



Laryngopharyngeal Symptoms and Gastroesophageal Reflux Disease: Pathophysiology, Diagnosis, and Management – A Literature Review

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Introduction

Gastroesophageal reflux disease (GERD) has a high worldwide prevalence, estimated at 13.3% to 17.3% [1,2], and represents a particularly relevant health problem in Latin America. It is characterized by the reflux of gastric contents into the esophagus and may present with a broad clinical spectrum, significantly affecting quality of life. Heartburn, regurgitation, and chest pain remain among its most recognized manifestations [2]; however, the disease has also been associated with extraesophageal symptoms.

In this context, laryngopharyngeal symptoms are of particular importance. Dysphonia or hoarseness, throat clearing, chronic cough, excessive pharyngeal secretions, and globus sensation may occur both in the presence and absence of typical reflux symptoms. Importantly, however, none of these findings alone is sufficient to diagnose laryngopharyngeal reflux disease (LPRD), as their etiology is often multifactorial. For this reason, the San Diego Consensus recommends the use of the descriptive term “laryngopharyngeal symptoms” (LPS), reserving the term LPRD for situations in which objective evidence supports the involvement of reflux in the pathogenesis of symptoms [3-5].

The relationship between gastroesophageal reflux and laryngopharyngeal symptoms is unlikely to result from a single mechanism. Direct exposure of the laryngopharyngeal mucosa to refluxed material and activation of neurogenic reflexes are the most widely discussed hypotheses. More recently, laryngeal hypersensitivity, neural hyperresponsiveness, and hypervigilance have been incorporated into this pathophysiological model, particularly to explain the persistence of symptoms in patients in whom the reflux burden does not appear sufficient to account for the clinical presentation [4,6,7].

Pathophysiology of laryngopharyngeal symptoms

The pathophysiology of extraesophageal manifestations attributed to GERD remains incompletely understood [8]. Current literature generally recognizes two main mechanisms, which are not mutually exclusive: direct contact of refluxate with the laryngopharyngeal mucosa and activation of esophageal reflex pathways, predominantly mediated by the vagus nerve [4,6,7].

In the direct exposure mechanism, gastroduodenal contents reaching the pharynx and larynx may exert a damaging effect

through acid, pepsin, and possibly bile salts. The laryngopharyngeal mucosa has defense mechanisms distinct from those observed in the esophageal epithelium and may be particularly vulnerable to such exposure. Nevertheless, laryngeal edema, erythema, and other inflammatory changes are not specific to reflux and therefore should not be interpreted outside the clinical context [4,7,9].

A second possibility involves indirect mechanisms. Esophageal exposure or even distension may activate vagal afferent pathways and trigger esophagobronchial and esophagolaryngeal reflexes. This phenomenon may contribute to cough, throat clearing, bronchoconstriction, and increased sensitivity of the aerodigestive tract, even when there is no evidence that the refluxate has directly reached the larynx [6,7].

This model becomes more comprehensive when the concepts of laryngeal hypersensitivity and central amplification of symptom perception are incorporated. In some patients, these alterations may perpetuate symptoms even in the absence of documented pathological reflux and may help explain why the response to acid suppression is sometimes incomplete or absent [4,7].

Main clinical manifestations

Dysphonia or hoarseness, chronic throat clearing, cough, excessive pharyngeal secretions, and globus sensation are among the complaints that most frequently raise the possibility of reflux involvement. However, the high frequency of these symptoms in clinical practice should not be mistaken for diagnostic specificity. In the initial evaluation, the most appropriate approach is to recognize them as laryngopharyngeal symptoms (LPS) and investigate their possible underlying causes before attributing them to LPRD [4,5].

In voice disorders, experimental and histopathological studies suggest that exposure to refluxate may interfere with the protective mechanisms of the vocal fold mucosa, with reported alterations in carbonic anhydrase III and protective mucins. In theory, these changes could promote inflammation, epithelial microtrauma, and deterioration of vocal quality. However, their clinical significance should be interpreted with caution, as these findings alone do not demonstrate a causal relationship with reflux [4,9].

Chronic throat clearing, defined as the recurrent need to “clear the throat,” is a very common and nonspecific complaint. When reflux involvement is suspected, several mechanisms may be

involved, including vagal hypersensitivity, impaired mucociliary clearance, and laryngeal hypersensitivity. These factors may sustain the persistent perception of secretions, irritation, or pharyngeal discomfort even in the absence of evident structural abnormalities [4,7,10].

Globus sensation refers to the persistent, painless perception of tightness, a “lump,” or a foreign body in the throat, generally without associated dysphagia or odynophagia [11]. Its causal relationship with GERD remains controversial. Reflux, motility disorders, visceral hypersensitivity, and functional factors may contribute to the condition, either individually or in combination. Therefore, isolated globus sensation does not constitute sufficient evidence for the diagnosis of LPRD [4,5,11].

Diagnosis and treatment

The evaluation of otolaryngological manifestations potentially related to GERD remains challenging, particularly because there is no single test that can serve as the gold standard for LPRD. Assessment should begin with a thorough clinical history and physical examination, with active investigation of common alternative causes, such as rhinosinusitis, allergic and pulmonary diseases, behavioral voice disorders, and medication effects [6,8]. The San Diego Consensus emphasizes that the presence or absence of concomitant esophageal symptoms should guide the diagnostic strategy and that laryngeal symptoms should not be automatically attributed to reflux [4,5].

Laryngoscopy plays an important role in the anatomical and functional assessment of the larynx, particularly because it allows the identification of alternative diagnoses, such as neoplasms, vocal fold paresis, benign mucosal lesions, and muscle tension dysphonia. Conversely, findings traditionally associated with reflux—such as edema, arytenoid erythema, and posterior commissure hypertrophy—have low specificity. Consequently, they should not be used in isolation to confirm LPRD [4,5,8,12].

Upper gastrointestinal endoscopy (esophagogastroduodenoscopy, EGD) is indicated in the presence of alarm features, such as dysphagia, gastrointestinal bleeding, and unintentional weight loss, and may also contribute to the evaluation of GERD, esophagitis, and other esophagogastric disorders. However, a normal EGD does not exclude pathological reflux and, by

itself, does not clarify the origin of laryngopharyngeal symptoms. In selected cases, the presence of heterotopic gastric mucosa in the proximal esophagus may be associated with these symptoms, although this finding should be interpreted in conjunction with other clinical data [8,13,14].

Ambulatory reflux monitoring becomes particularly relevant when patients present with isolated laryngopharyngeal symptoms and GERD has not yet been objectively established. In this setting, current practice tends to favor objective documentation of reflux rather than repeated empirical trials of antisecretory therapy. The choice between prolonged wireless pH monitoring and catheter-based pH-impedance monitoring depends on the clinical phenotype, test availability, and diagnostic question. In unproven GERD, testing is generally performed off antisecretory therapy; when GERD has already been objectively established and symptoms persist, pH-impedance monitoring on therapy may help assess ongoing reflux and the association between symptoms and reflux episodes [4,5,14].

Some tests remain of limited use in routine clinical practice. Oropharyngeal or pharyngeal pH monitoring still faces issues related to reliability and standardization. Although salivary pepsin measurement is biologically plausible as a marker of proximal reflux, its diagnostic performance varies across studies, partly due to heterogeneity in sampling methods and cutoff values. Therefore, it should not be used in isolation to establish the diagnosis of LPRD [4,8,15].

Treatment should be tailored to the clinical phenotype and to the strength of evidence that reflux is actually related to the symptoms. Dietary and behavioral measures remain part of the therapeutic approach, including avoiding large meals or meals close to bedtime, promoting weight management when indicated, and identifying individual dietary triggers. More structured dietary strategies have shown promising results, but substantial variation among protocols still precludes universal recommendations [16,17].

When typical concomitant GERD symptoms are present, proton pump inhibitors (PPIs) may be used in accordance with current recommendations for the management of the disease. The scenario is different in patients with isolated LPS: in these cases, indiscriminate and prolonged empirical use of PPIs should be

avoided. Moreover, treatment response—or lack thereof—neither confirms nor excludes LPRD. Recent reviews have shown variable outcomes with acid suppression and reinforce the need to tailor treatment according to the clinical phenotype [4,6,8,18,19].

Alginates represent a potential therapeutic option, either as monotherapy or as adjunctive treatment, particularly in patients with suspected postprandial reflux or non-acidic or mixed reflux episodes. However, the available evidence remains heterogeneous, and additional controlled studies are needed to more precisely define their role in different patient profiles [19-21].

When laryngeal hypersensitivity or a coexisting functional disorder appears to contribute to the clinical presentation, treatment should not be limited to reflux suppression. Behavioral strategies, voice therapy or speech-language pathology, and interventions targeting hypervigilance may be incorporated into a multidisciplinary approach [4,7].

Invasive procedures, including antireflux surgery, require careful patient selection. In general, they should be considered only when there is objective evidence of pathological reflux, consistency between physiological findings and the clinical presentation, and appropriate assessment of esophageal function [4,8,14].

Conclusion

Laryngopharyngeal symptoms are common, but their multifactorial nature makes it inappropriate to automatically attribute them to reflux. GERD may contribute to their pathophysiology through direct exposure to refluxate, activation of neurogenic reflexes, and hypersensitivity mechanisms; nevertheless, the presence of isolated LPS does not establish a diagnosis of LPRD. Current management favors a multidisciplinary approach, exclusion of alternative diagnoses, and judicious use of objective testing, with the aim of reducing both overdiagnosis and unnecessary exposure to antisecretory therapy. Treatment should therefore be individualized and guided by the patient's clinical phenotype and the strength of the evidence linking their symptoms to reflux [4,5,7,14,19].

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