Current Treatment of Gastroesophageal-Esophagitis Reflux Disease

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is a condition of reflux of gastric content into the esophagus, which could create clinical symptoms.

Reflux can occur under normal conditions, usually related to certain conditions, such as lying down after meals, and during vomiting. If reflux occurs, the esophagus would immediately contract to cleanse the lumen from the refluxate, preventing prolonged contact between the refluxate and the esophageal mucosa.[1,2,3]

According to the theory of balance (Shay theory), refluxate is an aggressive factor, with acid as its main component, while esophageal motility is a defensive factor, including lower esophageal sphincter tone.

Recurrent gastroesophageal reflux accompanied by disturbed cleansing of the esophageal lumen creates an inflammatory process in the esophageal mucosa. This inflammation creates complaints in the patient in the form of heart burn sensations and regurgitation.[4,5,6]

The incidence of GERD in Asia differs from that of Western countries. In Japan, GERD is found at a rate of approximately 2% each day. Complaints of heartburn are usually brought up among those over 40 years of age. Symptoms are usually mild. The most recent data from the United States reported a weekly prevalence of heartburn ranging from 18-42%.

The prevalence of esophagitis in an endoscopic study in Indonesia on 127 patients with dyspepsia was 22.8%, with a milder form in 90% of all cases. Similar data from Japan demonstrated a prevalence rate for esophagitis ranging between 1.29% and 9.96%, with a mild form in 70% of cases. Such low prevalence may be associated to a difference in diet and the number of parietal cells between Asian and Western populations.[1,2,3,7]

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PATHOPHYSIOLOGY

The development of abnormalities on the esophageal mucosa due to reflux of gastric content, according to the balance theory, may be classified into 2 types, as follows:

1. Defense of the Esophageal Mucosa

Defense of the esophageal mucosa may be classified into 3 levels, as follows:

1.1. Primary defense: anti-reflux barrier, which minimizes the frequency and volume of reflux.
1.2. Secondary defense: lumen cleansing, which minimizes contact between refluxate and body tissue (esophageal epithel).
1.3. Tertiary defense: epithelial resistance, which minimizes mucosal destruction during contact between tissue and refluxate.

2. Aggressive factors associated with the potential of refluxate

These factors may be classified into:

2.1. Gastric secretion
2.2. Pyloric competence

Defense of the esophageal mucosa can be classified into 3 levels, as follows:

1. Pre-epithelial defense; the role of mucus and bicarbonate.
2. Epithelial defense: classified into physical barriers, including cell membrane, junction, intercellular lipid, and mucine. Functional components consist of cell ability in controlling acid effect through epithelial transport of sodium, hydrogen, and chloride ions, as well as intracellular buffer through proteins and bicarbonate ions. In addition, epithelial ability to fix damages through epithelial restitution and cell replication.
3. Post-epithelial defense, conducted through blood flow in delivering oxygen, nutrients, and bicarbonate ions, as well as eliminating hazardous substances such as

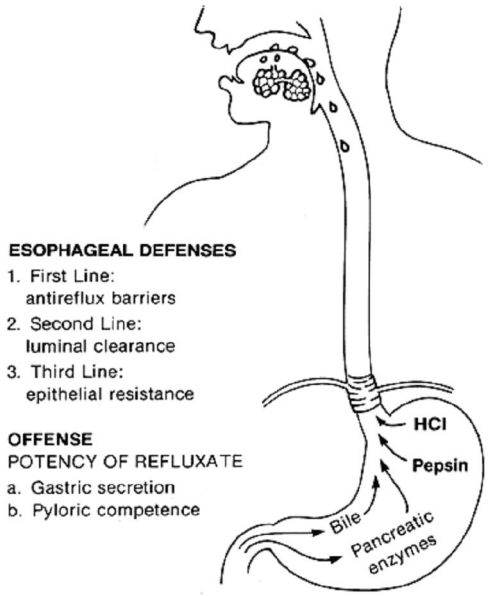


Figure 1. Balance theory of the esophageal mucosa

carbon dioxide and hydrogen ions. Metabolic products and dead cells are also eliminated through the blood.

In addition to mucosal defense, the lower esophageal sphincter tone (LEST) also determines the development of reflux. Various endogenous components influence the LEST, particularly for the process of relaxation, such as secretin, glucagon, VIP, nicotinic acetylcholine, dopamine, hystamine, as well as PGE.

Reduced LEST would facilitate the refluxate in repeatedly entering the esophagus, usually accompanied by reduced esophageal peristalsis, causing prolonged contact between the refluxate and esophageal mucosa.

The role of the refluxate as an aggressive factor is particularly influenced by gastric acid. Lower gastric acid increases the aggressiveness of the refluxate. Thus, even though motility is satisfactory, and the LEST is normal, mucosal abnormality may still occur. From 24-hour pH monitoring, we found 62% of reflux cases with a pH of less than 4. If we consider the two factors stated above, the refluxate factor was a little more dominant compared to motility factors (AGA, 1998). This greatly determines the choice of treatment in GERD cases.

Another clinical form of GERD is the non-erosive reflux disease (NERD). This abnormality is caused by hypersensitivity of esophageal mucosa to acid, associated with increased perception of pain.[1,2,3,4,5,6,8,9]

CLINICAL SIGNS AND SYMPTOMS

Clinical symptoms will develop when there are abnormalities in the esophageal mucosa. Typical symptoms are heartburn and regurgitation. In addition, atypical symptoms include non-cardiac chest pain, night time coughing and wheezing, hoarseness in the mornings (when waking), sore throat, and dental complaints. GERD symptoms often occur after meals, and often overlap with dyspepsia. Positive clinical symptoms without abnormalities in 24-hour pH are associated with a condition of transient lower esophageal sphincter relaxation (TLOSR). In this case, motility plays a more dominant role in producing symptoms.[1,2,3,7,8]

DIAGNOSIS

After typical clinical symptoms are found in an esophagitis reflux, there are several ways to establish a diagnosis. Endoscopic examination is a way to determine esophagitis reflux (Table 1), even though 50-60% of endoscopic results are negative. Histopathological examination will determine the presence of GERD according to the current classification, which is the Los Angeles classification (Table 1).

Table 1. Los Angeles Classification

Degree of abnormality	Description
A	Changes in the mucosa, at least in the form of mucosal folds with a size of less than 5 mm
B	At least one or more changes in the mucosa/mucosal fold, with a size of more than 5 mm, but without connection between the crest of one fold to the other
C	Presence of a connection between the peak of one mucosal fold to the other, without encircling the lumen
D	Circumferential lesion on the mucosa

Tests that can be performed to establish GERD, as well as several types of mechanism and consequences of GERD can be found in Table 2.[1,7]

Evaluation of the degree of endoscopic abnormality and evaluation of histological finding is crucial. Development of GERD into esophagitis, and then to Barret's esophagus and carcinoma are conditions that need adequate management.

During evaluation of LEST using manometry, most cases are found to be normal. In a study by Manan and Syafrudin on esophagitis cases, 60% of the results of LEST evaluation were found to be normal. This demonstrates that esophageal peristaltic function in maintaining lumen cleansing plays an important role.[1,2,8]

Table 2. Examinations for GERD

Test for reflux	
	Upper gastrointestinal serial endoscopy
	Standard reflux test
	pH monitoring
	scintiscan using 99m Tc radionuclide
Symptom-analysis testing	
	Bernstein test
	pH monitoring
	Acid suppression test
Test to determine extent of esophageal damage	
	Serial barium meal
	Endoscopy of the upper gastrointestinal tract
	Esophageal biopsy
	Measurement of difference in esophageal potential
Test to analyse the pathogenesis of esophagitis	
	Acid clearance test*
	scintiscan using 99m Tc radionuclide*
	Esophageal manometry
	Gastric acid analysis

* = principally investigated procedures

TREATMENT

GERD treatment can be classified into three types, which are:

1. Supportive
2. Medication
3. Surgery

Supportive therapy is aimed at changing the patient's lifestyle, particularly avoiding types of foods that have effect of LEST, and the patient's activity.

Medications can be symptomatic and definitive. Short-term use of antacids can reduce the patient's complaints.

Reducing refluxate aggressiveness by controlling pH is the treatment of choice. Medications that can be used are anti-acids that function as proton-pump inhibitors, with an optimal dose in the beginning of therapy, and continued at half dosage at subsequent stages. The choice of administering a single or a combination of drugs should be known. Studies demonstrate that the degree of esophageal abnormality greatly determines the therapy of choice.

In the year 1996, AGA conducted a comparison of treatment on various degrees of esophageal abnormality (Table 3).[1,10,11,12,13,14,15,16,17]

Medications can be classified as symptomatic and definitive treatment.

The use of antacids as gastric acid neutralizing agents and sucralfate to increase tissue resistance are symptomatic and supportive therapy.

Symptomatic therapy should only be administered for a short period of time. Definitive therapy should be administered for 4 weeks, and maintenance for another 4 weeks.

The most recent method of single-drug treatment is the step down method, which recommends the use of PPI with an initial dose of twice daily for 4 weeks, continued with half the initial dose for 4 weeks.

Clinical trials demonstrate different results for different PPIs. Among first generation PPIs, omeperazole was proven to be more effective than lansoprazole, and pantoperazole.

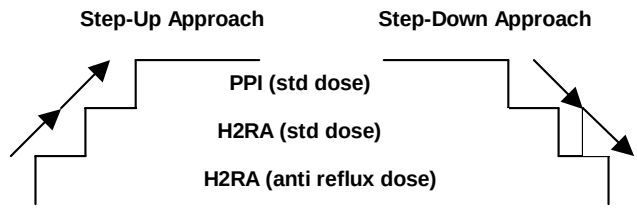
The most recent second generation PPI, esomeperazole, an isomer of omeperazole, demonstrated a far better result than first generation PPIs in clinical trials.[18]

Evaluation of the result of treatment is conducted clinically, and endoscopy is re-conducted to determine clinical improvement objectively.

Even though it is still under debate, eradication of H. pylori infection is considered necessary.[19]

The types of medicines that can be used to treat GERD- reflux esophagitis is adjusted to the clinical condition.[1,13]

The most recent approach for gastroesophageal reflux – reflux esophagitis is the step down method, using one kind of proton pump inhibitor starting with an initial



ADVANTAGES	ADVANTAGES
Cost Saving Define lowest effective maintanance dose Record of long-term safety	Q.D. dosing High rate of responders More complete relief Shorter time to symptom control Shorter time to lesion healing
DISADVANTAGES	**DISADVANTAGES**
B.I.D. DOSING High initial non responder Rate Incomplete relief	Higher cost Unsttled issues of l Long-term safety

Figure 2. The types of medicines that can be used to treat GERD- reflux esophagitis

Table 3. Efectiveness of therapies for GERD

Class of Drugs	How it works	Eliminate symtoms	Heal Esophagitis	Manage or Prevent Complications	Maintain remission
Antacids	Neutralize acid	+ 1	0	0	0
H_2 Blocker over-the counter	Mildly suppress acid	+ 1	0	0	0
Promility	Increase LES pressure; move acid from esophagus and stomach	+2	+1	0	+1
H_2 Blockers Prescription	Moderately suppress acid	+2	+2	+1	+1
H_2 Blcckers + Promotility	Moderately suppress acid; move acid from esophagus and stomach	+3	+3	+1	+1
High Dose H_2 Blockers	Moderately suppress acid	+3	+3	+2	+2
Proton Pump Inhibitor	Markedly suppress acid	+4	+4	+3	+4
Surgery	Improve barrier between stomach and esophagus to prevent acid reflux	+4	+4	+3	+4

Note : Rating scale; 0 (no effect) to +4 nearly 100%(Adapted from ACG,1996)

dose of 1-2 times daily for 4 weeks, depending on the drug, continued by half the initial dose for 4 weeks. If there are clinical symptoms, short-term treatment is administered (Genval, 1999).[18]

CONCLUSION

1. Gastroesophageal reflux disease is established from clinical signs and symptoms.
2. Abnormalities may take the form of reflux esophagitis to Barret's esophagus. Similar clinical findings are found in non-erosive gastroesophageal reflux disease.
3. Diagnosis is established by means of endoscopy and histopathology.
4. Treatment consists of supportive, medication, and surgical treatment. Medications using the step down method with proton pump inhibitors initiated with the optimal dose continued by half the dose, with cost-effectiveness in consideration.
5. Evaluation of treatment should be done regularly, bearing in mind that this disease can advance into carcinoma.

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