Peptic Ulcer Disease
Different Pathogenesis of Duodenal and Gastric Ulcer

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ABSTRACT

Despite decrease frequency of Helicobacter pylori (H. pylori) due to eradication therapy, peptic ulcer disease as a manifestation of this infection is still remain a health burden. Understanding the physiology of gastric acid secretion and its alteration by H. pylori induced inflammation will aid physician in differentiating peptic ulcer disease based on its location. Duodenal ulcer and gastric ulcer disease are two common condition that usually found in peptic ulcer. Recognition of symptoms and its pathogenesis may lead physician to understand the fate of each condition in the future. This article reviews concept of peptic ulcer pathogenesis according to ulcer etiology.

Keywords: *duodenal ulcer, gastric ulcer, pathogenesis, Helicobacter pylori (H. pylori)*

ABSTRAK

Walaupun Helicobacter pylori (H. pylori) menurun jumlahnya karena adanya terapi eradikasi, penyakit ulkus peptikum sebagai manifestasi infeksi ini masih merupakan beban kesehatan. Pengetahuan mengenai fisiologi sekresi asam lambung dan inflamasi akibat infeksi H. pylori akan membantu klinisi dalam membedakan penyakit ulkus peptikum berdasarkan pada lokasinya. Penyakit ulkus duodeni dan ulkus gaster merupakan dua kondisi yang sering dijumpai pada ulkus peptikum. Dengan mengetahui gejala dan patogenesis, klinisi dapat memahami kondisi yang mungkin terjadi pada masa yang akan datang. Artikel ini akan mengulas konsep patogenesis ulkus peptikum berdasarkan etiologi ulkus.

Kata kunci: *ulkus duodeni, ulkusgaster, patogenesis, Helicobacter pylori (H. pylori)*

INTRODUCTION

Peptic ulcer disease is a condition that still carries high disease burden in developing countries. One of its main etiologies is *Helicobacter pylori* (*H. pylori*) infection. Although eradication therapy has been established to combat this infection, peptic ulcer disease is still a main clinical problem. Increasing frequency of non-steroid anti-inflammatory drugs usage and high aspirin consumption for cardiovascular disease add risk factors for this disease.[1] Peptic ulcer disease itself can be differentiated into duodenal and gastric ulcer disease.

H. pylori infection which underlies both of this condition has important role in determine which

location the ulcer will develop. The disease expression shows high or low acid output based on *H. pylori* infection site. This review looks at the physiology of gastric acid secretion, *H. pylori* as the most common etiologic agent of peptic ulcer disease, and different pathogenesis concept of duodenal and gastric ulcer.

GASTRIC PHYSIOLOGY OF ACID SECRETION

The composition of gastric glands are determined according to their anatomic location. Cardia consist of less than 5% of gastric gland area and mainly contain mucous and endocrine cells. Most of gastric glands (75%) are found within the oxyntic mucosa and contain mucous neck, endocrine (G and D cells), parietal, chief, and enterochromaffine-like cells. Pyloric glands located in antrumconsist of mucous cells, G cells which release gastrin and D cells.[2]

Parietal cell is the main cell in the gaster that secretes acid through expression of H+,K+-adenosine triphosphatase (ATPase) in its tubulovesicle membrane. Gastrin stimulates parietal cells indirectly through histamine release by enterochromaffine-like cells which stimulates parietal cells, and directly to parietal cells, also cause growth of enterochromaffine-like and parietal cells. High acid output produced by parietal cells will induce inhibitory response by D cells which secretes somatostatin. Somatostatin inhibit acid production through its receptors in G cells, enterochromaffine-like cells, and parietal cells. The location of *H. pylori* infection decides which part of cells that affected and determine inflammatory zone and the fate of acid secretion, whether hyposecretion or hypersecretion (Figure 1).[2]

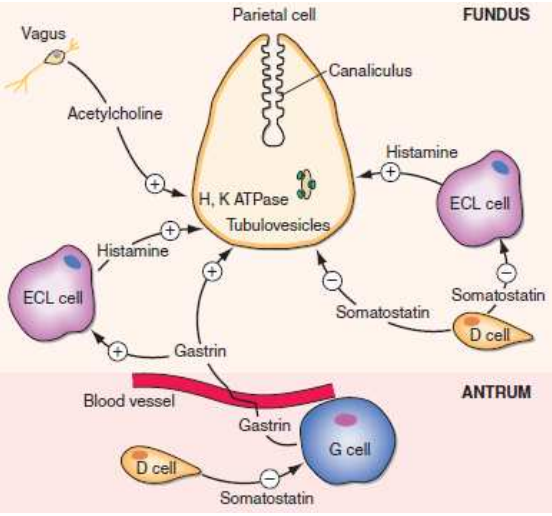

Figure 1. Physiology of acid secretion in stomach

PEPTIC ULCER DISEASE

Peptic ulcer disease is defined as breaks in the mucosal surface > 5 mm in size, with depth to the submucosa. Peptic ulcer disease itself has several etiologies such as *H. pylori* infection and non-steroid anti-inflammatory drugs. Based on its location peptic ulcer disease can be differentiated into duodenal ulcer and gastric ulcer.[2] Duodenal ulcers is commonly occur in the first portion of the duodenum (> 95%) while gastric ulcers in the other hand is located especially over lesser curve.[1] Peptic ulcer disease is typically present with symptoms of epigastrial pain. Symptoms of duodenal ulcers usually occurs 90 minutes to 3 hour after a meal and relieved by antacids or food while discomfort in gastric ulcers is precipitated by food. This causes duodenal ulcers patients had weight gain due to frequent eating while gastric ulcers is anorexic because of food avoidance. These symptoms may happen because of closure of pyloric sphincter to concentrate the stomach content while eating. Pain begins when stomach release digested food and acid into the duodenum. While in gastric ulcer patients food itself stimulate acid production in the stomach which directly expose to gastric mucosa.[2,3]

HELICOBACTER PYLORI AS MOST COMMON CAUSATIVE AGENT OF PEPTIC ULCER DISEASE

H. pylori has been known to infect more than half of the world's population, and still become problem in developing countries.[4] Over 80% *H. pylori* positive was found in developing countries.[5] In Indonesia, *H. pylori* prevalence data in peptic ulcer disease is varied between 90 until 100%.[6] As the discovery of this bacterium in 1984 by Barry Marshal and Robin Warren, research has been focused on handling its infection in people.[7] This gram-negative microaerophilic rod bacterium has S-shaped, sized 0.5-3 micron and has multiple sheathed flagella. This organism produce urease which alkalinizing the surrounding pH and generates ammonia that enable its survival. Its flagella and spiral-like form enable this bacteria to penetrate mucus layer and move toward the more neutral pH of gastric mucosa.[8] Although *H. pylori* maintain its vitality in an acid environment, it moves away from acid and search higher pH environment to stay alive. *H. pylori* normally cannot survive in gastric corpus which has low pH environment.[9] The presence of *H. pylori* is closely related with the presence of peptic ulcer disease. *H. pylori* has a high predilection in antrum due to its lack of parietal cells. Therefore gastritis usually

occurs at this level which then progress to corpus. The inflammation in corpus will cause atrophic part of its mucosa progressing into metaplasia.[10]

Some experts suggest that gastric ulcer and gastric cancer is the continuation of duodenal ulcer disease. This condition is strengthened from the observation that inflammation of the stomach extend from antrum to the corpus and followed by high gastric acid secretion to reduced gastric acid secretion below. Therefore there are different epidemiology between both condition, with duodenal ulcers begin earlier in the 20s and reached their peak in the 3rd until 4th decade, while gastric ulcers reached their peak in the 5th until 6th decade.[11,12] In several areas of Eastern Asia, where gastric cancer is quite high in frequency, healed duodenal ulcer were found in 1-7% patients.[13] Untreated *H. pylori* infection may lead to condition of gastric cancer.[14]

HIGH ACID OUTPUT IN DUODENAL ULCER DISEASE

Duodenal ulcers patients has twice parietal cells number compared to those with normal condition. Duodenal ulcer never happened in people with production of gastric acid less than 12-15 mmol per hour. This condition needs a normal gastric corpus to happen. *H. pylori* infection in antrum will most likely cause inflammation of D cells which cause negative inhibitory action and high acid output because of parietal cells secretion. Antral predominant gastritis also caused increased gastrin release which also increased acid secretion (Figure 2).[15] Prolonged exposure to acid and creation of supportive milieu for *H. pylori* in duodenum will cause gastric metaplasia in duodenum. Normally, due to occurrence of bile, *H. pylori* cannot infect duodenum. However, this condition can be breached by low pH that precipitates bile acid.[1] This area may be colonized by *H. pylori* due to its trophic effect on gastric type epithelium and cause inflammation (duodenitis) and continue to damage the mucosa. Besides pH alteration, *H. pylori* also induced shift of duodenal bicarbonate secretion causing decrease of defensive factors.[9] Hyperchlorrhydia leading to duodenal ulcer also occurred in patients with Zollinger-Ellison syndrome which has hypergastrinemia. Most case of duodenal ulcer was caused by *H. pylori* infection because eradication usually normalized this condition.

LOW ACID OUTPUT IN GASTRIC ULCER DISEASE

Infection of *H. pylori* in corpus, or so-called corpus predominant gastritis will cause inflammation or even progressive loss of parietal cells in that area. Patients with gastric ulcer has low acid secretion because of hyposecretion due to impairment of parietal cells. Some research said that there are gastric atrophy that caused loss of parietal cells. Low acid output caused by gland atrophy will provide high pH condition in the stomach (Figure 2).[15]

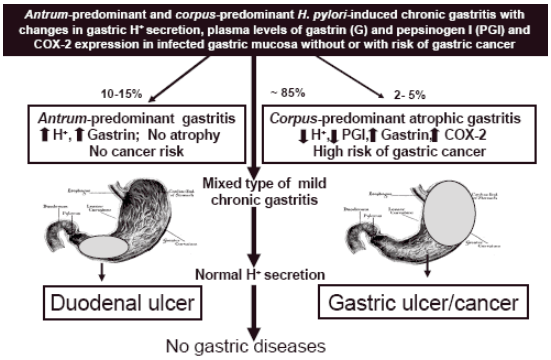

Figure 2. Hyperchlorrhydia is associated with duodenal ulcer disease while hypochlorrhydia usually obtained in gastric ulcer disease

Gastric ulcer is a precancer condition that may lead to gastric malignancy. Compared to duodenal ulcer, gastric ulcer are associated with more development into gastric cancer.[16] Fuccio et al stated that gastric ulcer patients had higher frequency to develop gastric cancer compared to duodenal ulcer.[17] Even some guideline mandates biopsy from gastric ulcer to find gastric cancer earlier.[18] International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) even declared in 1994 that *H. pylori* is a group 1 carcinogen in humans.[19] Some mechanisms may explains carcinogenesis. Such mechanism are as follows: impaired absorption of several antioxidant such as vitamin C that has proven efficacy in prevention of cancer, overgrowth of bacteria that occurred in high pH environment, and prolonged chronic inflammation which cause malignancy. Correa's hypothesis model of gastric carcinogenesis also showed that atrophy gastritis may lead to intestinal metaplasia and continued to gastric cancer, especially intestinal-type gastric cancer (Figure 3).[20]

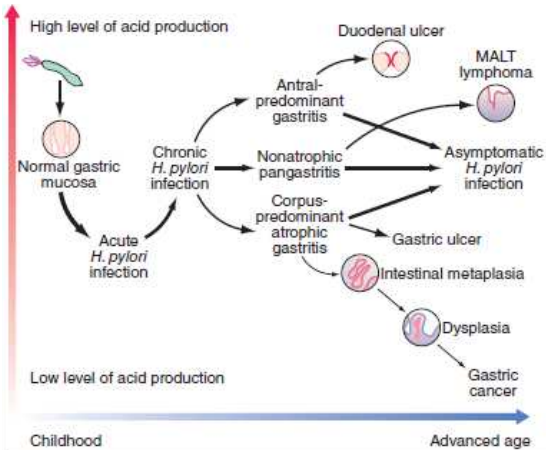

Figure 3. Correa cycle of gastric carcinogenesis

CONCLUSION

Until now peptic ulcer disease still remain issue in health care visits. Most patients come with complaints of dyspepsia need to be screened for possibility of peptic ulcer disease. Knowledge of gastric acid secretion is needed to acquire which part of gastric mostly affected by etiologic agent of peptic ulcer disease. Until now, *H. pylori* remains risk factor for development of peptic ulcer disease. The predilection site of this bacteria determine its clinical outcome. If the inflammation took place in antrum, high acid output will develop due to decrease inhibitory effect of somatostatin and develop into duodenal ulcer because of increase duodenal acid load. Gastric ulcer in the other hand occur after years of inflammation in corpus that cause gland atrophy and lack of acid secretion of parietal cells. Knowledge of peptic ulcer pathogenesis may aid physician to increase awareness toward complication that may occurred, such as gastric cancer.

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