

## CLINICAL TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE: WHAT DO THE LATEST STUDIES AVOID?

---

*Maria Karollina Almeida Passos*

Universidade Tiradentes, Aracaju

<http://lattes.cnpq.br/1762239145179344>

*Frederico Santana de Lima*

Universidade Tiradentes, Aracaju

<http://lattes.cnpq.br/3724611069152483>

*Bruno José Santos Lima*

Universidade Tiradentes, Aracaju

<http://lattes.cnpq.br/6158584238563073>

*Alana Darly Santos Andrade*

Universidade Tiradentes, Aracaju

<http://lattes.cnpq.br/1436644309178152>

*Ianne Jesus Santana*

Universidade Tiradentes, Maceió

<http://lattes.cnpq.br/3613119801404937>

*Rebeca Apolinário Sousa*

Universidade Tiradentes, Maceió

<http://lattes.cnpq.br/2961473495086242>

*Sara Mikaele Souza Santos*

Universidade Tiradentes, Maceió

<http://lattes.cnpq.br/8882896087667807>

*Letícia Almeida Meira*

Universidade Tiradentes, Maceió

<http://lattes.cnpq.br/6763020049224377>

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



***Déborah Esteves Carvalho***

Universidade Tiradentes, Aracaju  
<http://lattes.cnpq.br/9459988558420684>

***Natália Araújo Barreto***

Universidade Tiradentes, Aracaju  
<http://lattes.cnpq.br/0553473986481540>

***Gabriela Peres de Oliveira Krauss***

Universidade Tiradentes, Aracaju  
<http://lattes.cnpq.br/6223909536233030>

***Marina Déda Peixoto Leite***

Universidade Tiradentes, Aracaju

**Abstract: Introduction:** Gastroesophageal reflux is a physiological response of the body. When, for any reason, this reflux is associated with diseases, complications and impairment of quality of life, the condition is called gastroesophageal reflux disease (GERD). The clinical diagnosis of GERD is very sensitive, as most patients have the classic symptoms of the disease. The treatment can be clinical or surgical, depending on its dominant form of presentation and its main etiology. Surgery will rarely be a first option, as it must be reserved for cases that are refractory to medical treatment or for life-threatening situations. For this reason, the current discussion aims to investigate what the latest studies point out in the clinical treatment of GERD. **Methodology:** This is a bibliographic review whose secondary data were obtained through articles from Google Scholar, Scielo and PubMed databases. The descriptors were defined by the Decs BVS in “Gastroesophageal Reflux Disease”, “Clinical treatment” and “Non-pharmacological measures”, and hundreds of articles from national and international literature were identified. For the purpose of this literature review, only articles published in the last 2 years were included to discuss the clinical treatment of the disease. **Results:** The therapeutic approach to GERD includes two modalities, clinical and surgical treatment, the choice of which depends on the patient’s characteristics, in addition to other factors such as response to treatment, presence of erosions in the esophageal mucosa, atypical symptoms and complications. Clinical treatment aims to relieve symptoms, heal esophageal mucosal lesions and prevent the development of complications. It is based on non-pharmacological and pharmacological measures. Anti-reflux surgery must be reserved for patients who do not respond to medical treatment and/or who have life-threatening conditions. After the emergence

of more potent prokinetic agents and acid secretion inhibitors, the role of surgery as a definitive therapeutic weapon for complicated reflux has been questioned. **Conclusions:** Surgical treatment, when properly indicated, tends to be a definitive way to resolve the typical and atypical symptoms of GERD. On the other hand, considering the multidimensional etiopathogenesis of the disease, clinical treatment is still the best alternative to start with. It is understandable that the adjustment of doses, the association of classes, the combination with behavioral measures and the due adherence by the patient are presented as determinant measures for the therapeutic success, being able to avoid a surgical approach in most cases.

**Keywords:** Gastroesophageal Reflux Disease, Clinical treatment, Non-pharmacological measures.

## INTRODUCTION

Gastroesophageal reflux is a physiological response of the body characterized by a passive return of gastric contents to the esophagus and can be accentuated by specific behavioral and dietary habits. When, for any reason, this reflux is associated with diseases, complications and impairment of quality of life, the condition goes beyond physiological limits and is called gastroesophageal reflux disease (GERD) - one of the most important digestive disorders, given the high and increasing incidences, the intensity of symptoms and the severity of complications.

GERD has multifactorial causes that are based on the effectiveness of the anti-reflux barrier, such as the crural diaphragm and lower esophageal sphincter; the resistance of the gastric mucosa; of intragastric emptying and pressure and esophageal clearance (BICCAS et al., 2009). The lower esophageal sphincter (LES) is composed of smooth muscle and is under non-cholinergic and non-adrenergic

control. It is maintained in a state of constant contraction, mainly due to extrinsic myogenic activity, but its resting tone is affected by several neural and hormonal factors. The sphincter tone increases in response to increased intra-abdominal pressures and during gastric contractions (ANDREOLLO; COELHO-NETO; LOPES, 2010).

In its pathophysiology, the phrenoesophageal ligament is constituted by the subdiaphragmatic fascia and its function is to prevent the lower esophageal sphincter from being subjected to negative intrathoracic pressure. The diaphragmatic hiatus is formed by fibers from the right crura of the diaphragm, through which the esophagus enters the abdomen. During inspiration, the diaphragmatic hiatus contracts, increasing intraluminal pressure at the esophagogastric junction, preventing reflux. The angle of His is formed by the abdominal esophagus and the gastric fundus. Under normal conditions this angle is acute. Thus, the volume of gastric contents increases the pressure in the abdominal esophagus by extrinsic compression, due to distention of the stomach fundus. In the newborn, this angle is obtuse. The gastric rosette, formed by the concentric folds of the gastric mucosa, in the transition between the esophagus and the stomach, helps to contain the gastric content, preventing its passage into the esophagus.

Thus, hiatal hernias seem to be related to the severity and refractoriness to clinical treatment of reflux esophagitis. Permanent (obesity) or transient (deep inspiration, coughing, physical exercise, Valsalva maneuver, constipation and others) increase in intra-abdominal pressure and predominant posture in the decubitus are factors that predispose to reflux. In summary, the factors that contribute to pathological reflux are: excessive number of reflux episodes, prolonged or deficient esophageal clearance, lower mucosal resistance to the refluxed

content, or the interaction of acid reflux with dietary, behavioral and emotional co-factors. (RAPÔSO et al., 2010)

Among the clinical spectrum of the disease, typical and atypical symptoms stand out. The first are the most classic and involve heartburn (retrosternal burning sensation that can radiate) and regurgitation (return of acidic or food contents to the oral cavity). The second include chest pain, respiratory and otorhinolaryngological symptoms, the last two considered supraesophageal manifestations, since they are caused by the effect of refluxed gastric contents in regions that go beyond the esophagus (AGUERO et al., 2007).

The clinical diagnosis of GERD is very sensitive, as most patients have the classic symptoms of the disease. Thus, it becomes possible to carry out diagnosis, therapeutic testing and follow-up after a diagnosis made by good anamnesis and physical examination. When there is refractoriness or diagnostic doubt, the first exam to be is upper digestive endoscopy (EDA), through which the esophageal mucosa is evaluated, the presence of hiatal hernia and other upper digestive tract disorders are investigated. Technological advances in endoscopic exams have allowed the diagnosis of GERD to go beyond patients with hiatal hernia. Esophageal biopsy must be performed in all patients with suspected esophagitis, although some authors consider it unnecessary in cases without endoscopic esophagitis. Barrett's esophagus, characterized by the presence of intestinal metaplasia in the esophagus, is a premalignant condition.

Among other useful complementary exams, but with different levels of accessibility, there are: radiography of the esophagus, stomach and duodenum; manometry; scintigraphy; esophageal ultrasound; intraluminal impedancemetry, among others. It is also important to rule out the main differential diagnoses, such

as infectious and neurological diseases, bronchial hyperreactivity, peptic ulcer, colic in infants, among others.

Finally, the treatment can be clinical or surgical, depending on its dominant form of presentation and its main etiology. Goals include alleviating symptoms, healing established esophageal lesions, and preventing complications. Surgery will rarely be a first option, as it must be reserved for cases that are refractory to medical treatment or for life-threatening situations. For this reason, the current discussion aims to investigate what the latest studies point out in the clinical treatment of GERD.

## **METHODOLOGY**

This is a bibliographic review whose secondary data were obtained through articles from Google Scholar, Scielo and PubMed databases. The descriptors were defined by the Decs BVS in "Gastroesophageal Reflux Disease", "Clinical treatment" and "Non-pharmacological measures", and hundreds of articles from national and international literature were identified. For the theoretical foundation, studies were selected that contributed to the topic in non-therapeutic aspects, such as etiopathogenesis, clinical picture and diagnosis. For the purpose of this literature review, only articles published in the last 2 years (2020-2022) were included to discuss the clinical treatment of the disease.

## **RESULTS**

The therapeutic approach to GERD includes two modalities, clinical and surgical treatment, the choice of which depends on the patient's characteristics (age, treatment adherence, personal preference, presence of comorbidities), in addition to other factors such as response to treatment, presence of erosions in the esophageal mucosa, atypical symptoms and complications. Clinical

treatment aims to relieve symptoms, heal esophageal mucosal lesions and prevent the development of complications. It is based on non-pharmacological and pharmacological measures.

Non-pharmacological treatment concerns behavioral measures and includes: raising the head of the bed by 15 cm; moderate the intake of the following foods depending on the correlation with symptoms: citrus, coffee, alcoholic and/or carbonated drinks, mint, mint, tomato, chocolate; special care with potentially “risk” drugs: anticholinergics, theophylline, calcium channel blockers, alendronate; avoid lying down for two hours after meals; avoid copious meals; smoking cessation and body weight reduction in obese individuals. Such recommendations are considered useful and time-honored despite scientific controversies.

In addition to the recommendations, the patients’ diet must be individualized, taking into account the particular complaints regarding each food. Such measures improve the doctor-patient relationship and increase adherence to treatment.

## **DRUG TREATMENT**

This can be accomplished through hydrogen blockers, prokinetic agents and proton pump inhibitors.

### ***Proton pump inhibitor (IBPs)***

They represent the drugs of first choice. An example is Omeprazole, its mechanism of action is by inhibiting the production of acid by the parietal cells of the stomach. They are used for a period of four to eight weeks, and if there is no improvement in symptoms, the recommendation is to double the dose. After a certain period without the drug, if symptoms reappear, maintenance treatment must be administered, in which a minimum dose must be administered to keep the patient

asymptomatic. This is the initial therapeutic test.

### ***Hydrogen blockers***

Represent the second line. H<sub>2</sub> blockers reversibly bind to parietal cell H<sub>2</sub> receptors, inhibiting the acid secretory response of these receptors. They have proven effectiveness and are used by millions of people around the world. The clinical efficacy of the drug depends on the desired gastric inhibition and on aspects inherent to this inhibition. This class of drugs is most effective in inhibiting basal acid secretion, particularly nocturnal acid secretion. Cimetidine, ranitidine, famotidine and nizatidine are available on the market. Among these drugs, ranitidine is the most prescribed in our country (GUIMARÃES; MARGUET; CAMARGOS, 2006).

### ***Prokinetics***

Prokinetics have the property of accelerating gastric emptying, but have no effect on transient relaxations of the lower esophageal sphincter. The most used are metoclopramide and domperidone and must be indicated when the gastroparesis component is present. Domperidone is a peripheral dopaminergic antagonist with no cholinergic effects. Metoclopramide acts peripherally, increasing the action of acetylcholine on muscarinic synapses and antagonizing dopamine in the central nervous system. It increases LES pressure, facilitates gastric emptying, improves esophageal peristalsis, accelerates transit time from the duodenum to the ileocecal valve, but does not increase salivation and does not produce bronchospasm.

### ***Antibiotic therapy in *H. pylori****

An addendum of drug therapy must be made to the bacteria: *H. pylori*. The *Helicobacter pylori*, the first bacterial carcinogen to be

recognized, it is a Gram-negative, spiral-shaped, flagellated bacterium, responsible for promoting a natural colonization that develops in the protective mucous layer of the gastric lining (ANSARI SA, et al., 2018). the association of *H. pylori* with some pathologies still requires clarification, however several studies point to the existence of its influence on GERD, suggesting the idea of a defender role of this bacterium in the development of the pathology and raising, therefore, a possible benefit of such bacterial infection. On the other hand, with the understanding of the changes that this microorganism produces in the secretion of human gastric acid, the possibility of this pathogen aggravating the symptoms of GERD also arises (LIUL, et al., 2018), in addition to being importantly related to the incidence of gastric cancer.

The first line of eradication therapy *H. pylori* in western countries it consists of the use of Proton Pump Inhibitors (PPIs), clarithromycin and azithromycin, for a period of 7 to 14 days. It is a well-tolerated triple combination with proven efficacy in most patients. As an alternative, especially for refractory patients, bismuth-based quadruple therapy, which consists of a combination of metronidazole, tetracyclines, PPIs and bismuth, can be instituted, also for 7 to 14 days (MALFERTHEINER P, et al., 2016).

### ***What do the latest studies say?***

In first-line clinical treatment (PPI) refractoriness, reflux episodes seem to be mainly non-acid reflux, which may justify the fact that patients without erosive disease are more refractory to them. It is also noted that a very significant percentage of refractory patients end up being diagnosed with other pathologies when a diagnostic process is initiated using complementary diagnostic means, which presents a margin of error in the diagnosis provided by the clinical diagnosis

of GERD. as an important mechanism of refractoriness. Thus, when reviewing the potential mechanisms associated with the ineffectiveness of PPIs in these patients, it is understood that low therapeutic adherence, the occurrence of non-acid reflux and misdiagnosis must be the most important inherent mechanisms.

It is worth credible, for clinical therapeutic success, the weight loss in obese patients and the correct adherence to the PPI daily and at the appropriate time as consensual measures in the literature. Doubling the PPI dose appears to be effective in treating patients with esophagitis, but does not appear to be necessarily associated with symptom relief. This measure, however, seems to be effective in the treatment of patients with esophagitis, although it is not necessarily associated with symptom relief.

In this sense, a good clinical spectrum of the disease can be clinically optimized before opting for more invasive measures, such as surgery, or even another line of treatment, often adopted early.

## **SURGICAL TREATMENT**

By way of information, anti-reflux surgery (gastric fundoplication) is one of the three most commonly performed surgeries in children in the United States. The Nissen technique is the most used worldwide and, more recently, the laparoscopic approach has been gaining acceptance, especially due to the lower risk of complications and shorter recovery time. Anti-reflux surgery must be reserved for patients who do not respond to medical treatment and/or who have life-threatening conditions. After the emergence of more potent prokinetic agents and acid secretion inhibitors, the role of surgery as a definitive therapeutic weapon for complicated reflux has been questioned.

## CONCLUSIONS

Surgical treatment, when properly indicated, tends to be a definitive way to resolve the typical and atypical symptoms of GERD. The latest studies, therefore, in no way condemn the indications already established for this procedure. On the contrary, in recent years, advances in the surgical technique have increasingly allowed for safety, brevity and resolution, especially in patients with larger hiatal hernias and complications of the disease.

On the other hand, considering the multidimensional etiopathogenesis of the disease, clinical treatment is still the best alternative to start with. With the diverse arsenal of drug classes and different mechanisms of action, it is understandable that the adjustment of doses, the association of classes, the combination with behavioral measures and the due adherence by the patient are presented as decisive measures for the therapeutic success, being able to avoid a surgical approach in most cases.

## REFERENCES

1. BORTOLI, Victor Fajardo et al. Doença do refluxo gastroesofágico-uma revisão da literatura Gastroesophageal reflux disease-a review of the literature. **Brazilian Journal of Health Review**, v. 4, n. 3, p. 14245-14253, 2021.
2. DE SOUZA, André Luís Carvalho; AMORIM, Ítalo Filipe Cardoso. Relação entre o *Helicobacter pylori* e a doença do refluxo gastroesofágico: uma revisão integrativa. **Revista Eletrônica Acervo Saúde**, v. 13, n. 9, p. e8796-e8796, 2021.
3. DOMINGUES, Gerson; DE MORAES-FILHO, Joaquim Prado P. Doença do refluxo gastroesofágico: uma abordagem prática. **Arquivos de Gastroenterologia**, v. 58, p. 525-533, 2021.
4. MARET-OUDA, John; MARKAR, Sheraz R.; LAGERGREN, Jesper. Gastroesophageal reflux disease: a review. **Jama**, v. 324, n. 24, p. 2536-2547, 2020.
5. NORTON, Rocksane C.; PENNA, Francisco J. Refluxo gastroesofágico. **Jornal de pediatria**, v. 76, n. 2, p. 218-224, 2000.
6. SOUSA, Diogo Francisco Couto. Doença de refluxo gastroesofágico refratária. 2021.