

The symptomatology of the gastroesophageal reflux disease and the first line therapy

Teodora Hanghichel^{1,2}, Emanuela Strugaru², Oana Maria Ionescu¹, Lenuta Profire¹

¹ Department of Pharmaceutical Chemistry, Faculty of Pharmacy, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania

² Aris Pharmacy, Iasi, Romania

ABSTRACT

Over time, gastroesophageal reflux has undergone an unexpected and at the same time undesirable evolution towards the most commonly diagnosed upper gastrointestinal disease, called gastroesophageal reflux disease. The symptoms of gastroesophageal reflux disease are complex, difficult to treat and often recurrent. In order to prevent the disease recurrences, it is also necessary to establish the treatment in accordance with the gastroesophageal reflux symptoms. Unfortunately, nowadays, more and more patients of all ages go to the pharmacy with typical symptoms of gastroesophageal reflux, this ailment having a negative impact on the quality of life. This article aims to highlight the role of the pharmacist in recognizing the symptoms of gastroesophageal reflux and initiating first-line treatment.

Keywords: GERD, pharmacist, obesity, risk factors

INTRODUCTION

Statistically, gastroesophageal reflux disease (GERD) or gastroesophageal reflux (GER) has a prevalence that varies between regions and countries from 8.8% to 28% of the respective population [1]. GERD is a digestive disorder that affects the lower esophageal sphincter (LES), being one of the most common diagnosis managed in the gastroenterology clinics [2]. LES protects the esophagus from stomach acid and if it relaxes, the gastric content can flow back and cause acid reflux.

GERD can be classified as non-erosive reflux disease (NERD) and erosive reflux disease (ERD) based on the presence or absence of esophageal mucosal damage seen on endoscopy [3]. GERD is treatable with a combination of lifestyle, alimentation and basic therapy. If symptoms persist, medical advice is required to determine the underlying cause. If GERD is not properly treated, patients with persistent acid reflux may be at risk for a number of complications like erosive esophagitis, peptic stricture, Barrett's esophagus (defined as intestinal metaplasia of the esophagus) [4], esophageal adenocarcinoma and finally pulmonary disease [3].

Corresponding author:
Teodora Hanghichel
E-mail: teodora-l-hanghichel@d.umfiasi.ro

Article History:
Received: 18 June 2021
Accepted: 5 July 2021

TABLE 1. Foods that may cause acid reflux

Foods high in fat, salt or spice	Other food that can cause acid reflux
Fried food	Carbonated beverages
Fast food	Peppermint
Pizza	Chocolate
Chips/processed snacks	Citrus fruits
Pepper, chili powder	Tomato sauce
Bacon	-
Cheese	-

GERD SYMPTOMS

Symptoms of GERD can be classified as: (i) typical symptoms (heartburn, regurgitation of gastric and/or esophageal contents); (ii) atypical symptoms (epigastric pain, epigastric fullness, epigastric pressure, dyspepsia, bloating, nausea, belching) and (iii) extraesophageal symptoms (chronic cough, wheezing, bronchospasm, hoarseness, sore throat, asthma, laryngitis, dental erosions) [3].

RISK FACTORS IN GERD

Multiple mechanisms are involved in GERD pathogenesis. First of them are motor abnormalities, like damaged LES resting tone with spontaneous and transient LES relaxation (TLESRs) of 10-60s duration and damaged esophageal acid clearance. Anatomical risk factors include hiatal hernia (prevalance of 43%) [8] and obesity (prevalance of 35.8%) [5]. Hiatal hernia is considered to be a significant anatomical factor, because it increases the frequency of TLESRs and decreases esophageal clearance [6]. A possible mechanism through which obesity aggravates GERD consists in increasing abdominal pressure, delaying gastric emptying, increasing frequency of TLESRs and reducing LES resting pressure. For the patients with moderate obesity, with body mass index (BMI) >40, some bariatric procedures like ballons or bands can aggravate the reflux [7]. The incidence of reflux symptoms rises progressively with increasing BMI [6]. Metabolic syndrome and especially hypertriglyceridemia have been common associated with erosive esophagitis or reflux symptoms [8].

GERD risk factors include also a considerable number of genetic factors. Numerous single-nucleotide polymorphisms (SNPs) have been proposed as potential factors in the appearance of reflux disease [6]. Physiological conditions, such as pregnancy, are another factor associated with reflux disease, which can cause GERD, especially in the second or third trimester of pregnancy [1].

Some commonly used groups of drugs can cause GERD through various mechanisms and can also lead to an increase in the existing symptoms of GERD. The mechanism that causes reflux includes the potential for drugs to cause damage and inflammation to the esophageal mucosa [9].

The use of non-steroidal anti-inflammatory drugs (NSAIDs) aggravates GERD symptoms. Acetylsalicylic acid may slightly increase the risk of developing GERD, which increases with the combination of nonsteroidal anti-inflammatory drugs. The use of calcium channel blockers can lead to GERD and exacerbate existing reflux symptoms. Theophylline, an antiasthmatic drug, can increase the number of GERD episodes in asthma patients and can also exacerbate existing reflux symptoms. Anticholinergic drugs can also increase the number of episodes of reflux [10]

GERD TREATMENT



The treatment for GERD aims to prevent and to relieve symptoms, to heal the damage caused by the acid and to stop the development of the disease, thus avoiding further complications. Although GERD symptoms vary from patient to patient, the treatment can be addressed from two perspectives: *nonpharmacological and pharmacological* approach.

Nonpharmacological approach

Both lifestyle changes and eating habits are the first line of treatment in reducing the symptoms of GERD. The elevation of the head of the bed is a proven lifestyle modification which decreases esophageal acid exposure and esophageal clearance time, thus reducing the GERD symptoms [11]. Several changes in lifestyle can prevent from developing symptoms: eating smaller servings, eating slowly and at least 2 to 3 hours before bedtime. Foods that may cause acid reflux are presented in Table 1. Persons with GERD should avoid this type of foods because they can irritate the esophagus and can relax LES [11]. Stopping daily habits like smoking, alcohol and caffeine intake is important to reduce GERD symptoms [6].

Also, those aliments that have a low pH, are acidic and thus they are more likely to cause reflux. Contrariwise alkaline foods can help offset strong stomach acid and watery foods can dilute it. These are presented in Table 2. New studies highlight the protective effect of curcumin in esophageal diseases, including gastroesophageal reflux, reflux esophagitis,

TABLE 2. Foods that can help avoid acid reflux

		High fiber aliments	Alkaline aliments	Watery aliments
Brown rice Couscous		Whole grain	Bananas Melons	Cucumber Watermelon
Sweet potatoes Beets Carrots		Root vegetables	Cauliflower Fennel Nuts	Herbal tea Broth-based soupe
Asparagus Broccoli Green beans		Green vegetables	-	-

required. These patients are named partial responders or nonresponders, depending on the degree of symptom alleviation [7]. If it is necessary to do an endoscopy, it is not recommended for patients with typical symptomatology unless they don't respond to PPIs treatment [10].

Barett's esophagus and last but not least esophageal carcinoma [13].

Pharmacological approach

Where necessary, therapeutic strategies should be focused on the GERD phenotype and revolve around the severity of the symptoms reported by the patients [12]. We can look at managing the GERD from two perspectives. First is to progressively introduce the use of antacids followed by/or together with H2 blockers and in case of persisting symptoms, switching to PPIs [1]. Second perspective is to start with the most effective approach and then gradually reduce the intensity of the treatment to the use of antacids and even give up treatment [1].

Antacids have the role of neutralizing the pH level in the stomach, providing relief from the burning sensation caused by the acidity. The most common antacids contain aluminum hydroxide, magnesium hydroxide, calcium carbonate, sodium bicarbonate [1]. The role of *H2 blockers* is to inhibit histamine stimulation of the parietal cell, thus decreasing gastric acid secretion. Among H2 blockers, more used are famotidine, ranitidine and cimetidine. *PPIs therapy* decrease the acid secreted from parietal cells into the gastric lumen. The most potent class used in GERD therapy are PPIs, prodrugs that are converted into active compounds in the acidic environment of the gastric lumen [10,11]. PPIs needed to be administered once daily, at the same time every day [10]. Statistically, 10% of patients who administrate full-dose PPIs still suffer from heartburn and regurgitation [7]. Overmore, some patients report refractory symptoms when the PPIs therapy is finished. So, what's to be done for these patients?

If the patients cannot tolerate antacid treatment because of the side effects (usually diarrhea and hypomagnesemia), or the symptoms persist in spite of optimized PPIs therapy, the antireflux surgery is

THE ROLE OF THE PHARMACIST IN GERD MANAGEMENT

Often times, pharmacists are the first healthcare professionals that patients come in contact with to ask for advice concerning their health. It is important for the pharmacists to have a proper knowledge of basic GERD symptoms in order to determine the right approach for this ailment. Since patients with GERD have varied symptomatology, which sometimes interferes with other pathology, the pharmacist plays a very important role in recognizing symptoms and advising the patient about the diet and treatment.

For the proper management of GERD treatment it is important that the patient answer a few questions like: "When did the symptoms start?", "(Do you) have acidic taste in the mouth?", "(Do you) experience heartburns? Are they connected to food intake or not?", "When does the symptoms appear more frequently?", "Is the heartburn linked with regurgitation?", "(Do you) find it hard to swallow?", "(Do you) feel pain in the chest?", "(Do you) take any other medication?", "Are you pregnant?", "Do you have a family history of gastric and/or esophageal reflux?", "How frequently are the symptoms occurring?", "Have you tried any lifestyle changes or medications that have made your symptoms better or worse?". Usually, heartburn and acid regurgitations are sufficient to suspect GERD [1,11,12].

Also, the pharmacist should be aware that the medication presented in the previous chapter can predispose patients to reflux and potentially exacerbate the symptomatology.

It is the duty of the pharmacist to ask basic questions in order to identify the severity of the ailment and then to choose and present treatment options. Also it is important to give clear information about the duration and proper administration of the selected medication. A notable role that the pharmacist plays

is to also educate the patients about the potentially adverse effects as well as of the consequences of long-term use of the medication.

Not to be neglected is the involvement of the pharmacist in the follow-up of the treatment adopted by the patients. This way, if GERD symptoms persist or worsen, the patient could be guided to seek medical attention and benefit from advanced investigations.

CONCLUSIONS

In conclusion, the treatment of gastroesophageal reflux can be successful, only if the non-pharmaceuti-

cal aspects of the therapy like lifestyle changes are complementary to the pharmaceutical treatments. Because frequent reflux symptoms are not optimally treated with alginates or antacids, a short-term treatment with PPIs is required in patients without alarm symptoms. The importance of pharmacists in ameliorating reflux disease cannot be forgotten because, by customizing the treatment scheme, the fastest and best results can be obtained. Also, as they are able to guide the treatment, it is essential to stay up to date with the available products, both medications and over-the-counter products.

Conflict of interest: none declared

Financial support: none declared

REFERENCES

1. Nirwan J, Yousaf M, Conway B, Usman Ghori M. Management of gastrointestinal disorders and the pharmacist's role: gastroesophageal reflux disease. *Encyclopedia of pharmacy practice and clinical pharmacy* 2019;336-350.
2. Yadlapati R, Pandolfino JE. Personalized approach in the work-up and management of gastroesophageal reflux disease. *Gastrointest Endoscopy Clin N Am*. 2020;227-238.
3. Badillo R, Francis D. Diagnosis and treatment of gastroesophageal reflux disease. *World J Gastrointest Pharmacol Ther*. 2014;5(3):105-112.
4. Shaheen NJ, Richter JE. Barrett's oesophagus. *Lancet* 2009;373:850-861.
5. Cicala M. New classifications of GERD and impact on clinical management. *Global J Dig Dis*. 2017;14-15.
6. Argyrou A, Legaki E, Koutserimpas C, Gazouli M, Papaconstantinou I, Gkiokas G, Karamanolis G. Risk factors for gastroesophageal reflux disease and analysis of genetic contributors. *World J Clin Cases* 2018;6(8):176-182.
7. Lundell L. Borderline indications and selection of gastroesophageal reflux disease patients: is surgery better than medical therapy? *Dig Dis*. 2014;32:152-155.
8. Li CH, Hsieh TC, Hsiao TH, Wang PC, Tseng TC, Lin HH, Wang CC. Different risk factors between reflux symptoms and mucosal injury in gastroesophageal reflux disease. *Kaohsiung J Med Sci*. 2015;31:320-327.
9. Böhmer AC, Schumacher J. Insights into the genetics of gastroesophageal reflux disease (GERD) and GERD-related disorders. *Neurogastroenterol Motil*. 2017;29.
10. Mungan Z, Pınarbaşı Şimşeki B. Which drugs are risk factors for the development of gastroesophageal reflux disease?. *Turk J Gastroenterol*. 2017;28(Suppl 1);38-43.
11. Clarrett D, Hachem C. Gastroesophageal Reflux Disease (GERD). *Missouri Medicine* 2018;115(3):214-218.
12. Gyawali CP, Kahrilas PJ, Savarino E, et al. Modern diagnosis of GERD: the Lyon Consensus. *Gut*. 2018;67:1351-1362.
13. Kwiecien S, Magierowski M, Majka J. Curcumin: a potent protectant against esophageal and gastric disorders. *Int J Mol Sci*. 2019;20,1477.