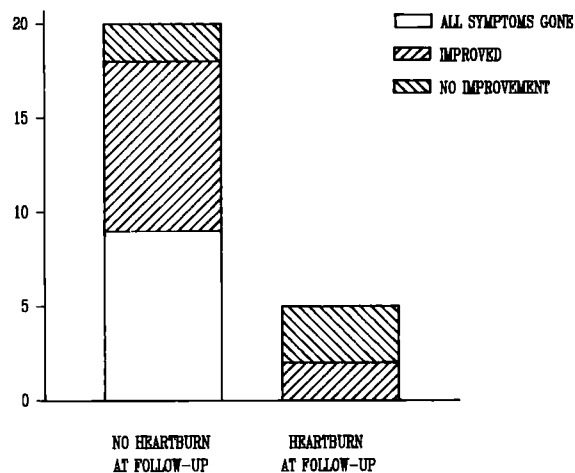


Fig 1. Comparison of improvement of cough or hoarseness in patients with and without heartburn at follow-up.

Twenty patients had no heartburn at follow-up. The absence of heartburn was strongly predictive of successful therapy for the atypical symptoms (Figure 1). Cough and hoarseness improved in only two of the five patients with residual heartburn symptoms compared to 18 of 20 (90%) of patients with no heartburn ($P < 0.04$).

All nine patients with complete resolution of atypical symptoms had no heartburn at follow-up. If heartburn was eliminated, cough resolved in nine of 16 (56%) patients, while hoarseness resolved in eight of 14 (57%) patients.

Patients who had a complete resolution of cough and hoarseness had slightly more reflux in the distal esophagus. However, there was no significant difference in any parameter on ambulatory pH monitoring of the proximal esophagus, between partial and complete responders (Table 1).

Pretreatment heartburn scores were similar between patients with and without atypical symptoms (3.0 vs 3.1). Of those having endoscopy, thirteen of 22 (59%) of patients with atypical symptoms had esophagitis compared to seven of twelve (58%) patients with typical symptoms only. There were more proximal reflux episodes in patients without atypical symptoms. Otherwise, there were no statistically significant differences in any parameter on ambulatory pH monitoring between these two groups (Table 2). Proximal esophageal reflux was common in patients in the patients with severe reflux but no atypical symptoms. Proximal reflux time correlated well only with total distal esophageal reflux time ($P < 0.01$; Figure 2). Proximal reflux time did not correlate with age ($P = 0.17$) or with severity of symptoms, ie,

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TABLE 1. COMPARISON OF REFLUX PARAMETERS BETWEEN PATIENTS WITH PARTIAL AND COMPLETE IMPROVEMENT IN ATYPICAL SYMPTOMS*

	<i>Partial responders</i>	<i>Complete responders</i>
Distal esophagus		
Total reflux time (%)	12.5, 13.5	22.8, 26.0
Reflux episodes	107.0, 85.5	130.0, 81.0
Episodes > 5 min	7.0, 12.0	13.0, 13.5
Upright reflux time (%)	18.9, 21.9	35.9, 28.5
Upright reflux episodes	98.0, 62.5	104.0, 51.5
Upright reflux episodes > 5 min	7.0, 6.5	9.0, 11.5
Supine reflux time (%)	4.0, 12.2	11.4, 28.8
Supine reflux episodes	3.0, 7.0	15.0, 29.5
Supine reflux episodes > 5 min	1.0, 1.5	5.0,† 7.5
Proximal esophagus		
Total reflux time (%)	1.6, 1.5	1.0, 3.6
Reflux episodes	40.0, 13.0	27.0, 44.5
Reflux episodes > 5 min	0.0, 1.0	0.0, 2.5
Upright reflux time (%)	2.1, 3.6	2.0, 4.0
Upright reflux episodes	32.0, 17.5	27.0, 36.0
Upright reflux episodes > 5 min	0.0, 1.0	0.0, 1.0
Supine reflux time (%)	0.0, 0.9	0.2, 2.8
Supine reflux episodes	1.0, 2.0	2.0, 8.0
Supine reflux episodes > 5 min	0.0, 0.0	0.0, 1.5

*Values are expressed as median, interquartile range.

† $P < 0.05$.

heartburn ($P = 0.27$), cough ($P = 0.52$), hoarseness ($P = 0.18$), or asthma ($P = 0.36$).

DISCUSSION

There is little question that gastroesophageal reflux can cause chronic cough or hoarseness in some patients. The differences in published incidence rates probably represent selection bias. Our report repre-

sents one of the largest treatment-oriented studies in the literature. The variable response in other studies may be a result of the antireflux therapy. McNally et al found improvement in only two of six patients with hoarseness using ranitidine 150 mg twice a day (12). Kamel et al, however, found improvement in 13 of 16 patients with posterior laryngitis using omeprazole (19). Eighty percent of our patients improved with

TABLE 2. COMPARISON OF REFLUX PARAMETERS BETWEEN PATIENTS WITH AND WITHOUT ATYPICAL SYMPTOMS*

	<i>Atypical symptoms</i>	<i>Typical symptoms</i>
Distal esophagus		
Total reflux time (%)	15.3, 16.1	18.0, 17.8
Reflux episodes	95.0, 69.0	95.0, 93.0
Episodes > 5 min	7.0, 7.0	11.0, 7.0
Upright reflux time (%)	18.9, 24.1	18.0, 11.1
Upright reflux episodes	88.0, 61.0	83.0, 92.0
Upright reflux episodes > 5 min	7.0, 6.5	6.0, 8.0
Supine reflux time (%)	7.7, 17.1	20.0, 19.7
Supine reflux episodes	5.0, 13.0	12.0, 18.0
Supine reflux episodes > 5 min	1.0, 4.0	2.0, 3.0
Proximal esophagus		
Total reflux time (%)	1.6, 2.2	1.8, 3.0
Reflux episodes	28.0, 25.0	50.0,† 55.0
Reflux episodes > 5 min	0.0, 1.0	1.0, 2.0
Upright reflux time (%)	2.2, 4.0	2.4, 3.7
Upright reflux episodes	28.0, 19.0	39.0, 58.0
Upright reflux episodes > 5 min	0.0, 1.0	0.0, 2.0
Supine reflux time (%)	0.1, 0.8	0.1, 2.7
Supine reflux episodes	2.0, 4.0	2.0, 9.0
Supine reflux episodes > 5 min	0.0, 0.0	0.0, 1.0

*Values expressed as median, interquartile range.

† $P < 0.05$.

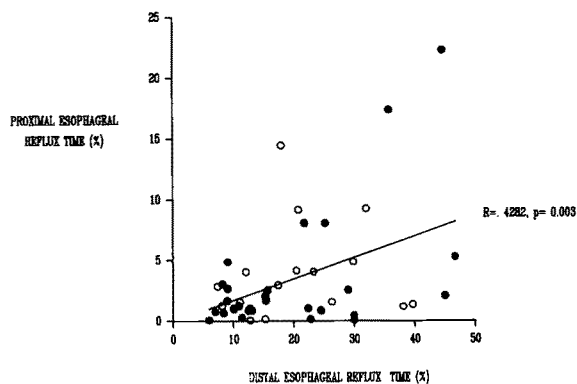


Fig 2. Correlation of proximal esophageal reflux time with distal esophageal reflux time in patients with atypical symptoms (solid spheres) and patients without atypical symptoms (hollow spheres).

aggressive antireflux therapy. While one cannot exclude a placebo effect, it seems less likely when the results are so dependent on successful antireflux therapy. Kamel et al found prompt relapse of laryngitis symptoms after stopping therapy, again arguing against a significant placebo affect.

Ambulatory esophageal pH monitoring may be used to verify gastroesophageal reflux. Unfortunately, results of this test in these patients have been variable. Some studies have identified GER predominantly in the upright position (13, 16), while others found GER in the supine position (12, 17). While, some studies found reflux episodes to be brief (16), others found them prolonged (12). Attempts to correlate reflux episodes with episodes of cough have met with mixed results (12, 20). We found no special significance of finding reflux in the upright or supine position. Patients with findings of reflux laryngitis are noted to have significant proximal esophageal or hypopharyngeal reflux (16, 17, 19). The laryngitis probably results from hypopharyngeal reflux of small amounts of gastric acid. The proximal pH electrode is generally placed 20 cm above the manometric lower esophageal sphincter and is therefore still in the esophagus in most patients. It was hoped that finding acid in the proximal esophagus would correlate with atypical reflux symptoms (21). However, many of our patients without atypical symptoms had proximal reflux. Proximal esophageal acid reflux had no predictive value for the presence of atypical symptoms or the response to therapy.

In summary, acid reflux is probably responsible for most of the problems seen in these patients. Patients with GER-related cough or hoarseness frequently respond to aggressive antireflux therapy. The initial

goal of therapy should be to eliminate heartburn. We found that there is a small chance for improvement and virtually no chance for cure if heartburn continues. Ambulatory esophageal pH monitoring is of limited value in distinguishing which patients with severe gastroesophageal reflux disease will respond to therapy. We found no special significance of finding reflux in the proximal or distal esophagus. This test should probably be reserved for difficult patients, such as those who have no typical heartburn symptoms or those who do not respond to aggressive antireflux therapy.

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