Dyspepsia and Gastroesophageal Reflux Disease (GERD): Is There Any Correlation?

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ABSTRACT

Dyspepsia is a syndrome characterized by symptoms and signs of upper gastrointestinal tract and the adjacent organs. It is estimated that 25% of the community have symptoms of dyspepsia syndrome. One-third of patients who visit general physician practices are patients with dyspepsia syndrome; and half of patients who visit gastroenterologists are also patients with dyspepsia syndrome. Dyspepsia syndrome and gastroesophageal reflux disease (GERD) are very prevalent in the community throughout the world.

Gastroesophageal reflux disease (GERD) is more and more commonly found in daily medical practice. Until now, the natural history of disease on GERD and dyspepsia is hardly understood, even though many scientists studied both conditions and there are frequently overlapping. In an individual, GERD and dyspepsia may occur simultaneously and therefore they are hardly to be discriminated.

The management of GERD is performed in keeping with Indonesia and Asia Pacific consensus, life-style modification and administering the acid suppression agents (Proton pump inhibitor (drug of choice), H₂-receptor antagonist, etc), prokinetic agents (Cisapride, domperidone, etc). Life-style modification shall be performed as follows, i.e. sleep with 30-45 degree elevated head or upper chest, do not avoid sour beverages, chocolate, coffee or alcohol, avoid fat and various fried foods, sour food, less stress, stop smoking, small but frequent feeding, etc. There is a correlation between dyspepsia syndrome and gastroesophageal reflux disease (GERD), particularly between the functional dyspepsia and non-erosive gastroesophageal reflux (NERD). More appropriate definition is necessary to differentiate the dyspepsia syndrome and GERD. Further studies are needed to establish distinct definition and criteria between dyspepsia syndrome and GERD.

Key words: dyspepsia, gastroesophageal reflux disease (GERD).

INTRODUCTION

Dyspepsia syndrome and gastroesophageal reflux disease (GERD) are very prevalent in the community throughout the world. Dyspepsia is a syndrome characterized by symptoms and signs of upper gastrointestinal tract and the adjacent organs. It is estimated that 25% of the community have symptoms of dyspepsia syndrome. One third of patients who visit general physician practices are patients with dyspepsia syndrome; and half of patients who visit gastroenterologist are also patients with dyspepsia syndrome. In America and western countries, ¼ of population have dyspepsia syndrome. However, there are only ¼ of such patients who seek treatment by visiting doctors; while the rest mostly try to cure themselves by using over-the-counter drugs sold in stores or supermarkets. Sixty percent of patients with dyspepsia have functional dyspepsia type, in which the endoscopic and other examinations reveal no significant abnormality.

The term dyspepsia is derived from the word duo and merely as mentioned by Rind and Watson in 1968. Duo is originated from the word dus, which literally means bad; while merely is originated from the word peptien, which means to digest. Thus, the term dyspepsia is meant for bad digestion.

Gastroesophageal reflux disease (GERD) is more and more commonly found in daily medical practice. The prevalence of GERD is recently increasing in children and adult patients and it has become a global disease that occurs in all over the world. It is estimated that there are approximately 20% population in the community having symptoms of heartburn or regurgitation for at least once a week. Until now, the natural history of disease on GERD and dyspepsia have been hardly understood, even though many scientists studied
both conditions and there are frequently overlapping symptoms. In an individual, GERD and dyspepsia may occur simultaneously and therefore they are hardly to be discriminated.5

DEFINITION

Dyspepsia syndrome is persistent and recurrent pain or discomfort centered in the upper abdomen.3,5 The discomfort sensation felt by the patients are bloating, distension, anorexia, post-prandial fullness or nausea.

Functional dyspepsia according to the Rome III (2006) criteria is defined as the presence of dyspepsia symptoms originated from the gastroduodenal region such as abdominal pain or discomfort which occurs in the last 3 months, with onset at least 6 months previously to the diagnosis, in the absence of any organic, systemic, or metabolic disease that is likely to explain the symptoms. Other terms are used only for study/experiment and the term of functional dyspepsia is replaced by more obvious abnormality: (1) a meal-related dyspeptic symptoms (post-prandial distress syndrome), and (2) epigastric pain syndrome. Patients with symptoms of post-prandial fullness, early satiety, or post-prandial epigastric pain/heartburn are considered as patients with dyspepsia.

Gastroesophageal reflux disease is an upper gastrointestinal tract disease caused by reflux of gastroduodenal content into esophagus.

CLASSIFICATION

Based on the presence of ulcer, dyspepsia syndrome can be classified into ulcer and non-ulcer types. The non-ulcer type, according to its symptoms, is initially categorized into 4 subgroups such as ulcer-like, dismotility-like, reflux-like and non-specific dyspepsia. Ulcer-like dyspepsia is the most frequent subgroup of all dyspepsia types. All of such subgroups have similar or overlapping symptoms, and therefore, they are difficult to differentiate.

By the progression of disease, the reflux-like dyspepsia may cause dangerous organic disease such as esophageal cancer and other complications. Thus, the world scientists have agreed to classify it as a disease entity which has obvious pathophysiology and complications, i.e. the gastroesophageal reflux disease (GERD). However, a patient may usually have overlap between GERD and gastric disorders such as gastritis, ulcer, etc.

Considering the presence of organic disorders in the stomach, duodenum and the adjacent organs such as pancreas, liver, and biliary duct, we may classify dyspepsia syndrome into organic and functional (non-organic) dyspepsia. The organic disorder includes peptic ulcer, gastric-duodenal neoplasm (benign and malignant), stone in biliary duct/gall-bladder, acute/chronic pancreatitis, acute/chronic hepatitis, cholecystitis and cholangitis.

Based on the abnormality findings by endoscopic examination, gastroesophageal reflux disease (GERD) can be classified into erosive and non-erosive types.

PATHOPHYSIOLOGY

The exact cause of dyspepsia syndrome and gastroesophageal reflux disease (GERD) has not been clear and has been hardly understood until now. There are overlaps of symptoms in both conditions which have no definite explanation and lead us to the consideration of general pathophysiology mechanism.2,5

Dyspepsia syndrome: The experts have agreed that the development of dyspepsia syndrome (both organic and functional) is due to imbalance of aggressive and defensive factors, i.e. the aggressive factors have become stronger than the diminished defensive factors. The aggressive factors include gastric acid, pepsin, bicarbonate, and Helicobacter pylori infection and the presence of free radical. The defensive factors are the mucosal circulation (microcirculation), surface epithelial cells, prostaglandin, phospholipids/surfactan, mucin/mucus, bicarbonate and motility of gastrointestinal tract.

Gastroesophageal reflux disease (GERD): similar pathophysiology has been agreed by the experts, i.e. the imbalance between aggressive and defensive factors, i.e. there are more dominant aggressive factors than defensive factors. The aggressive factors are the potency of jeopardizing reflux content (Hydrochloride acid, pepsin, pancreatic and biliary enzymes) into esophagus, gastric secretion, gastric motility, pyloric competence, etc; while defensive factors include anti-reflux barrier at gastroesophageal junction, the ability of emptying gastric content from the esophageal lumen, relaxation time of lower esophageal sphincter, etc.

CLINICAL MANIFESTATIONS

The dominant symptoms of ulcer or non-ulcer-like are epigastric pain. Major symptom of non-ulcer dyspepsia is dismotility, including epigastric discomfort (early satiety and post-prandial fullness) followed by belching, nausea, vomiting and loss of appetite.

The symptoms of reflux-like dyspepsia are heartburn, epigastric pain, sour or bitter tongue taste,
hypersalivation, etc.

The symptoms of gastroesophageal reflux disease (GERD) are similar to dyspepsia symptoms, i.e. heartburn, dominant epigastric pain, followed by bitter/sour taste, hypersalivation and extra-esophageal complications.

There are no predominant symptoms or typical symptoms in non-specific or mixed dyspepsia.

The symptoms of gastroesophageal reflux disease (GERD) are classified into esophageal and extra-esophageal symptoms. Esophageal symptoms found are burning sensation or hot sensation in the chest area, sour or bitter tongue taste due to acid regurgitation into the mouth, nausea, excessive salivation (hypersalivation). The patients in Asia mostly present with severe epigastric pain, difficult breathing, and complication symptoms such as dysphagia (due to stricture), bleeding, perforation, etc. The heartburn occurs repeatedly everyday, at night or after meal, and exacerbates when bending or drinking alcohol, sour juice, coffee, hot or cold beverages. Extra-esophageal symptoms found are oropharyngeal disorders such as sore throat, laryngitis symptoms, cough, teeth problem (caries). The symptoms of laryngeal disorder include husky voice, laryngeal stricture, apnea. The symptoms of bronchopulmonary symptoms include difficult breathing (dyspnea), asthma, pneumonia, bronchial asthma, and bronchiectasis.

There are alarm signs in dyspepsia syndrome and GERD, and it is an indication to perform immediate invasive examination. The alarm signs are severe vomiting, fever, hematemesis, anemia, jaundice and loss of weight. Based on study results, the alarm signs are very significantly correlated to organic disease of upper gastrointestinal tract.

The symptoms of dyspepsia syndrome and gastroesophageal reflex disease (GERD) are frequently overlapped and consequently, it is difficult to differentiate both conditions. However, both conditions may occur in an individual simultaneously (co-incidence). A study in America (1) demonstrated that of 180 patients with GERD, 132 of them (70%) had belching symptom; in contrast to 63 of 78 patients (80%) with dyspepsia who also had belching symptom. One hundred sixty three of 180 patients with GERD (90%) reported the heartburn symptom; versus 64 of 78 patients with dyspepsia (82%) \( (p = \text{not significant}) \) who also had heartburn symptom. The interview evaluation revealed no significant difference on the severity of belching symptoms between both groups. But, the heartburn/burning sensation in the chest area and acid regurgitation were significantly more severe in patients with GERD. There is a significant and strong correlation between heartburn/burning sensation in chest area as well as belching and the amount of acid reflux in patients with GERD compared to patients with dyspepsia. In addition to patients with GERD and dyspepsia, although the belching and heartburn/burning chest sensation was significantly improved, but the belching score in patients with dyspepsia remained unchanged following the treatment by using proton-pump inhibitor (PPI) agents.1

**PHYSICAL EXAMINATION**

In dyspepsia syndrome, we may find epigastric/umbilical tenderness on palpation, abdominal mass, jaundice (due to liver and biliary abnormality) and pallor or anemia.

In gastroesophageal reflux disease (GERD), there is often no abnormal finding on the abdomen. If there are bronchopulmonary complications, we may find wheezing, prolonged expiratory sound, rales, fever, etc. If there is bleeding complication, pale conjunctiva (anemia) will be found.

**Further Tests**

Similar further tests are necessary for dyspepsia syndrome and GERD, i.e. routine examinations and sophisticated examinations. The necessary routine examinations are complete peripheral blood test, pancreas function test (amylase, lipase serum level), liver function test (AST/ALT, total bilirubin, direct bilirubin, gamma GT, alkaline phosphatase), fecal examination (occult blood test, stool microscopy for worm eggs and parasites), tumor marker (CEA, Ca-19-9), thyroid function test (TSH, T4, T3 to exclude hypo-hyperthyroidism), post-prandial fasting blood glucose test.

ECG is necessary to exclude coronary heart disease in patients over 40 years of age.

Sophisticated examinations needed are esophagogastroduodenoscopy (for hospital with such facility) or double-contrast radiographic examination of esophagus, stomach and duodenum, CT-scan of the upper abdomen, abdominal ultrasonography, MRI and MRCP, ERCP, EUS, etc.

Other special examinations needed are electrogastrography, manometry of upper gastrointestinal tract, PH-metri of upper gastrointestinal tract.

**DIAGNOSIS**

The diagnosis of dyspepsia syndrome and GERD is established based on history, physical examination,
Dyspepsia syndrome and gastroesophageal reflux disease is one of the most frequent reasons for patients to visit a gastroenterologist, especially if there is no improvement following 2-4 week-treatment. Functional dyspepsia and non-erosive reflux disease most often cause difficulties for patients and doctors and they are frequently found in the community, which has prevalence approximately 70% of GERD patients in the community. It is frequently hard to differentiate functional (non-ulcerative) dyspepsia and non-erosive reflux disease (NERD) or reflux disease with negative endoscopic results based on their definition and pathophysiology. Recent studies found that both conditions are correlated and they may represent the same components of disease spectrum regarding symptoms and pathophysiology. Some theories proposed that the etiologies of both conditions include acid exposure, visceral hypersensitivity, and disrupted accommodation of gastric fundus, slow gastric emptying and infection of Helicobacter pylori. The clinical definitions of both conditions (functional dyspepsia and gastroesophageal reflux disease) remain unclear. In addition, experts and patients frequently interpret the definition differently. Although, there has been a consensus on the new terminology for dyspepsia and gastroesophageal reflux disease such as Rome II and Rome III criteria, clinical studies are still using different diagnostic terminology. The Committee in Rome Consensus has deleted dyspepsia with burning sensation symptoms and it is included in the gastroesophageal reflux disease. They think that dyspepsia syndrome and GERD are originated from different organs, i.e. esophagus and stomach; whereas in fact many experts also think that differentiation of both entities is frequently not possible (impossible) in clinical setting. There have been evidences of studies that dyspepsia with burning/predominant heartburn sensation is very responsive to acid suppression treatment. Both entities/such conditions bring great socioeconomic impact, resulting approximately £250 million of annual expense for treatment by doctors in United Kingdom.

Several studies found that although both entities are differentiated by definitions, they (functional dyspepsia and NERD) are correlated and have brought impact to the community in terms of quality of life and complication and therefore, appropriate diagnosis and treatment are necessary.

To broaden our knowledge about overlap between dyspepsia and NERD, we have to understand the pathophysiology of both entities. Various potential mechanisms have been reported to have role on the development of symptoms. Visceral hypersensitivity has the strongest role in functional dyspepsia and NERD and we assume that it occurs in 30-40% cases. Some studies have demonstrated that such sensitivity result not only from mechanical distension but also by exposure of some factors including gastric acid and lipid solution. Samson et al reported in their study that patients with functional dyspepsia are more sensitive to acid introduced into duodenum. Mearing et al demonstrated that such hypersensitivity is exceedingly visceral, i.e. there is no difference between patients with dyspepsia and healthy control regarding the somatosensoric response. However, Bouin et al found in their study that patients with functional gastrointestinal disorder have earlier pain sensation and have lower tolerance to pain than the normal control subjects. Hypersensitivity is also found in patients with NERD, as proven by studies that showed response to balloon dilatation and acid. In such patients with NERD, the 24-hour-pH-metry found that the 24-hour-acid exposure in 33-50% patients demonstrated normal results, and there was no abnormality found in esophagus by endoscopic examination. Although the terminology of NERD according to the Rome III criteria has been made, it is still possible to revise the terminology since there is still overlap between NERD and functional dyspepsia. Several data reported that there is dysfunction of the upper part of stomach in patients with NERD. It may possibly caused by numerous reflux episodes since the lower esophageal sphincter and gastric fundus strongly have role in inducing transient relaxation of lower esophageal sphincter, which may precipitate the reflux episodes. Several studies reported that dismotility or dyspepsia symptoms are found in up to 50% patients with NERD. Intestinal dismotility such as delayed gastric emptying is found either in patient with NERD or in functional dyspepsia, which may explain its correlation to treatment failure by using the proton-ump inhibitor agents for both entities.  

Clinical Implication of GERD and Dyspepsia

Overlap between both entities causes implication on diagnosis and treatment strategies for both conditions. Should we evaluate all patients who present with burning sensation/heartburn and/or dyspepsia by endoscopy, which is invasive and time-consuming? How about patients with functional dyspepsia? Should we
perform the test and treat them adequately? Those questions need appropriate randomized controlled studies.

In general, acid suppression is not so effective in patients with NERD compared to patients with erosive esophagitis, which more likely results from the failure to normalize the symptoms of burning/functional heartburn. However, there are evidences that patients with overlap, particularly functional dyspepsia with burning/heartburn sensation, will respond to PPI treatment. Prokinetic treatment is expected to give beneficial result for heartburn in functional dyspepsia and NERD which has shown treatment failure by PPI agents. However, a study in EUROPE found that less than half of patients with NERD will experience long remission period by administering cisapride.6

MANAGEMENT

The management on dyspepsia syndrome consists of:
A. Supportive: Nutrition, Fluid-electrolyte balance, avoiding aggressive food-beverages and drugs, health promotion
B. Specific (in keeping with Indonesia and Asia Pacific consensus)
C. Other treatment: Psychological, Acupuncture, Gastric Ulcer (Cytotprotecter).

The management of GERD is performed in keeping with Indonesia and Asia Pacific consensus, life-style modification and administering the acid suppression agents (Proton pump inhibitor (drug of choice), H₂-receptor antagonist, etc), prokinetic agents (Cisapride, domperidone, etc). Life-style modification shall be performed as follows, i.e. sleep with 30-45 degree elevated head or upper chest, do not avoid sour beverages, chocolate, coffee or alcohol, avoid fat and various fried foods, sour food, less stress, stop smoking, small frequent feeding, etc.

CONCLUSION

There is a correlation between dyspepsia syndrome and gastroesophageal reflux disease (GERD), particularly between the functional dyspepsia and non-erosive gastroesophageal reflux (NERD).

More appropriate definition is necessary to differentiate the dyspepsia syndrome and GERD.

Further studies are needed to establish distinct definition and criteria between dyspepsia syndrome and GERD.
Dyspepsia and Gastroesophageal Reflux Disease (GERD)

REFERENCES


Figure 2. Treatment for patients with dyspepsia by gastroenterologist/internist with endoscopy facility