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A review of GERD and its treatment

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A review of GERD and its treatment

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Pharmacists have many responsibilities to patients. One of the most important is to educate their patients regarding therapeutic drug and nondrug options. Another unique responsibility is that of intervention and referral of patients who cannot adequately manage health-related issues on their own. A considerable number of people experience heartburn, giving pharmacists the opportunity to share their knowledge. The vast number of over-the-counter products designed to treat heartburn can cause confusion among consumers; therefore, pharmacists need to be able to step in and assist in product selection. Additionally, this allows pharmacists the opportunity to work up a patient and determine whether or not the problem is self-treatable. A condition known as



gastroesophageal reflux disease (GERD) is often mistaken for heartburn and will often require medical attention. Pharmacists should be aware that intervention in this area can prove greatly beneficial.

The Agency for Healthcare Research and Quality defines GERD as heartburn and/or acid regurgitation occurring weekly. Even though GERD is not considered to be a high-cost disease to treat, costs associated with GERD in 2000 were upwards of \$10 billion. GERD occurs when the lower esophageal sphincter (LES), which connects the esophagus to the stomach, is weak or relaxes, allowing stomach contents to reflux into the esophagus. Patients with GERD often experience a sensation known as heartburn in the chest and/or throat. This uncomfortable

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GOAL

To provide information on the treatment of GERD in order to educate pharmacists and technicians regarding appropriate therapies and when patients should be referred

CREDIT

This lesson provides two hours of CE credit and requires a passing grade of 70%.*

OBJECTIVES

Upon completion of this article, the pharmacist and technician should be able to:

- ✓ Explain when to recommend OTC products for heartburn and when to refer patients to their physicians
- ✓ Identify typical and atypical symptoms of GERD
- ✓ List the tests that may be preformed to diagnose GERD
- ✓ Discuss medications and their role in the treatment of GERD
- ✓ Discuss lifestyle changes to improve the symptoms of GERD

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feeling is a result of delicate esophageal tissue coming into contact with harsh stomach acid. This condition may also present as chest pain not classified as heartburn, difficulty swallowing, hoarseness in the morning, tightness in the throat, or even dry cough. The distinction between occasional heartburn and GERD is the frequency of events.

Heartburn is commonly experienced by people of all ages and occurs infrequently. A recent Gallup poll found that 44% of Americans experience heartburn at least once a month. Another poll estimated that 19.8% of Americans experience heartburn at least once a week. The diagnosis of GERD requires symptoms to occur two or more times per week. Symptoms of this disease can range from mild to severe, and chronic symptoms can lead to other serious complications.

While the exact etiology of GERD is unknown, there are several proposed pathophysiologies. Various foods associated with GERD include acidic fruits, chocolate, fried foods, drinks containing caffeine, onions, mint flavorings, and tomato-based products. These so-called trigger foods can reduce the tone of the LES, thereby causing a backflow of stomach contents. Hiatal hernias, caused by a disorder in which the top of the stomach extends past the diaphragm, have also been thought to play a part. Normally, the diaphragm helps the LES keep stomach contents from entering the esophagus. When this partnership is compromised, reflux occurs. Additional factors that may predispose a person to developing GERD are pregnancy, obesity, smoking, and the use of alcohol. It is believed, however, that compromised LES tone and hiatal hernias account for most cases of severe GERD. Some studies have claimed that these two conditions are independent predictors of GERD in more than 70% and 75% of cases, respectively. Excessive production of stomach acid and hyperchlorhydria are also strongly linked to severe GERD.

Another theory is a motility disorder, transient LES relaxations (TLESRs), believed to be the cornerstone in causing mild to moderate GERD. Normally after swallowing, a peristaltic wave propels food to the distal esophagus and LES relaxation occurs for several seconds.

Table 1
Medications that worsen GERD

Theophylline
Nitrates
Calcium-channel blockers
Meperidine
Beta₂ adrenergic agonists
Oral contraceptives
NSAIDs (may increase injury)

Source: *Med Clin N Am* 2005; 89

Swallowing will not initiate TLESRs; they occur without regard to esophageal peristalsis and last more than 10 seconds. TLESRs occur more frequently in GERD patients and may account for 80% of their reflux episodes.

Last, delayed gastric emptying may also contribute to GERD by stimulating TLESRs because of gastric distention. This may play an important role in diabetes patients with GERD.

Patients suspected of having GERD should be encouraged to seek medical attention. Occasionally, symptoms may be resolved with lifestyle modifications.

If lifestyle modifications do not resolve the problem, or if patients prefer pharmacologic therapy, doctors may suggest OTC products or prescription medications. Special refractory cases may require surgical intervention.

Proper treatment of GERD is essential to prevent long-term complications, including bleeding and ulceration of the esophagus or esophageal stricture. A more serious consequence may be the development of Barrett's esophagus, which occurs in approximately 5% to 15% of patients with chronic GERD. Due to this condition, esophageal tissue cells become abnormally shaped and colored. Ultimately Barrett's esophagus may lead to cancer. Endoscopy is required for detection of Barrett's esophagus. Even without progression to Barrett's esophagus, GERD is an independent risk factor for the development of esophageal adenocarcinoma. This further increases the need to treat people with chronic GERD. Research has also shown that untreated GERD may exacerbate chronic conditions such as asthma, pulmonary fibrosis, and chronic cough.

Diagnosis

The diagnosis of GERD is primarily made by symptom assessment obtained through a thorough history of the patient. The most commonly reported symptoms of GERD are heartburn and acid regurgitation. Patients will most often seek medical attention when these symptoms interfere with their daily lives. The frequency, severity, and timing of these symptoms should be determined during the patient history. Symptoms may be described as a burning pain that spreads to the throat and neck. The burning may be worsened by meals, lying down, bending over, or drinking acidic beverages. It is also important to assess what OTC treatments the patient has used and whether they were effective in relieving the symptoms.

Heartburn and acid regurgitation are not always present in patients with GERD. Patients may experience atypical symptoms, which include chest pain, asthma, hoarseness, dental enamel loss, recurrent sore throat, and chronic cough. A patient who has a cough may induce GERD episodes causing a cycle of reflux. Another theory explaining why cough is a symptom of GERD involves the stimulation of the esophageal-bronchial reflex by the reflux episodes. This is the most common theory presented linking GERD to cough. The cough may be a dry cough or a productive cough and may be present at night in some patients. Patients initiated on antireflux therapy in these cases have responded well, even if they have not reported symptoms of heartburn and

Table 2
Conditions that increase the risk of GERD

Pregnancy	Scleroderma
Hiatal hernia	Cystic fibrosis
Chronic hiccups	Diabetes mellitus
Cerebral palsy	Obesity
Down's syndrome	Family history
Gastrinoma	Alcoholism
Smoking	

Source: *Med Clin N Am* 2005; 89

acid regurgitation.

Empiric therapy may be initiated after a complete history is positive for typical GERD symptoms. Therapy may consist of a histamine-2 receptor antagonist (H2RA) twice daily or a proton pump inhibitor (PPI) taken once daily 30 minutes before a meal. PPIs are considered first-line due to their superiority over other treatments. A rapid response to a normal dose of PPI (PPI test) is often thought of as a valid diagnosis of GERD. Studies examining the validity of the PPI test have produced differing results. Despite the conflicting information, empiric therapy is regularly initiated and should continue for four to eight weeks. Drug selection should be based on the frequency and severity of symptoms. There are two approaches to therapy: step up and step down. Patients started on H2RA therapy may step up to a PPI if symptoms persist after the initial eight weeks of therapy. Step-down therapy involves initial therapy with a PPI for eight weeks of treatment, which should then be streamlined to the lowest effective dose of a PPI or an H2RA.

Complicated GERD may involve the alarm symptoms of dysphagia, gastrointestinal bleeding, anemia, vomiting, weight loss, early satiety, and painful swallowing. In cases when a patient has atypical or alarm symptoms, diagnostic testing should be conducted before therapy initiation. Diagnostic testing may include endoscopy, laboratory tests, pH testing, and esophageal manometry.

Diagnostic testing

Esophagrams are used to document reflux and detect mucosal injury due to reflux. They will also identify hiatal hernia, Barrett's esophagus, peptic stricture, and adenocarcinoma. Esophagrams are also useful in

Table 3
Lifestyle modifications

- Elevate the head of the bed
- Sleep on left side
- Eat small meals
- Avoid high-fat meals
- Avoid eating three hours before lying down
- Lose weight
- Wear loose-fitting clothing
- Avoid foods that exacerbate symptoms
- Avoid alcohol, caffeine, tobacco

Source: *American Journal of the Medical Sciences* 11/03

diagnosing other upper gastrointestinal diseases (e.g., ulcers, gastric malignancy). This diagnostic test utilizes barium and is relatively inexpensive and noninvasive. Esophagrams are not commonly conducted, since they are less sensitive (60% for single contrast, 90% for double contrast) for detecting reflux esophagitis than esophagogastroduodenoscopy (EGD). Esophagrams are best used when trying to identify Schatzki's rings, webs, diverticula, and strictures. Patients with dysphagia may undergo an esophagram to identify these lesions. Patients who are intolerant of or who refuse EGD will also have an esophagram.

EGD is the most valuable clinical test for GERD. It has a high sensitivity, high specificity, and is safe. EGD can detect the severity and extent of injury to the mucosal lining as well as existing complications. The severity of esophagitis is determined and graded according to the Los Angeles grading system, the Savary-Miller grading system, or the Hetzel classification. Disadvantages associated with EGD include cost, degree of invasiveness, and discomfort. Also, EGD will not detect nonerosive reflux disease and may fail to identify up to 40% of acid reflux cases that have been identified in pH testing. The cases missed are generally mild and uncomplicated disease. If esophagitis is not present, EGD may fail to diagnose extra-esophageal manifestations of GERD. Patients who have an EGD may also have a biopsy conducted at the time of the procedure. This should be done in patients with strictures or an esophageal mass.

Ambulatory pH monitoring is the most sensitive test for diagnosing acid reflux. This is a 24-hour test for diagnosing GERD due to acid reflux. It cannot detect GERD caused by nonacid reflux or mucosal damage from this refluxate. This test produces the best results in

CONTINUING EDUCATION

patients with typical symptoms that are refractory to traditional antireflux therapy without evidence of esophagitis at EGD, patients presenting with extraesophageal symptoms of undetermined etiology, and patients preparing for antireflux surgery. Previously a catheter was placed transnasally into the esophagus with the pH electrode placed in the esophagus 5 cm above the LES. This technique is uncomfortable and disrupts the patient's daily activities. To avoid these problems, the Medtronic Bravo pH system does not utilize a catheter. Instead, a capsule is inserted by EGD and attached to the esophageal mucosa 6 cm above the gastroesophageal junction.

During the 24-hour pH test, the acid exposure time is measured and is defined as the amount of time the pH is less than 4. To accomplish this, esophageal pH will transmit to a small receiver that is then uploaded onto a computer for analysis. After the test, the catheter is removed, or, with the Bravo pH system, the capsule passes into the stool when the esophageal mucosa sloughs off. It is uncommon that the capsule requires endoscopic removal. Patients are also instructed to record their regular daily routine in an effort to stimulate the events that cause acid reflux. Symptoms and time of symptoms should be recorded in a diary of events in order to correlate acid reflux with symptoms.

Duodenogastroesophageal reflux may be diagnosed by scintigraphy or by esophageal bilirubin monitoring. Scintigraphy is a noninvasive test that uses intravenous technetium-99m iminodiacetic acid. The radioactive substance is concentrated in the liver and then excreted by the bile ducts into the mid-descending duodenum. It is then available for duodenogastroesophageal reflux because it can be detected as radioactivity from the radiolabeled iminodiacetic acid in the esophagus. Scintigraphy is expensive, technically difficult, and has a restricted application; therefore, esophageal bilirubin monitoring is more likely to be done. The Bilitec device

is more quantitative and more versatile. This is an ambulatory procedure that measures bilirubin concentration of esophageal fluid. Elevated bilirubin levels in the esophagus have been associated with Barrett's esophagus.

Patients may have nonacidic reflux, which is not detected in pH monitoring. This type of reflux may be detected by a decrease in esophageal impedance. Fluid will conduct electricity better than solids or mucosa. Air would cause an increase in esophageal impedance because it conducts electricity more poorly than solids. The Bilitec device will differentiate between swallows and reflux. Impedance monitoring may be done simultaneously with pH monitoring, allowing detection of acid reflux or nonacid reflux. This procedure may replace the esophageal bilirubin monitoring, have use in evaluation of refractory symptoms of GERD, and provide a useful way to evaluate nonacid regurgitation.

Esophageal manometry has limited use in the diagnosis of GERD. It may be used prior to antireflux surgery to eliminate other diagnoses, to evaluate LES tone, and to assess esophageal body function. It is useful to

Table 4

Symptoms and treatment options for GERD

Symptoms	Definition of symptoms	Level of care	Treatment options
Mild	Occasional heartburn, regurgitation	Self-medicate	Lifestyle modifications, OTC antacids, H2RA, PPI (therapy <2 weeks)
Moderate	Frequent symptoms responsive to standard therapy	Primary care physician	Lifestyle modifications, H2RA, PPI
Severe	Persistent and/or severe symptoms resistant to standard therapy	Gastroenterologist	Lifestyle modifications, high-dose PPI, surgery, endoscopic procedures, prokinetics, baclofen

Source: *American Journal of the Medical Sciences* 11/03

CONTINUING EDUCATION

Table 5
Medications used in the treatment of GERD

Medication class	Names	OTC dose	Rx dose (max/day)	Common side effects+	Drug interactions+
Antacids Alginic agent	Aluminum and magnesium (Maalox, Mylanta) Calcium (Tums) Gaviscon	10 ml-20 ml p.r.n. 2-4 tabs p.r.n. 15 ml-30 ml q.i.d. p.r.n.	NA	Constipation Diarrhea Acid rebound with Ca++	Antacids may decrease the absorption of certain drugs and should be separated from each other (instruct patient to take antacids up to 4 hours before or 2 hours after the interacting drug).
Histamine (H₂)-receptor antagonists (H2RAs)*	Nizatidine Famotidine Cimetidine Ranitidine	75 mg b.i.d. 10 mg q.d.-b.i.d. 200 mg q.d.-b.i.d. 75 mg q.d.-b.i.d.	150 mg b.i.d. 20 mg b.i.d. (80 mg) 800 mg b.i.d. 150 mg b.i.d. (600 mg)	Dizziness, headache, constipation, diarrhea	3A4 inhibitor (weak) Inhibits 1A2, 2C8/9, 2C19, 2D6, 2E1, 3A4 Substrate of 1A2, 2C19, 2D6; inhibits 1A2 and 2D6
Proton pump inhibitors (PPIs)	Omeprazole Lansoprazole Rabeprazole Pantoprazole Esomeprazole	20 mg q.d.	20 mg q.d. (40 mg) 15 mg q.d. (30 mg) 20 mg q.d. (40 mg) 40 mg q.d. (80 mg) 20 mg q.d. (40 mg)	Headache, diarrhea, constipation, nausea, vomiting	Substrate 2C19, inhibits 2C8/9, 2C19 Substrate 2C19, 3A4, inhibits 2C19 Substrate 2C19, 3A4, inhibits 2C19 Substrate 2C19, inhibits 2C8/9 Substrate 2C19, 3A4
Prokinetic agents	Metoclopramide Bethanechol	NA	10 mg t.i.d. 25 mg q.i.d.	Drowsiness, restlessness, EPS, diarrhea Hypotension, tachycardia, headache, malaise, diarrhea	Opiates, anticholinergics, haloperidol Cholinergic drugs, procainamide, quinidine, anticholinergics
Gamma-aminobutyric acid₂ receptor agonist	Baclofen	NA	20 mg t.i.d.	Drowsiness, dizziness, ataxia, weakness, headache, constipation	CNS depressants

*All decrease the effect of itraconazole and ketoconazole

+Lists are not all-inclusive

CONTINUING EDUCATION

exclude motility defects, esophageal spasms, and achalasia.

Treatment

The treatment of GERD depends heavily on the frequency and severity of symptoms. Goals of therapy include relief of symptoms, healing of any esophageal lesions, keeping the patient symptom-free and disease-free, and preventing complications and adverse events of therapy. Ideally, one would like to obtain the above goals in the most cost-effective manner possible. Treatments either strengthen the LES or reduce acid exposure to the esophagus. Lifestyle changes are aimed at strengthening the LES and reducing or blocking the secretion of acid. Lifestyle modifications must be incorporated into the treatment of all patients; however, reduction of acid exposure has become the mainstay of therapy for GERD.

The addition of lifestyle modifications is simple and should be implemented by all patients with GERD. Elevation of the head of the bed by six inches helps to promote acid clearance of the esophagus and decreases the overall acid exposure time. Modifications such as sleeping on one's left side and avoiding meals three hours before bedtime will also improve GERD symptoms. Decreasing intragastric pressure will make a difference in relieving symptoms. Weight loss, wearing loose-fitting clothing, and avoiding bending over at the waist are ways to reduce the pressure. Pregnancy may also increase intragastric pressure; however, symptoms should resolve after delivery. Diets that include spicy foods, chocolate, peppermint, fatty foods, acidic and caffeinated drinks, and alcohol may exacerbate GERD symptoms. Avoiding these foods may strengthen the LES tone and improve patient symptoms. Tobacco is another substance that may contribute to a decrease in LES tone.

Medications including calcium-channel blockers, beta agonists, alpha-adrenergic agonists, theophylline, and nitrates may also contribute to GERD symptoms. Alendronate (Fosamax) and nons-

teroidal anti-inflammatory drugs should be avoided if exacerbation of esophageal injury is a concern. If lifestyle modifications are not completely effective in alleviating symptoms or symptoms are frequent and severe, medication therapy should be initiated.

Antacids: Antacids work by neutralizing gastric acid secretions and are proven to be more effective than placebo. Antacids such as Maalox and Mylanta temporarily (one to two hours) buffer stomach acid to provide relief of heartburn. Products available most often contain calcium, magnesium, or aluminum salts. Those containing calcium may cause rebound heartburn and should be avoided. Antacids with alginic acid, such as Gaviscon, float above the gastric contents and act as a barrier to reflux. This floating barrier is most effective when patients are in the upright position.

Adverse effects from antacids include diarrhea from magnesium and constipation from aluminum products. Diarrhea may be a serious problem if the patient is taking the antacid for more than occasional relief of heartburn. An increase in aluminum absorption and a decrease in phosphorus may occur if aluminum products are taken on a chronic basis. The liquid products are the most beneficial for quick relief of symptoms but are less popular due to the chalky taste. Antacids are best for patients who require quick and infrequent relief of symptoms and as adjuvant therapy for breakthrough heartburn and pregnancy-related heartburn.

H2RAs: Histamine-2 receptor antagonists provide relief to more than 50% of GERD patients after only a few weeks of treatment. Several randomized, controlled trials have proven H2RAs are more effective than placebo. They exert their actions by inhibiting the H2 receptor on the gastric parietal cells, therefore inhibiting acid secretion. Standard doses of H2RAs are effective in some patients; however, higher doses (twice the standard dose) and more frequent administration may increase the

CONTINUING EDUCATION

effectiveness in treating esophagitis. These higher doses increase the cost, making them equivalent in cost to PPI therapy. Increasing the frequency and dose may also contribute to poor compliance.

H2RAs are available OTC in half the standard prescription dose. They are recommended in patients with mild GERD, patients with breakthrough symptoms despite other therapies, and patients who are able to predict when they will have symptoms of GERD. H2RAs may also be used when symptoms occur or if additional symptom control is needed at night. Patients who use H2RAs continuously or frequently and who have breakthrough symptoms should seek medical attention. One limitation of H2RA therapy is that tolerance may develop when the treatment duration is longer than 30 days. The doses of these medications may need adjustment in renally insufficient patients and in the elderly. H2RAs are generally well tolerated, but there have been case reports of cytopenias, gynecomastia, liver function test abnormalities, and hypersensitivity reactions. Overall, H2RAs are beneficial when prompt relief of symptoms is desired. All four agents available (ranitidine, famotidine, cimetidine, nizatidine) may be used interchangeably, although the pharmacist should interview patients on their medication history to identify any drug-drug interactions.

PPIs: Proton pump inhibitors inhibit the parietal cell H⁺/K⁺ ATPase pump, which then suppresses acid secretion. PPIs are best at treating moderate to severe GERD and erosive esophagitis and its complications, and at preventing GERD symptoms. This group of medications includes omeprazole, lansoprazole (Prevacid), rabeprazole (Aciphex), pantoprazole (Protonix), and esomeprazole (Nexium). They are most often taken once daily. All of the agents are equally effective based on studies, but the patient response may be different with each agent. This inpatient variability allows physicians to switch to a different PPI if the patient does not respond well or tolerate the current therapy. Omeprazole is also available OTC in the 20-mg strength. Current labeling recommends

a short treatment period of 14 days, and patients should seek medical attention if the need for treatment exceeds this. Esomeprazole is the S-isomer of omeprazole, and patients with more severe disease may find it more effective than the other agents in this class.

Patients should be counseled on appropriate administration of PPIs, which includes taking them 30 minutes before a meal. This is so that the medication is on board when the proton pumps have been activated by a meal. Educating your patients regarding this is especially important in those patients who take their PPI twice daily, because they tend to take the second dose at bedtime. Twice-daily dosing is often needed in patients with inadequate esophageal healing and atypical symptoms such as asthma, cough, and laryngitis. It is best to give a standard dose twice daily instead of doubling the dose and giving it once daily.

When nocturnal symptoms continue to occur despite PPI therapy, an H2RA may be added at night. Previously this was thought to decrease the efficacy of the PPI, but studies have demonstrated similar acid control after PPI alone or PPI plus H2RA. Patients most commonly complain of headache and diarrhea when taking PPIs. They may be changed to an H2RA after successful treatment with a PPI, but relapse rates may be as high as 70% (versus less than 20% with continued PPI therapy). Once failure of PPI therapy has been established, patients should undergo further diagnostic testing.

Prokinetic agents: Metoclopramide, bethanechol, and cisapride are prokinetic agents that have been used in the treatment of GERD. They are thought to be beneficial because these agents decrease the amount of time the stomach contents are available for reflux, therefore decreasing esophageal acid contact time. Overall, these agents are not widely used due to lack of efficacy and bothersome side effects. Cisapride increases LES pressure by aiding in esophageal peristalsis and accelerating the emptying time. Due to the cardiovascular side effects of cis-

CONTINUING EDUCATION

apride, it is available only for compassionate use for the treatment of gastroparesis.

Bethanechol, a cholinergic agonist, increases esophageal peristalsis and stimulates gastric secretion. It will alleviate GERD symptoms due to an increase in LES pressure but will not heal esophagitis. Bethanechol is dosed at 25 mg four times a day, and its side effects include diarrhea, abdominal cramping, and blurred vision. Metoclopramide works by inhibiting dopamine receptors. It will increase LES pressure and improve gastric emptying. Like bethanechol, metoclopramide improves GERD symptoms without healing esophagitis. The use of metoclopramide is limited by its side effects, which include extrapyramidal side effects (EPS), lethargy, and menstrual dysfunction. Tardive dyskinesia may occur in patients taking metoclopramide and can be permanent.

Tegaserod (Zelnorm) has been utilized in the treatment of GERD. A small, randomized, double-blind, placebo-controlled study demonstrated a 50% improvement in postprandial esophageal acid exposure with tegaserod doses of 1 mg/day or 4 mg/day 30 to 60 minutes prior to the morning and evening meal. Potential mechanisms of action include increased esophageal acid clearance, improved gastric emptying, and a reduction in TLESRs. Common reported side effects were diarrhea, abdominal pain, gas, vomiting, and headache. Tegaserod may have a potential role in the treatment of GERD, but further studies with a larger sample size need to be conducted to determine efficacy and mechanism of action. Domperidone and erythromycin enhance gastric emptying time but are not routinely used due to side effects.

Future therapies: Research has been focusing on the development of TLESR inhibitors. TLESR inhibitors attack the major mechanism behind GERD and would treat both acidic and nonacidic reflux. Baclofen is a gamma-aminobutyric acid receptor agonist and blocks TLESR. It reduced the frequency of reflux by 60% compared with placebo.

Candidates for treatment with baclofen may be patients who have persisting reflux symptoms despite treatment with high-dose PPIs. Baclofen is generally well tolerated, with side effects consisting of dizziness, somnolence, and transient nausea. In addition to potential side effects, the use of baclofen may be limited due to its three-times-daily dosing regimen.

The medications discussed above may be used in combination. Studies with PPIs, H2RAs, and prokinetics often use antacids as treatment for breakthrough heartburn. Therefore, it is reasonable to recommend antacids to patients for heartburn not resolved by their chronic therapy. When antacids are consistently utilized more than four times daily while on other therapy, a patient should return to his physician for further evaluation.

The addition of prokinetics to H2RAs and PPIs improves healing of esophagitis compared with therapy without prokinetics. However, one should consider initiating a PPI alone before considering addition of a prokinetic agent to an H2RA. This is because PPI therapy increases compliance with once-daily dosing and has a better side-effect profile. As previously discussed in this article, H2RAs may be added to PPIs for nocturnal heartburn. Patients with nocturnal heartburn have an increase in acid secretion at night, which may be reduced by the addition of an H2RA. Other than in the case of nocturnal heartburn, the use of H2RAs in combination with PPIs has been avoided due to conflicting mechanisms. H2RAs suppress acid secretion from the parietal cell rendering the cell inactive, and PPIs bind only to active parietal cells. Long-term benefit of the addition of H2RAs for nocturnal heartburn is uncertain in light of the tolerance that may develop with their use.

Surgery for GERD has been an option for many years and is very effective in appropriate patients. The two procedures available are the Nissen and Toupet funduplications; the Nissen is the most common. In both procedures the goal is to increase the LES pressure by wrapping the upper stomach around the distal esophagus. The procedure may be an open procedure but is most often done by laparoscopy. Some reasons

CONTINUING EDUCATION

patients may be considered for surgery include failure of medical therapy or intolerance or noncompliance to PPI therapy, and aspiration and asthma not responding to PPI therapy. Surgery may also be used in young patients with moderate to severe GERD. Prior to surgery, patients will be evaluated by esophageal manometry, upper GI endoscopy, 24-hour esophageal pH monitoring, barium esophagogram, and gastric-emptying studies.

Initial complications (e.g., esophageal hemorrhage, perforation, gastric volvulus) from surgery are rare and usually occur in the first two months after the procedure. Long-term complications include bloating, dysphagia, gas, diarrhea, and flatulence. Simethicone is not effective in treating the gas and bloating. Surgery success rates are as high as 90%, but some patients may also need additional antireflux medication to achieve further symptom relief.

The recent development of endoscopic treatment for the prevention of GERD has allowed patients to reduce medication use, increased their quality of life, and decreased symptoms without the complications and cost of surgery. Medication use is either decreased or eliminated in 50% to 75% of patients with these procedures. The Stretta procedure uses a balloon to deliver radiofrequency (RF) energy at the gastroesophageal junction. It is proposed that RF ablation decreases the number of TLESRs. Patients who suffer from chronic heartburn without a hiatal hernia >2 cm, severe esophagitis, or complications from GERD may benefit from the Stretta procedure.

Another method of preventing GERD is endoscopic suturing near the LES, which creates a barrier to reflux. The devices available are the EndoCinch, Sew-Right, Ti-Knot, and knot-clipping devices, which vary some in technique. This procedure is contraindicated in patients with hiatal hernias >2 cm, dysphagia, grade 3 or 4 esophagitis, or obesity. Improvements in symptoms and esophageal acid exposure parameters have been published. Endoscopic injection with a chemically inert substance (Enteryx) into the LES will form a ring and barrier

around the LES after it solidifies. This treatment is a recent addition to the endoscopic procedures to prevent GERD, and patients should be chosen carefully. Patients who received Enteryx had improvement of symptoms and a decrease in the need for PPIs. These are new treatments for GERD that are promising, but more information must be collected and reported on their techniques, mechanism of action, long-term effectiveness, and safety.

Conclusion

GERD is a chronic condition that is prominent in the adult population and requires long-term treatment. First-line treatment begins with lifestyle changes, which are economical and simple to initiate but must be continued for a lifetime. If the addition of lifestyle changes does not alleviate the symptoms completely, acid suppression therapy should be added. This therapy will range from the occasional antacid to chronic therapy with PPIs. Acid suppression therapy with PPIs is successful and safe in treating GERD and healing the esophageal mucosa, but several patients will require combination therapy with antacids, H2RAs, or prokinetics. If symptoms continue after eight weeks of therapy, further evaluation of the patient is needed to determine whether the symptoms are related to acid, nonacid, or nongastroesophageal reflux. Antireflux surgery is effective and should be included in the therapy options for those patients that are candidates. Endoscopic procedures are relatively new in the treatment of GERD and should be reserved for patients with chronic heartburn without other complications. These procedures need more long-term data and head-to-head trials with other GERD treatments.

Pharmacists can play a key role in the continuity of care provided to patients with GERD. They have the opportunity to initiate care with OTC products and to counsel patients regarding lifestyle changes. By listening to patients and asking questions to determine the history of their symptoms, pharmacists will be able to make a recommendation to

CONTINUING EDUCATION

self-treat or to refer them to their physician. Whether the patient self-treats or seeks additional medical care for GERD, the pharmacist continues to play an important role in evaluating and optimizing drug therapy.

References are available upon request.

Key reference: Cappell, MS. Clinical presentation, diagnosis, and management of gastroesophageal reflux disease. *Med Clin N Am.* 2005; 89:243-291.

TEST QUESTIONS

Mark the most appropriate answer. The answer form follows the test questions.

1. The diagnosis of GERD requires the frequency of symptoms to occur:
 - a. At least once monthly
 - b. Two or more times per week
 - c. Once per week
 - d. Two or more times monthly
2. Which of the following statements concerning proposed pathophysiologies of GERD is *true*?
 - a. There is an increase in LES tone.
 - b. Hiatal hernias do not exacerbate GERD.
 - c. Food and medications do not play a role in GERD symptoms.
 - d. Transient TLESRs occur more frequently and may account for 80% of reflux episodes in GERD.
3. What percentage of patients with chronic GERD has been found to develop Barrett's esophagus?
 - a. 0% to 1%
 - b. 1% to 10%
 - c. 5% to 15%
 - d. 15% to 20%
4. Complications of GERD include:
 - a. Esophageal adenocarcinoma
 - b. Heartburn
 - c. Chest pain
 - d. Cough
5. At what point do patients often seek medical attention?
 - a. When the patient has symptoms of heartburn monthly
 - b. When the patient experiences heartburn and acid regurgitation interrupting his or her daily life
 - c. When the patient has heartburn after eating a spicy meal or chocolate
 - d. When heartburn worsens when lying down
6. Atypical symptoms of GERD include:
 - a. Chest pain, hoarseness, and asthma
 - b. Sore throat, chest pain, and heartburn
 - c. Chronic cough, acid regurgitation, and chest pain
 - d. Asthma, dental enamel loss, and heartburn
7. Which of the following statements is *true* about a PPI test?
 - a. It is a valid test to diagnose GERD.
 - b. The PPI test is not often initiated prior to diagnostic testing.
 - c. The test consists of a regimen with a PPI for four to eight weeks.
 - d. An H2RA should be initiated for 12 weeks.
8. A patient with dysphagia, weight loss, coughing, and hoarseness:
 - a. Should be started on antacids as needed for heartburn
 - b. Is a good candidate for the PPI test
 - c. Should be sent to the ER for immediate medical treatment
 - d. Should be referred to his physician for further diagnostic testing
9. Which diagnostic test is the most effective for GERD?
 - a. pH monitoring
 - b. Esophagram
 - c. Esophageal endoscopy
 - d. Esophagogastroduodenoscopy
10. Ambulatory pH monitoring is recommended in which of the following patients?
 - a. Patients with atypical symptoms of GERD
 - b. Patients with typical symptoms resistant to traditional antireflux therapy
 - c. Patients who may require a biopsy of the mucosal lining
 - d. Patients with suspected motility defects
11. Lifestyle changes are:
 - a. A simple treatment that should be initiated for all patients with GERD
 - b. A simple treatment that should be discontinued when drug therapy is initiated
 - c. Complicated and difficult to implement
 - d. Often implemented but do not decrease symptoms of GERD

TEST QUESTIONS

- 12.** Which of the following lifestyle modifications has not been found to help the symptoms of GERD?
- a. Eating smaller meals
 - b. Sleeping on left side
 - c. Using extra pillows
 - d. Wearing loose-fitting clothes
- 13.** Which class of agents is best to use in patients requiring quick relief of infrequent heartburn?
- a. Antacids
 - b. H2RAs
 - c. PPIs
 - d. Prokinetics
- 14.** Which of the following statements about PPIs is *true*?
- a. Lansoprazole is available OTC.
 - b. PPIs are best for rapid relief of heartburn.
 - c. Higher doses of PPIs are better taken daily versus twice daily.
 - d. Patients should be counseled on the importance of taking their PPI 30 minutes prior to a meal.
- 15.** Therapy with prokinetic agents should be:
- a. Initiated with a PPI in patients with severe GERD
 - b. Used rarely because of multiple side effects and lack of efficacy
 - c. Used when patients have esophagitis
 - d. Used because they increase gastric emptying time
- 16.** Which agent is being studied for its unique mechanism of action as a TLESR inhibitor?
- a. Baclofen
 - b. Metoclopramide
 - c. Erythromycin
 - d. Tegaserod
- 17.** Which combination of agents is best for patients who still experience nocturnal symptoms with monotherapy?
- a. PPI + antacid
 - b. PPI + H2RA
 - c. PPI + PPI
 - d. PPI + prokinetic
- 18.** When should antireflux surgery be considered in the treatment of GERD?
- a. When patients fail or are intolerant of drug therapy
 - b. In older patients with mild GERD
 - c. After successful treatment with a PPI
 - d. When combination therapy is required
- 19.** The development of endoscopic treatments for GERD has:
- a. Decreased quality of life due to complications of the procedure
 - b. Reduced or eliminated the requirements of medication use
 - c. Eliminated the need for drug therapy entirely
 - d. Eliminated all symptoms of GERD in all patients
- 20.** Which surgical measure involves using a balloon to deliver radiofrequency energy?
- a. Nissen fundoplication
 - b. Endoscopic injection
 - c. Stretta procedure
 - d. EndoCinch suturing

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ANSWER FORM

A review of GERD and its treatment

JANUARY 8, 2007 ACPE # 012-999-06-220-H01

Test questions start on previous page

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