

Peptic Ulcer Diseases in Korea

Peptic ulcer disease (PUD) is one of the most commonly encountered gastroenterologic diseases in Korea. The trend in diagnosis and treatment of PUD in Korea has changed in the past decade with the introduction of endoscopy and potent acid suppressants such as proton pump inhibitors. The discovery of *Helicobacter pylori* has opened a new era for the understanding of pathogenesis and management of PUD. In this review, we tried to look back at the history of PUD in Korea and the changes of epidemiologic features and treatment of PUD in Korea. (**Korean J Helicobacter Up Gastrointest Res 2012;12:19-22**)

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INTRODUCTION

Peptic ulcer disease (PUD) is one of the most commonly encountered gastroenterologic diseases. It is defined as a break in the lining of the mucosa, with appreciable depth at endoscopy or histologic evidence of involvement of the submucosa. It is named because pepsin (proteolytic in acidic solution) plays a key role in causing the mucosal breaks regardless of the causes (e.g., *Helicobacter pylori* [*H. pylori*], aspirin, non-steroidal anti-inflammatory drugs). It is often complicated to hemorrhage and/or to perforation and some of the victims reach to death.

Previous management for PUD was focused on neutralization of gastric acid or on reducing acid secretion. Complicated pa-

tients with PUD usually undergo surgical management. The treatment paradigm for PUD has been shifted to eradication of *H. pylori* after the findings by Marshall and Warren¹ for its causative role in PUD.

Here, we are going to review the history, epidemiology, etiology, treatment, and complications of PUD in Korea.

HISTORY OF PUD IN KOREA

Dr. Hur Jun (1539-1615), the most famous doctor of oriental medicine in Chosun Dynasty, described PUD for the first time in Korea. In his book of Oriental Medicine, the patients with gastric lesion and/or gastritis usually complain of symptoms such as indigestion, bloating, loss of appetite, weight loss, nau-

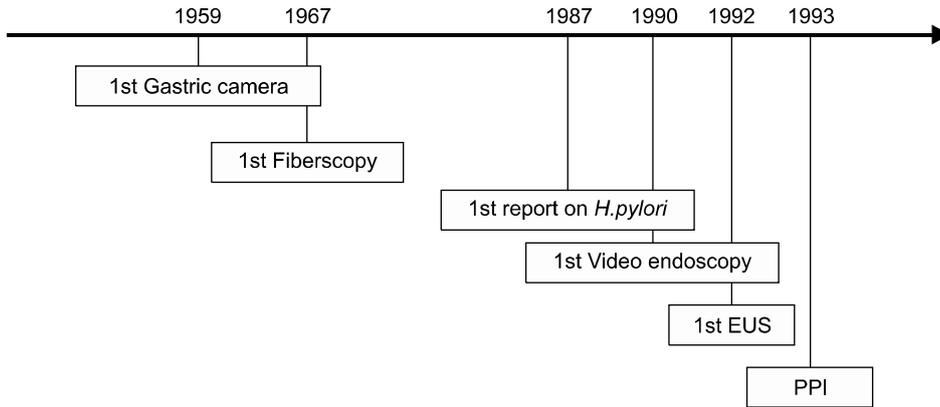


Fig. 1. History of gastroenterology in Korea. *H. pylori*, *Helicobacter pylori*; EUS, endoscopic ultrasonography; PPI, proton pump inhibitor.

sea, acid belching, and/or hiccups. In addition, patients with PUD show yellowish discoloration of faces, easy fatigue and tend to lying down.

Western medicine was first introduced in Korea by Japan (Jesaeng Clinic) in Busan in 1877 and by Allen, an American missionary, who established Royal Hospital (Gwanghyewon), changed the name to Jejungwon in Seoul in 1855.

Gastrointestinal endoscopy (gastric camera) was first introduced in Korea by Dr. Keuk-Soo Chung (Kyongpook National University) and Dr. Heung-Jae Choi (Yonsei University) in 1959. Fiberscopic biopsy was performed for the first time in 1969 and videoendoscopy was clinically used in 1990. *H. pylori* infection in Korea was first reported in 1987. Before the introduction of gastrointestinal endoscopy, PUD was diagnosed with barium studies in Korea (Fig. 1).

EPIDEMIOLOGIC DATA

Before 1980's, experts in gastroenterology described PUD several times and analyzed them into complicated and un-complicated ones in patients who underwent surgical treatment. However, epidemiological studies for PUD was first described in 1984 and 8 epidemiological studies were published so far.²⁻⁹ Two studies included data of 1970's, 6 studies included data of 1980's, 3 studies included data of 1990's, and one study included data of 2000's.

We have been performed a series of surveys for PUD in the 8 institutes of the Catholic University of Korea over two decades. These serial surveys included over 1,000 patients each time, with questionnaires on general life style, medical histories, and endoscopic findings of PUD patients. The first survey was performed between 1988 and 1989, second one between

1996 and 1997, and now third one is under way which contains over 250 enrolled patients so far.

1. Incidence and prevalence

Data on incidence and prevalence of PUD in Korea is very limited. Retrospective nation-wide survey shows that the prevalence of PUD is 18.0~20.2% between 1995 and 2005, and showing significant increased the prevalence of peptic ulcer (PU), and gastric ulcers (GUs) also showed an increasing trend (9.6, 10.5, and 12.0%, $P < 0.001$).¹⁰ In one retrospective study for the past two decades in a single institute, admission due to PUD has not been changed for that period.¹¹ We compared people who underwent endoscopic examination for routine health check-up and patients who visited gastroenterology outpatient clinic, Incheon St. Mary's Hospital from 1995 to 2007 (unpublished data). Overall prevalence has not been changed much during this period both in routine health check-up group and outpatient clinics despite starting the *H. pylori* eradication therapy. GU was more commonly found in out patients group (6.5~11.9%) than in routine health check-up group (2.0~10.8%). Duodenal ulcer (DU) was more common in outpatient group (3.7~7.1%) than in routine health check-up group (1.4~7.8%). Combined GU and DU shows similar patterns (1.0~2.0% in outpatient group vs. 0~2.0% in routine health check-up group). This result suggests that asymptomatic PUD patients are not uncommon.

Considering the previous epidemiological data, while the ratio of GU, DU, and combined GU and DU has not been changed much from 1970's to 2000's, it is likely that the ratio of GU is increasing compared to DU in our serial data.

2. Age and sex

The mean ages of patients with GU and DU tend to increase both in the previous epidemiological data and in our serial data. Peak ages of PUD also have been increased for the past two decades, i.e., peak age of GU changed from 40's to 50's, peak age of DU changed from 30's to 50's, and peak age of combined GU and DU changed from 40's to 50's.

Male over female ratio is declining in GU but not in DU in the previous epidemiologic studies and in our serial data. It is plausible that the increasing consumption of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) both in male and female elderly patients is associated with this tendency.

3. Complications

The incidence and prevalence of complicated PUD such as bleeding and perforation have been reported in various ranges in previous epidemiologic studies. Bleeding was reported in 3.9~10.4% of GU, 6.2~12.4% of DU, and 0~14.4% in combined GU and DU groups. Perforation was reported in 0.1~0.7% of GU, 0.1~2.7% of DU, and 0% in combined GU and DU groups. Obstruction was found in 1.7~2.6% of GU and in 2.3~2.8% of DU groups. In our serial data, complaints of hematemesis/melena are increasing, suggesting that bleeding ulcers are increasing.

4. Etiology

Little is known about the etiology of PUD in the previous studies, but the ratios of smokers were higher than general population in both GU and DU groups in our serial data. It has known that alcohol drinking is not associated with the development of PUD. Regarding ABO blood types, type O was associated with PUD in some reports but this should be elucidated in the future.

1) Drugs (aspirin and NSAIDs): Aspirin and NSAIDs are well-known causes of PUD and drug-associated lesions were more common in GU than in DU. In our serial studies, drug-related GU tends to increase, though statistically not significant. Ischemic heart diseases and degenerative musculoskeletal diseases will be increased as a result of increased life expectancy and it will naturally follow the increased incidence and prevalence of drug-related PUD in the future.

2) *H. pylori* infection: *H. pylori* infection is one of the most common causes of PUD. However, *H. pylori* infection rate is

now decreasing in Korea and *H. pylori*-associated PUD tends to be decreased. In one study, annual *H. pylori* infection rate in PUD has been gradually decreased.⁹ Our serial studies also show the same results.

3) Idiopathic (non-*H. pylori*, non-drug-related) PUD: There was one report on PUD not related to *H. pylori* or drugs and the characteristics of this type was not much different from *H. pylori* or drug-related PUD.¹²

5. PUD in the elderly

There was some reports on PUD in the elderly comparing to younger patients in Korea.^{2,13-15} In these data GU was more common than DU and the ratio of GU over DU was 1.4 to 4.8. PUD related to ingestion of drugs (aspirin, NSAID, steroid, etc) was commonly found in the elderly than younger patients. Subsequent complicated ulcers such as bleeding was also common. However, *H. pylori*-associated PUD was relatively less common this complication.

TREATMENT

Treatment of PUD was focused on conservative managements such as bed rest and blend diet. However, researches unveiled that PUD developed as a result of insult from gastric acid and pepsin. This led to the discovery of H₂ receptors of parietal cells, which contributed to the development of H₂ receptor blockers. The final pathway of acid secretion is through the proton pumps of parietal cells and proton pump inhibitor (PPI) is now widely accepted as a standard therapy. Acid pump antagonist, a reversible blocker of potassium influx into parietal cell, was first introduced in Korea and now in the market.

The discovery of *H. pylori* made a great progress in the treatment of PUD. In Korea, *H. pylori* eradication therapy was introduced in 1990's. Standard triple therapy, PPI and two antibiotics such as clarithromycin and amoxicillin, for 7 days is now the most commonly used regimen for *H. pylori* eradication in Korea. However, the eradication rate of this regimen is declining in Korea¹⁶ and the development of more effective regimen is anticipated very soon. The clarithromycin-resistant *H. pylori* strains have increased significantly recently, and there was also increasing tendency for the emergence of strains with multi-drug resistance. The increase in clarithromycin-resistant strains results in a decrease in eradication rate for *H. pylori*. In areas with high clarithromycin resistance, new alternative

first-line treatment combination should be considered.¹⁷

Endoscopic treatment of complicated PUD is now very popular in endoscopists in Korea. An article on endoscopic hypertonic saline injection for PUD was published 1992 for the first time in Korea. Then endoscopic management by ethanol injection (1995), by band ligation (1995), by hemoclip (1997), by heaterprobe (1998), and by lasertherapy (1998) was published. Intravenous administration of PPI and oral administration of PPI was also published in 1990's.

Surgical treatment still plays a role in the management of PUD. The number of patients who underwent surgical treatment due to complicated PUD has not been decreasing much for the past decades.

Most PU heals within eight weeks of initiation of anti-secretory therapy. Nevertheless, there is a small, but considerable significant number of the patients whose ulcers persist despite conventional treatment. Such ulcers can be considered refractory. Unfortunately, we do not have data on this refractory PUD in Korea.

SUMMARY AND CONCLUSIONS

Prevalence rate of PUD in Korea has been increased during last decades and it reached more than 20% in 2005. GU was significantly increased during last 15 years but DU was not changed. Age of patients with PUD has been gradually increased during last decades. Male over female ratio is also declining in GU but not in DU. The most important and frequent causes of PUD are drugs (e.g., NSAIDs) and *H. pylori* in Korea. Prevalence of *H. pylori*-related PUD is now decreasing due to improved hygiene and eradication of the organism. Drug-related PUD, by for example NSAIDs, aspirin, and steroids expected to be gradually increased near future. PPI is now the most frequently used regimen for the treatment of PUD in Korea. Eradication rate of *H. pylori* in PUD is decreasing gradually due to the emergence of resistant strains to antibiotics. It is imminent for the development of more effective regimens. For treatment of complications of PUD, for example bleeding, stenosis or obstruction, endoscopic treatment is actively involved in Korea. Surgical treatment still plays a role in the management of PUD as the number of patients who underwent surgical treatment due to complicated PUD has not been de-

creasing much for the past decades.

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