**Chronic Cough Associated with Gastroesophageal Reflux Disease: An Integrative Review of Physiological and Psychogenic Mechanisms and Therapeutic Strategies**

**ABSTRACT**

**Aims:** This study investigates the association between gastroesophageal reflux disease (GERD) and chronic cough with psychogenic components, identifying both physiological and psychological mechanisms that contribute to symptom persistence. It also evaluates therapeutic strategies including pharmacological treatments, such as proton pump inhibitors (PPIs), baclofen, and neuromodulators, alongside behavioral interventions like cognitive-behavioral therapy (CBT).

**Study Design:** Integrative literature review.

**Place and Duration of Study:** Databases searched (PubMed, SciELO, BVS, LILACS, Medline) between March and June 2025.

**Methodology:** This study followed PRISMA guidelines for integrative reviews. Searches were performed using descriptors including "Cough," "Gastroesophageal Reflux," "Psychogenic," and "Therapeutics." Studies were included if published between 2014 and 2024, freely available in full text, and methodologically robust (randomized controlled trials, systematic reviews, or well-defined observational studies). After applying eligibility criteria and qualitative analysis, 17 studies were selected for inclusion.

**Results:** GERD-related chronic cough was found to involve both vagal-mediated reflexes and microaspiration, with esophageal hypersensitivity as a contributing factor. Psychogenic influences—such as anxiety, stress, and sensory hypervigilance—amplified symptom perception and limited response to acid suppression alone. PPIs showed modest effectiveness, particularly in non-acid or functional reflux cases. Adjunct therapies including baclofen, gabapentin, and CBT demonstrated improved symptom control, while Nissen fundoplication surgery was effective in selected refractory cases. Integrative treatment combining medical, surgical, and psychological approaches yielded the best outcomes.

**Conclusion:** Chronic cough associated with GERD is a multifactorial condition requiring individualized, multidisciplinary treatment. Optimal management involves not only acid reflux control but also the inclusion of behavioral and neuromodulatory strategies. Future studies should further investigate these integrated therapeutic pathways.

1. **INTRODUCTION**

Chronic cough, defined as a symptom lasting more than eight weeks, is a major complaint in respiratory care and can severely affect patients' quality of life. One of its leading causes is Gastroesophageal Reflux Disease (GERD), frequently associated with extraesophageal manifestations such as laryngitis, hoarseness, and refractory cough [1,2].

The link between GERD and chronic cough involves multiple pathways. Physiological mechanisms include activation of the vagal esophageal reflex and microaspiration of gastric contents, which sensitize airway receptors [3-5]. However, psychosocial factors such as anxiety and sensory hypervigilance also play a crucial role in maintaining symptoms, revealing a relevant psychogenic component [5-8].

Although proton pump inhibitors (PPIs) are widely used as the first-line treatment, many patients show unsatisfactory clinical response, particularly in the presence of non-acid reflux or psychological comorbidities [8-10]. In these cases, the use of neuromodulators such as baclofen and behavioral strategies like cognitive-behavioral therapy have shown promising results [7-12].

Given the multifactorial nature of chronic cough associated with GERD, this study aims to provide an integrative review of the physiological and psychogenic mechanisms involved, as well as current and emerging therapeutic approaches, to support more effective and individualized clinical practice.

1. **MATERIAL AND METHODS**

This integrative review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, with the objective of identifying, evaluating, and synthesizing recent evidence on the relationship between Gastroesophageal Reflux Disease (GERD), chronic cough, and psychogenic or neurogenic factors, as well as related therapeutic strategies.

The literature search was conducted between March and June 2025 using the PubMed, SciELO, LILACS, BVS, and Medline databases. Controlled descriptors (MeSH/DeCS) and free-text terms were used in Portuguese, English, and Spanish, combined using Boolean operators (AND/OR). The search strategy included: (“cough” OR “chronic cough”) AND (“gastroesophageal reflux” OR “GERD”) AND (“psychogenic” OR “anxiety” OR “sensory hypersensitivity”) AND (“treatment” OR “therapy” OR “intervention”).

Inclusion criteria comprised studies published from 2014 to 2024, available in full text with free access, and written in Portuguese, English, or Spanish. Eligible study types included randomized controlled trials, systematic reviews, meta-analyses, observational studies, and narrative reviews with clearly defined methods. Case reports, editorials, letters to the editor, duplicates, and articles that did not directly address the association between GERD and chronic cough were excluded.

The selection process occurred in three phases. Initially, two independent reviewers screened titles and abstracts. In the second phase, the full texts of potentially relevant articles were assessed. Lastly, eligibility criteria were applied, and disagreements between reviewers were resolved by a third evaluator.

Data extraction covered author, publication year, study type, population, objectives, interventions, and key outcomes. The synthesis was qualitative and thematically organized into three categories: pathophysiological mechanisms, psychogenic factors, and therapeutic approaches. At the end of the selection process, 17 articles met all criteria and were included in this review.

1. **RESULTS AND DISCUSSION**

A total of 17 studies published between 2014 and 2024 were included, examining the relationship between gastroesophageal reflux disease (GERD), chronic cough, and psychogenic or neurogenic factors. Findings were organized into three primary domains: pathophysiological mechanisms, psychological influences, and therapeutic approaches.

GERD has been consistently linked to chronic cough through two main mechanisms: (1) esophagotracheal reflex via vagal nerve activation and (2) direct microaspiration of gastric contents into the upper airway. Acid exposure in the esophagus stimulates vagal afferents that trigger the cough reflex, even in the absence of aspiration [12-17]. Microaspiration contributes to chronic inflammation and sensitization of cough receptors in the upper respiratory tract [15-21]. Additionally, esophageal hypersensitivity and motility disorders have been associated with chronic cough, particularly in cases involving non-acid reflux [5,6, 9, 16].

Psychogenic components play a critical role in cough persistence, especially when GERD is well-controlled. Studies show that anxiety, central sensitization, and cough hypersensitivity syndrome are common among refractory patients [21-23]. In these cases, reduced response to proton pump inhibitors (PPIs) is typical, highlighting the role of neuroplasticity and central processing in cough perception [8, 9, 24].

Therapeutically, PPIs remain the frontline treatment for GERD-related cough. However, their efficacy is limited, especially in patients with non-acid reflux or underlying psychosomatic components [25-28]. Baclofen and gabapentin have shown moderate effectiveness in refractory cases by modulating lower esophageal sphincter relaxation or central cough reflex sensitivity [6,11,19]. Cognitive-behavioral therapy (CBT), laryngeal desensitization techniques, and superior laryngeal nerve blocks have been beneficial in patients with idiopathic or neurogenic cough [9,10,16, 17, 19].

Surgical interventions, particularly Nissen fundoplication, were effective in selected patients with objective reflux and poor response to medical therapy, achieving symptomatic resolution in 70–85% of cases [4,17, 22]. Moreover, herbal regimens such as Ojeok-San plus Saengmaek-San have demonstrated promise in randomized trials, showing improvements in cough severity and gastrointestinal symptoms [19].

Table 1. Mechanisms linking GERD to chronic cough

| Mechanism | Description |
| --- | --- |
| Vagal esophagotracheal reflex | Acid stimulates vagal afferents triggering cough reflex |
| Microaspiration | Gastric contents inflame upper airway, activating cough receptors |
| Esophageal hypersensitivity | Heightened perception to normal esophageal stimuli |
| Motility dysfunction | Lower esophageal sphincter impairment permits non-acid reflux |

Table 2. Therapeutic interventions and outcomes

| Therapy | Primary Indication | Reported Effectiveness |
| --- | --- | --- |
| PPIs | Documented acid reflux | ~52% symptom improvement |
| Baclofen / Gabapentin | Non-acid reflux, neurogenic cough | Moderate symptom reduction |
| CBT and desensitization therapies | Idiopathic/psychogenic cough | Reduced frequency and distress |
| Fundoplication surgery | Confirmed reflux, failed pharmacological therapy | 70–85% complete symptom remission |
| OJS + SMS herbal combination | Functional GI and cough symptoms | Significant improvement in RCT |

1. **DISCUSSION**

This integrative review reinforces the multifactorial etiology of chronic cough associated with gastroesophageal reflux disease (GERD), highlighting the interplay between physiological mechanisms, central sensitization, and psychological comorbidities. While acid reflux and microaspiration remain primary culprits in cough induction, a significant portion of patients exhibit persistent symptoms even after achieving adequate acid suppression with proton pump inhibitors (PPIs) [1,5,11].

The vagal esophagotracheal reflex has emerged as a key pathway through which non-acid reflux may provoke coughing episodes, explaining why PPI therapy often fails in these cases [3,14, 25]. Additionally, studies demonstrate that esophageal hypersensitivity and transient lower esophageal sphincter relaxations (TLESRs) contribute to persistent cough in patients with functional or non-acid reflux [6,14,17, 26]. This mechanistic understanding justifies the modest but consistent benefit observed with agents like baclofen and gabapentin, which act on neural reflexes rather than gastric acidity [6,11,17, 25].

Importantly, our findings underscore the role of psychogenic factors—especially anxiety, stress, and hypervigilance—in amplifying symptom perception and perpetuating cough via central neuroplasticity mechanisms [7,8]. These patients frequently meet criteria for chronic refractory cough or cough hypersensitivity syndrome, where traditional GERD-focused treatments alone prove insufficient. This highlights the emerging value of multimodal interventions, combining pharmacological therapy with cognitive-behavioral therapy (CBT) and respiratory retraining [8,9,10].

Surgical options such as fundoplication remain viable for selected patients with documented reflux and persistent cough despite optimized medical management. However, the risks, cost, and variable outcomes necessitate careful patient selection [4,17]. Finally, complementary approaches like herbal therapies (e.g., Ojeok-San plus Saengmaek-San) have shown promise in randomized trials, although broader validation is still needed [17].

1. **CONCLUSION**

Chronic cough associated with GERD is a complex and multifactorial condition, often extending beyond acid reflux to involve neurogenic and psychogenic pathways. While PPIs remain the first-line treatment, a significant number of patients benefit more from integrated strategies that include neuromodulators, behavioral therapy, and, in selected cases, surgical intervention. Clinicians should adopt a personalized, multidisciplinary approach when managing refractory chronic cough, taking into account both physiological and psychological contributors to symptom persistence.

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