

Management of Gastroesophageal Reflux Disease

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ABSTRACT

Even though there are still no epidemiological data on the prevalence of Gastro Esophageal Reflux Disease (GERD) in Indonesia, data from The Division of Gastroenterology Department of Internal Medicine Cipto Mangunkusumo Hospital demonstrate signs of esophagitis in 22.8% of all patients with dyspepsia who underwent endoscopic examination. Western countries report a higher rate of GERD than Asian and African countries, possibly due to dietary factors and increased obesity.

Besides adequate history and physical examination, there are many other supporting examinations that could be performed to establish the diagnosis of GERD, especially endoscopy of the upper gastrointestinal tract and 24-hour esophageal pH monitoring. Even though this condition is rarely fatal, GERD patients should still receive adequate management. Most patients demonstrate a satisfactory response towards therapy, which includes life-style modification as well as medication.

Currently, the drugs of choice for GERD are proton-pump inhibitors. A combination of proton-pump inhibitors and prokinetics produces a better effect. Patients resistant to medical treatment or those with recurrent esophageal stricture should be considered for anti-reflux surgery.

Key words: Gastroesophageal reflux, diagnosis, prokinetics, proton-pump inhibitor.

INTRODUCTION

GERD is common in Western populations and is still relatively infrequent in Asian and African countries. Reports from The United States revealed that one of five adults suffers from symptoms of reflux (heartburn and/or regurgitation) once a week and more than 40% of the population suffers from such symptoms once in a month. The prevalence of esophagitis in The United States is around 7%, but non-Western countries report a much lower rate (1.5% in China, 2.7% in Korea). There is still no epidemiological data of this condition in Indonesia, but The Division of Gastroenterology Department of Internal Medicine Cipto Mangunkusumo Hospital report 22.8% cases of esophagitis in all patients who underwent endoscopic examination due to dyspepsia.¹ The high prevalence of reflux symptoms in Western countries is possibly due to dietary factors and increased obesity.

CLINICAL MANIFESTATIONS OF GERD

A characteristic clinical symptom of GERD is epigastric or lower retrosternal discomfort. Discomfort is usually described as heartburn, sometimes accompanied with dysphagia, nausea or regurgitation. If regurgitation occurs during sleep, patients would feel a bitter bile taste on their tongue or hypersalivation. This illness could also cause various and atypical extra-esophageal symptoms, such as non-cardiac chest pain, hoarseness, laryngitis, cough due to aspiration, even bronchiectasis or asthma. GERD usually occurs slowly, and rarely causes acute or life-threatening episodes. For this reason, most patients with GERD require medical management.

PATOPHYSIOLOGY OF GERD

The esophagus and the stomach are separated by a high-pressure zone produced by tonic contraction of specialized smooth muscle of the Lower Esophageal Sphinc-

ter (LES). In normal individuals, this functional barrier is maintained except to allow the antegrade flow associated with swallowing and the retrograde flow associated with belching and vomiting. Flow across the LES only occurs when the LES tone is absent or very low (less than 3 mmHg). Acid gastro-esophageal reflux in patients with GERD occurs by three mechanisms:

1. Spontaneous reflux during inappropriate LES relaxation
2. Retrograde flow prior to recovery of LES tone after swallowing
3. Increases in intra-abdominal pressure overcoming the weak barrier of chronically hypotensive LES

The three things mentioned are caused by multiple factors, including:

a. An incompetent LES

However, the majority of GERD patients have normal LES pressure. Conditions that could lower the LES pressure include the following: presence of hiatal hernia; the total length of LES (the shorter the LES, the greater the likelihood of LES incompetence); drugs, such as anticholinergics, beta adrenergic agonists, theophylline, benzodiazepine, calcium-channel blockers and opiate; hormonal factors (during pregnancy, the increased level of progesterone causes a decrease of LES pressure).

b. Transient LES relaxation (TLESR).

With the development of the manometry technique, it becomes clear that in GERD cases with normal LES pressure the reflux process is caused by transient LES relaxation (TLESR). This condition refers to spontaneous LES relaxation that takes approximately 5 seconds without being preceded by the process of swallowing.

c. Deficient or delayed esophageal acid clearance

d. Gastric abnormalities that increase physiologic reflux are gastric dilation, outlet obstruction and delayed gastric emptying

Other conditions that also play a role in the development of GERD symptoms are reduced esophageal mucosa epithelial resistance and the chemical composition of the refluxate.

DIAGNOSIS

Besides adequate history and physical examination, the following examinations can be performed to establish the diagnosis of GERD:

1. Upper G.I. endoscopy and biopsy

- To assess macroscopic changes in the esophageal mucosa caused by gastroesophageal re-

flux. However, GERD may exist without any visible esophageal damage.

- To exclude other pathological conditions that may cause the symptoms.

The discovery of peptic esophagitis by endoscopy confirms the clinical suggestion that symptoms of heartburn and regurgitation are caused by GERD.

2. Esophageal radiography using barium meal

Even though this examination is not sensitive enough to establish the diagnosis of GERD, this examination has a greater value than endoscopy in certain cases such as: minor degrees of esophageal stenosis secondary to peptic esophagitis resulting in dysphagia and the features of an associated hiatus hernia

3. 24-hour pH monitoring

Episodes of gastroesophageal reflux result in esophageal acidification of the distal esophagus. Such episodes can be monitored and recorded by placement of a pH microelectrode in the distal esophagus.

4. Bernstein testing

This is a test of mucosal sensitivity by transnasal esophageal intubation and perfusion of the distal esophageal mucosa with diluted (0,1 M) HCl over less than a one hour duration. This test can be complementary to pH monitoring in patients whose atypical symptoms are infrequent and do not happen to occur during a pH monitoring study.

5. Esophageal manometry

This test may sometimes be useful in the evaluation of patients with symptoms of dysphagia in addition to those of heartburn and regurgitation, where barium meal and endoscopy results have been normal.

6. Gastroesophageal scintigraphy

The patient is given a liquid or mixed liquid-solid meal labelled with a non-absorbable radioisotope, usually technetium. Transit of the labelled meal through the esophagus is then monitored by an external gamma counter.

The sensitivity and specificity of this test in the diagnosis of GERD has been disputed.

TREATMENT

Even though this condition is rarely fatal, bearing in mind possible long-term complications such as ulceration, esophageal stricture, or the pre-malignant condition of Barrett's esophagus, this condition should receive ad-

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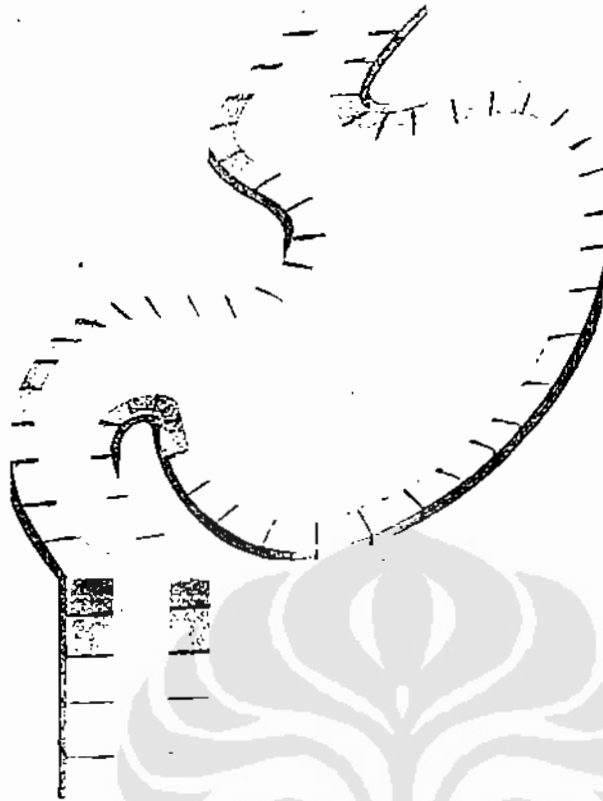
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equate management. Medical management for GERD consists of:

1. Lifestyle modification
2. Drugs

Both are beneficial in reducing mucosal damage caused by refluxate and increasing the effectiveness of esophageal defense mechanism (antireflux barrier, esophageal clearance mechanism and epithelial resistance).

Lifestyle Modification

Lifestyle modification is a part of the initial management of GERD to reduce symptoms and prevent relapse. Attention should be paid towards the following:

1. Elevating head position during sleep and avoiding meals prior to sleep. This could increase acid cleansing during sleep and prevent acid reflux from the gaster to the esophagus.
2. Stopping smoking and consuming alcohol, since the two could reduce pressure of the lower esophageal sphincter and directly affect epithelial cells.
3. Reducing fat consumption and total food intake.
4. Overweight patients should endeavour to lose weight and avoid tight clothing.
5. Avoiding food and drinks such as chocolate, tea, peppermint, coffee and soft drinks.
6. If possible, avoiding the following drugs: anticholinergics, theophylline, narcotics, diazepam, calcium-channel blockers, beta-adrenergic agonist (isoproterenol), progesteron, alpha-adrenergic agonist (fentolamine)

Drugs

The following drugs play an important role in the management of gastroesophageal reflux:

1. Antacids

Antacids are quite effective and safe in reducing symptoms and healing esophageal lesions. Other than serving as a buffer against HCl, these drugs could increase the pressure of the LES.

The disadvantages of these drugs include the following: unpleasant taste, antacids can cause diarrhea, especially those with magnesium content and constipation, especially those that contain aluminium; limited use in patients with renal dysfunction. Dosage: 4 x 1 tablespoon daily, administered 1 hour after meals and before sleep.

2. Gavescon (a combination of antacid and alginic acid)

This drug is safe and quite effective in reducing symptoms and is often used as a supplementary therapy in more severe conditions. It acts as a buffer against HCl and reduces reflux through mechanical

barrier mechanisms. The dose is 4 x 2-4 tablets daily, administered 1 hour after meals and before sleep.

3. H₂ receptor antagonists

This group of drugs include cimetidine, ranitidine, famotidine, and nizatidine. As acid-secretion inhibitors, these drugs are effective in the management of gastroesophageal reflux if administered at twice the dose administered for ulcer therapy. These drugs are only effective for the management of mild to moderate esophagitis. The dosage is as follows: cimetidin: 2 x 800 mg or 4 x 400 mg; ranitidin: 4 x 150 mg; famotidin: 2 x 20 mg; nizatidin: 2 x 150 mg.

All of them are administered after meals and before sleep.

4. Prokinetic drugs

Metochlorpramide

This drug acts as a dopamine-receptor antagonist. It has a low effectiveness rate in reducing symptoms and does not play a role in the healing of esophageal lesions except if used in combination with H₂ receptor antagonists or proton-pump inhibitors. Since this drug has the ability to pass through the blood-brain barrier, it could have effects on the central nervous system such as drowsiness, dizziness, agitations and dyskinesia. The dose is 4 x 10 mg, half of an hour before meals and before sleep.

Domperidon

This drug acts as a dopamine-receptor antagonist with fewer side effects compared to metochlorpramide, since it does not pass through the blood-brain barrier. Even though its effectiveness in reducing symptoms and healing esophageal lesions has not been greatly reported, this drug is known to increase the tone of the lower esophageal sphincter and increase gastric emptying. The dose is 3 x 10-20 mg daily.

Cisapride

As a 5-HT₄ receptor antagonist, this drug could increase gastric emptying and increase the tone of the LES. It is more effective in reducing symptoms and healing esophageal lesions than domperidon. The dose is 4 x 10 mg daily.

5. Sucralphate (aluminum hydroxide and octasulphate sucrose)

This drug increases the esophageal mucosal defense mechanism, acts as a buffer against HCl in the esophagus as well as binding pepsin and bile salts. This group of drugs is quite safe for administration because they work topically (cytoprotection). Dosage: 4 x 1 grams, administered 1 hour after meals

Tabel 1. The effectiveness drug therapy for GERD

Group of medications	Alleviation of symptoms	Healing of esophageal lesion	Prevention of complication	Prevention of relapse
Antacids	+ 1	0	0	0
Prokinetics	+ 2	+ 1	0	+ 1
H ₂ Receptor Antagonists	+ 2	+ 2	+ 1	+ 1
H ₂ Receptor Antagonists + prokinetics	+ 3	+ 3	+ 1	+ 1
High dose of H ₂ Receptor Antagonists	+ 3	+ 3	+ 2	+ 2
Proton-pump inhibitors	+ 4	+ 4	+ 3	+ 4
Surgery	+ 4	+ 4	+ 3	+ 4

and before sleep.

6. Proton-pump inhibitors

These are the drugs of choice for GERD management. These drugs are highly effective in alleviating symptoms and healing esophageal lesions, even severe erosive esophagitis, and are effective in those that do not respond to H₂ receptor antagonists. The dose administered omeprazole : 2 x 20 mg, lansoprazole: 2 x 30 mg, pantoprazole: 2 x 40 mg, labeprazole: 2 x 10 mg. To prevent relapse, patients are encouraged to continue taking the drugs once daily. Most therapy is administered for 6-8 weeks. The effectiveness of these drugs increases if combined with prokinetic agents.

The following table describes the effectiveness of therapy with the drugs listed above.

Treatment Strategy

Martin (Australia) recommends the following strategy for the management of GERD.

Mild degree:

- Lifestyle modification
- Intermittent administration of antacids and H₂ receptor antagonists

Moderate degree:

- Lifestyle modification

- Regular administration of full-dose H₂ receptor antagonists, with or without prokinetic agents.

Severe degree:

- Lifestyle modification
- Regular full-dose of proton-pump inhibitors.
- Surgery, if necessary.

The American Gastroenterology Association recommends the following algorithm for the management of GERD (figure 1).

MANAGEMENT OF COMPLICATIONS

Esophageal Stricture

Drugs treatment is recommended for patients with stricture. If the patient develops dysphagia with a stricture diameter of equal to or less than 13 mm, bougie dilation may be performed (Hurst bougie, Maloney bougie, or Savary bougie). Surgery is indicated if dilation fails.

Barrett's Esophagus

Barrett's esophagus is a condition where there is a transition of distal esophageal mucous from squamous to columnar epithel due to continuous irritation. This is often associated with a pre-malignant condition.

Barrett's esophagus could be treated using drugs. The following algorithm explains the management of gastroe-

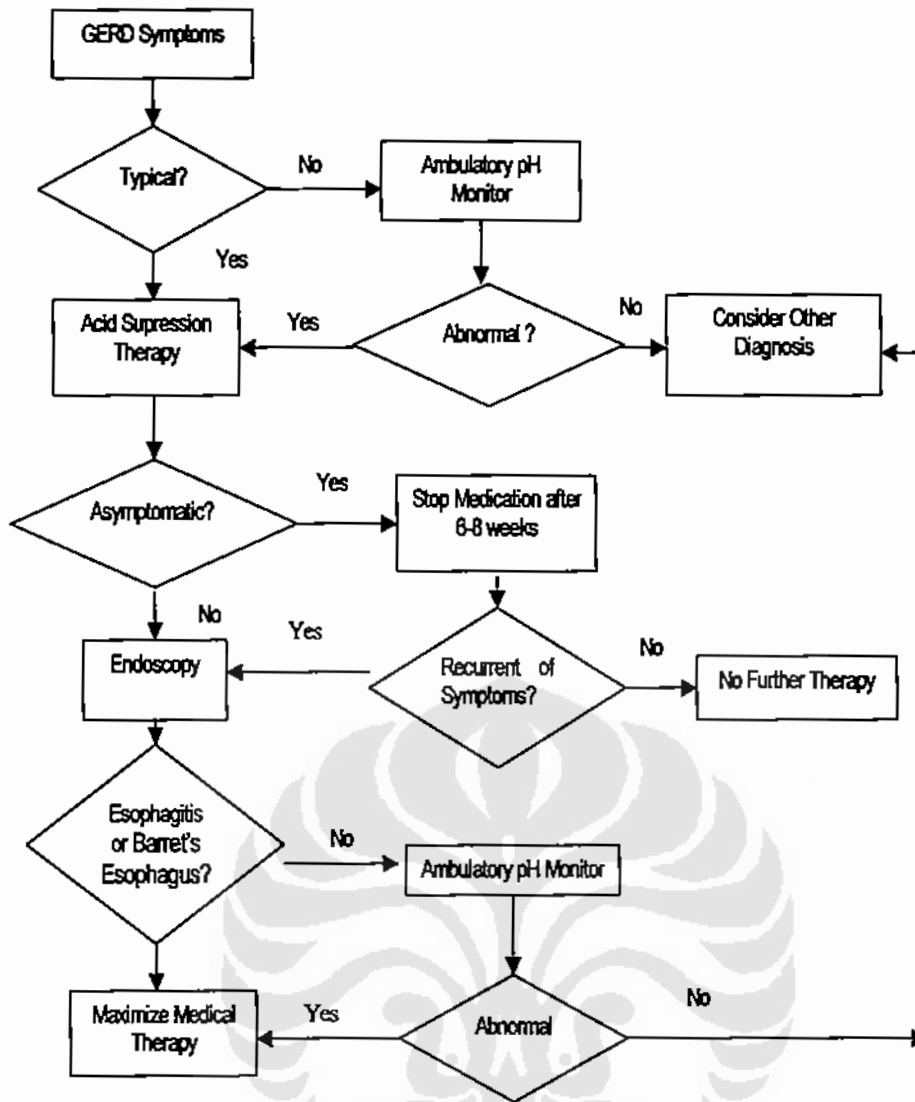


Figure 1. The algorithm for the management of GERD by The American Gastroenterology Association

sophageal reflux with a complication of Barrett's esophagus (figure 2).

SURGICAL THERAPY IN MEDICALLY REFRACTORY PATIENTS

There are many reasons why proton-pump inhibitors (PPI) may fail to relieve the symptoms of GERD:

1. The bioavailability of PPI varies considerably between subjects and may be decreased further when the drug is taken with food.
2. Only actively secreting ATPase molecules, recruited to the surface of the parietal cells by food intake, are inhibited by PPI.

3. In patients with *H. pylori* associated gastritis, the acid suppression effect of PPI is increased. It is more common to see *H. pylori* negative patients fail to have their gastric acidity controlled by standard doses of PPI.
4. PPIs are metabolized by the hepatic cytochrome P-450 2 C enzymes, the capacity of which is genetically regulated. Rapid metabolizers of PPI show decreased effect of PPI on gastric acidity than slow or intermediate metabolizers.
5. Hypersecretors may have a decreased effect, although this is uncommon.

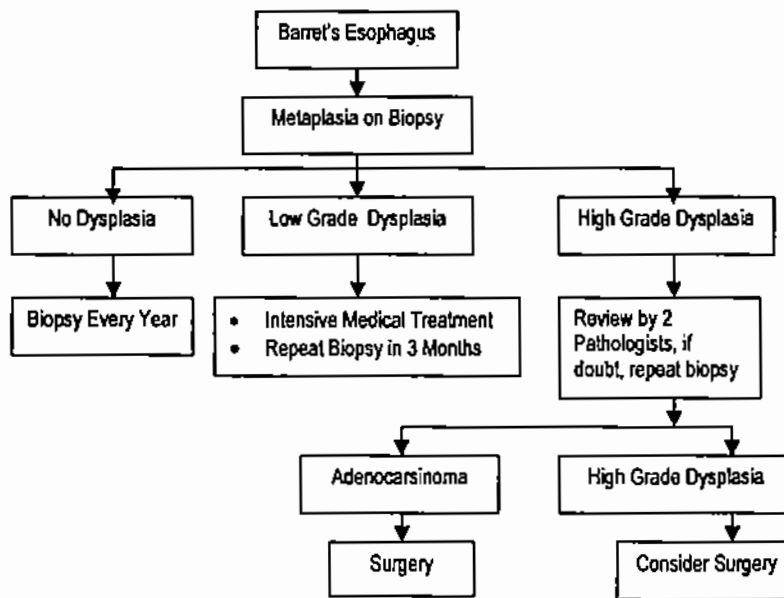


Figure 2. Algorithm for the management of gastroesophageal reflux with a complication of Barrett's Esophagus

Even when adequate acid suppression is achieved, there are situations when PPI therapy fails or seems to fail. The most common explanations are:

1. Incorrect diagnosis
2. Patients with GERD often have other symptoms, including bloating, early satiety and nausea. These symptoms will often not respond to PPI therapy and may be unmasked when reflux symptoms improved.
3. With endoscopy examination, some patients heal slowly and will need more than 8-12 weeks for full recovery from esophagitis.
4. With endoscopy, Barrett's esophagus or even cancer may be mistaken for esophagitis.
5. Peptic strictures will often need balloon dilation.
6. Gastric stasis, LES dysfunction or ineffective esophageal peristaltics may contribute to persisting symptoms.

Some studies have shown that if nocturnal acid breakthrough occurs in a patient with predominantly night-time symptoms, we can add an H₂ receptor antagonist at bed time (ranitidin 150 or 300 mg).

Surgical antireflux therapy is still an important alternative to medical therapy. A recent study also showed good results in patients resistant to therapy with PPI. Surgical therapy is also indicated in patients with recurrent esophageal stricture.

Fundoplication is commonly performed by creating a sort of artificial valve at the gastroesophageal junction

by closing or stitching the gastric fundus close to the lower esophagus.

SUMMARY

1. The incidence of GERD is caused by many factors that are basically always related to a failure of the anti-reflux mechanism (especially LES) and potential damage caused by refluxate.
2. Even though this condition is rarely fatal, because of its high prevalence and possible severe complications patients with GERD should receive adequate management.
3. GERD patients require medical management in the form of lifestyle modification and medication. A range of drugs can be utilized to alleviate symptoms and heal esophageal lesions but the drug of choice is the proton-pump inhibitor.
4. Anti reflux surgery is indicated in patients for whom medical therapy fails and in patients with recurrent esophageal stricture.

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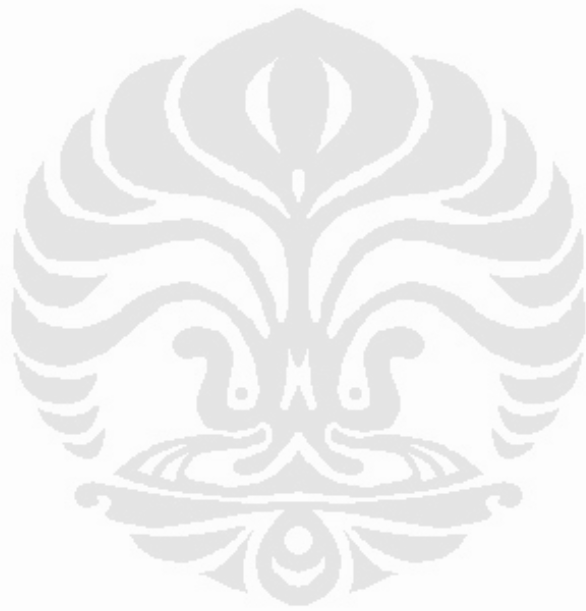
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