

AN OVERVIEW OF CAUSES, DIAGNOSIS AND MANAGEMENT OF PEPTIC ULCER DISEASE

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ABSTRACT

Peptic ulcer is a multifactorial disease and it is one of the most prevalent diseases in gastrointestinal field. Peptic ulcer disease (PUD) is a break in the inner lining of the stomach, first part of the small intestine or sometimes the lower esophagus. It has been one of the most prevalent diseases in the world, and some of its complications have been the major causes of morbidity and mortality. An ulcer in the stomach is called a gastric ulcer, while that in the first part of the intestines is a duodenal ulcer. Although there is a lot of evidence that the eradication of *Helicobacter pylori* (*H.pylori*) prevents ulcer recurrence, the development of ulcers only occurs in several percent of persons infected with *H. pylori*. Although stress is associated with ulcer development in 30–40% of all patients with peptic ulcer, many persons who are under stress do not suffer from this disease. The organ affected by stress varies depending on many factors, including individual predisposition (vulnerable organ), smoking, drinking, and dietary habits. This review focus the causes, diagnosis, management and nutritional care in peptic ulcer diseases.

Keywords: Peptic ulcer, *Helicobacter pylori*, Dietary habits, Drugs

INTRODUCTION

Peptic ulcer disease is a problem of the gastrointestinal tract characterized by mucosal damage secondary to pepsin and gastric acid secretion. Peptic ulcer refers to acid peptic injury of the digestive tract, resulting in mucosal break reaching the submucosa. Peptic ulcers are usually located in the stomach or proximal duodenum, but they can also be found in the oesophagus [1,2]. They are usually formed as a result of inflammation caused by the bacteria *H. pylori*, as well as from erosion from stomach acids. *Helicobacter pylori* had been thought as the main etiological factor for 90% duodenal and 80% gastric ulcers [3]. Peptic ulcer has a multifactor etiology. Environmental elements such as alcohol and nicotine can inhibit or reduce secretion of mucus and bicarbonate, increasing acid secretion. Genetic factors can influence, and children of parents with duodenal ulcer are three times more likely to have ulcer than the population. The most common symptoms of a duodenal ulcer are waking at night with upper abdominal pain or upper abdominal pain that improves with eating. With a gastric ulcer the pain may worsen with eating [4]. The pain is often described as a burning or dull ache. Other symptoms include belching, vomiting, weight loss, or poor appetite. About a third of older people have no symptoms. Complications may include bleeding, perforation and blockage of the stomach. Bleeding occurs in as many as 15% of people [5].

EPIDEMIOLOGY

Peptic ulcers are common and it has been estimated that upto 10% of the population has an ulcer and annual incidence of symptomatic peptic ulcer about 0.3%. Duodenal ulcers are 4 times as common as gastric ulcers and occur mainly in the duodenal cap. Gastric ulcer occurs mostly in lesser curvature of the stomach. These are benign, sometime develop as a tumor (5%). Gastric malignancy is common in Japan, Chile, Iceland and Finland than other world countries because of environmental and diet factor. Prevalence is higher in third world countries where it is estimated at about 70% of the population, whereas developed countries show a maximum of 40% ratio. Overall, *H. pylori* infections show a worldwide decrease, more so in developed countries. Transmission is by food, contaminated groundwater, and through human saliva[6].

CAUSES OF PEPTIC ULCER DISEASE

H. pylori infection and the use of Non Steroidal Anti-Inflammatory Drugs (NSAIDs) are the predominant causes of peptic ulcer disease accounting for 48 and 24 percent of cases [7]. A variety of other infections and comorbidities are associated with a greater risk of peptic ulcer disease (e.g., cytomegalovirus, tuberculosis, Crohn's disease, hepatic cirrhosis, chronic renal failure, sarcoidosis, myeloproliferative disorder). Critical illness, surgery, or hypovolemia leading to splanchnic hypoperfusion may result in gastroduodenal erosions or ulcers (stress ulcers); these may be silent or manifest with bleeding or perforation [8]. Genetic factors play a role in the pathogenesis of ulcer disease. Smoking, stress, hypercalcemia, alcohol and irregular diet increases the risk of ulcer recurrence and slows healing.

Protective vs. Hostile Factors

Excessive gastric acid secretion is only one factor in the pathogenesis of peptic ulcer disease. Decreased mucosal defense against gastric acid is another cause. The integrity of the upper gastrointestinal tract is dependent upon the balance between "hostile" factors such as gastric acid, *H. pylori*, NSAIDs and pepsin, and "protective" factors such as prostaglandins, mucus, bicarbonate, and blood flow to mucosa affecting gastrointestinal mucosa. Injury to gastric and duodenal mucosa develops when deleterious effects of

gastric acid overwhelm the defensive properties of the mucosa. Inhibition of endogenous prostaglandin synthesis leads to a decrease in epithelial mucus, bicarbonate secretion, mucosal blood flow, epithelial proliferation, and mucosal resistance to injury. Lower mucosal resistance increases the incidence of injury by endogenous factors such as acid, pepsin, and bile salts as well as exogenous factors such as NSAIDs, ethanol and other noxious agents.

Helicobacter pylori

Helicobacter pylori, a gram-negative, helical, rod-shaped bacterium, colonizes the gastric mucosa of approximately one-half of the world population and an estimated 30% to 40% of the U.S. population [9]. *H. pylori* is present in 95% of patients with duodenal ulcers and in 70% of those with gastric ulcers [10]. It is typically transmitted via the fecal-oral route during early childhood and persists for decades. The bacterium is a known cause of gastric and duodenal ulcers [11] and is a risk factor for mucosa-associated lymphoid tissue (MALT) lymphoma and gastric adenocarcinoma. *H. pylori* induced ulcer development is influenced by a variety of host and bacterial factors. Ulcers mostly occur at sites of most severe mucosal inflammation [12]. Decreased acid output, usually in the gastric transitional zone between corpus and antrum, give rise to gastric ulcer disease. If acid production is normal to high, the most severe inflammation usually is found in the distal stomach and proximal duodenum, giving rise to juxta-pyloric and duodenal ulcer disease. An individual's ultimate clinical outcome is dependent on the cytokine response and on the gastric acid secretion [13,14]. An increase in stimulated acid production predisposes to duodenal ulceration and decreased acid production predisposes to corpus gastritis or pangastritis which in turn predisposes to gastric ulceration, atrophic gastritis, and gastric carcinoma. The intragastric distribution of gastritis is thought to be dependent on host genetic factors, bacterial virulence factors and environmental factors including age at onset of infection.

Non Steroidal Anti-Inflammatory Drugs (NSAIDs)

Severe ulcer complications and gastrointestinal damages have been associated with NSAIDs. Risk factors for the development of NSAIDs-associated gastric and duodenal ulcers include advanced age, history of previous ulcer disease, concomitant use of corticosteroids and anticoagulants, higher doses of NSAIDs, and serious systemic disorders. The concept of gastroduodenal mucosal injury has evolved from the notion of topical injury to concepts that involve multiple mechanisms. NSAIDs initiate mucosal injury topically by their acidic properties, by diminishing the hydrophobicity of gastric mucus, endogenous gastric acid and pepsin may injure surface epithelium. Systemic effects of NSAIDs appear to play a predominant role through the decreased synthesis of mucosal prostaglandins. The precursor of prostaglandins, arachidonic acid, is catalyzed by the two cyclo-oxygenase isoenzymes, cyclo-oxygenase-1 and cyclo-oxygenase-2. NSAIDs tend to influence the cyclo-oxygenase (cox) pathways which lead to the production of prostanoids (prostaglandins, prostacycline, and thromboxane). This impacts the mucosal protection by reducing the effectiveness of the mucus bicarbonate barrier; gastric acid, and possibly also pepsin, plausibly causing damage, as most NSAIDs are also weak acids may also be a contributory factor in ulceration[15].

Gastrinoma (Zollinger-Ellison Syndrome)

The classic triad of Zollinger-Ellison syndrome involves peptic ulcers in unusual locations (i.e., the jejunum), massive gastric acid hypersecretion, and a gastrin producing islet cell tumor of the pancreas (gastrinoma). Zollinger-Ellison syndrome is a rare disorder that occurs when one or more tumors form in the pancreas and duodenum. The tumors, called gastrinomas, release large amounts of gastrin that cause the stomach to produce large amounts of acid. Normally, the body releases small amounts of gastrin after eating, which triggers the stomach to make gastric acid that helps break down food and liquid in the stomach. The extra acid causes peptic ulcers to form in the duodenum and elsewhere in the upper intestine. The tumors seen with ZES are sometimes cancerous and may spread to other areas of the body. ZES is rare and only occurs in about one in every 1 million people [16]. Although anyone can get ZES, the disease is more common among men 30 to 50 years old. A child who has a parent with MEN1 is also at increased risk for ZES [17]. Zollinger-Ellison syndrome signs and symptoms are similar to those of peptic ulcers. A dull or burning pain felt anywhere between the navel and midchest is the most common symptom of a peptic ulcer. This discomfort usually occurs when the stomach is empty between meals or during the night and may be briefly relieved by eating food. Other symptoms include: diarrhea, bloating, burping, nausea, vomiting, weight loss and poor appetite.

Hypercalcemia

Hyperparathyroidism causes increased levels of calcium in the blood which leads to increased serum levels of gastrin and acetylcholine. These changes result in increased gastric acid secretions and peptic ulcer disease [18]. Intravenous calcium infusion in normal volunteers induces gastric acid hypersecretion. Additionally, calcium has been demonstrated *in vivo* and *in vitro* to stimulate gastrin release directly from gastrinomas.

Genetic Factors

Genetic factors play a role in the pathogenesis of ulcer disease. The lifetime prevalence of developing ulcer disease in first-degree relatives of ulcer patients is about three times greater than the general population. Approximately 20–50% of duodenal ulcer patients report a positive family history; gastric ulcer patients also report clusters of family members who are likewise affected. Some

research results suggest that there is a significant association between genetic polymorphism at the PGR-RFLP gene locus and gastric body ulcer [19,20]. The inheritance of blood group 0 is associated with modest (1.3 fold) increase in duodenal ulcer [21].

Alcohol and smoking

Consumption of alcohol and smoking are risk factors. Chronic alcohol disturbs gastric mucosal barrier by inhibiting COX 1 receptor enzymes which reduce the production of cytoprotective prostaglandin. Pure ethanol is lipid soluble and results in frank, acute mucosal damage. Because most humans do not drink absolute ethanol, it is unlikely there is mucosal injury at ethanol concentrations of less than 10%. Ethanol at low concentrations (5%) may modestly stimulate gastric acid secretions; higher concentrations diminish acid secretion. Cigarette smoking causes reduction of circulating epidermal growth factor and increase free radical production in gastric mucosa [22-24]. Smokers are about two times more likely to develop ulcer disease than nonsmokers. Cigarette smoking and *H. pylori* are co-factors for the formation of peptic ulcer disease. There is a strong association between *H. pylori* infection and cigarette smoking in patients with and without peptic ulcers. Cigarette smoking may increase susceptibility, diminish the gastric mucosal defensive factors, or may provide a more favorable milieu for *H. pylori* infection.

Diet and Stress

Some types of food and beverages are reported to cause dyspepsia. There is no convincing evidence that indicates any specific diet causes ulcer disease. Stress due to serious health problems such as those requiring treatment in an intensive care unit is well described as a cause of peptic ulcers, which are termed stress ulcers [25,26]. Acute stress results in increases in pulse rate, blood pressure and anxiety, but only in those patients with duodenal ulcers did acute stress actually result in significant increases in basal acid secretion. Caffeinated, decaffeinated, or cola-type beverages, beer, or milk also commonly thought to cause or exacerbate ulcer disease. Dietary alteration, other than avoidance of pain-causing foods, is unnecessary in ulcer patients. Skipping of meals allows gastric acid to directly act on surface mucosa of the stomach causing irritation which ultimately leads to gastric ulcers. Gastric ulcers cause abdominal pain which aggravate with meals [27].

SYMPTOMS

An ulcer may or may not have symptoms. When symptoms occur, they may include: A gnawing or burning pain in the middle or upper stomach between meals or at night, Bloating, heartburn, nausea or vomiting, burping and water brash. In severe cases, symptoms can include, dark or black stool (due to bleeding), vomiting blood (hematemesis), weight loss, severe pain in the mid to upper abdomen. If not properly treated, ulcers can lead to serious health problems, including bleeding (gastric acid or peptic ulcer breaks a blood vessel), perforation (ulcer grows deeper and breaks through the wall of the stomach or duodenum), gastric outlet obstruction from swelling or scarring that blocks the passageway leading from the stomach to the small intestine and peritonitis is a very serious abdominal infection. It may develop if the ulcer eats completely through the wall of the stomach or intestine.

Other clinical presentations include

Acute presentation-natural, voluntary, or accidental *H.pylori* acquisition can cause acute upper gastrointestinal illness with nausea and upper abdominal pain [28], chronic colonization in most persons after acquisition *H.pylori* persists for years, if not for decades, duodenal ulceration in the absence of medication-associated ulceration, more than 90 % of patients with duodenal ulceration carry *H.pylori*, an occurrence that is significantly more common than in age-matched controls[29,30]

DIAGNOSIS

The diagnosis is mainly established based on the characteristic symptoms. Stomach pain is usually the first signal of a peptic ulcer. The following tests that can confirm a diagnosis include:

Physical Exam

A physical exam may help the health care provider diagnose the cause of peptic ulcer disease. During a physical exam, a health care provider usually, checks for abdominal bloating, listens to sounds within the abdomen using a stethoscope, taps on the abdomen checking for tenderness or pain.

Blood test

A blood test involves drawing a sample of a patient's blood at a health care provider's office or a commercial facility and sending the sample to a lab for analysis. The blood test can show the presence of *H. pylori*.

Urea breath tests

Urea breath tests require the ingestion of urea labeled with the nonradioactive isotope carbon 13 or carbon 14. Specificity and sensitivity approach 100%. Urea breath testing is one option for test of cure and should be performed four to six weeks after completion of eradication therapy. Proton pump inhibitors (PPIs) must be stopped for at least two weeks before the test, and accuracy is lower in patients who have had distal gastrectomy. Cost and inconvenience are disadvantages of this test [31].

Stool monoclonal antigen tests

Stool antigen tests using monoclonal antibodies are as accurate as urea breath tests if a validated laboratory-based monoclonal test is used [32]. They are cheaper and require less equipment than urea breath tests. Like urea breath tests, stool antigen tests detect only active infection and can be used as a test of cure. PPIs should be stopped for two weeks before testing, but stool antigen tests are not as affected by PPI use as are urea breath tests.

Serologic tests

Serologic antibody testing detects immunoglobulin G specific to *H. pylori* in serum and cannot distinguish between an active infection and a past infection. Serologic tests may be most useful in mass population surveys and in patients who cannot stop taking PPIs (e.g., those with gastrointestinal bleeding or continuous NSAID use) because the tests are not affected by PPI or antibiotic use [33,34].

Endoscopy with biopsy

Endoscopy with biopsy is recommended to rule out cancer and other serious causes in patients 55 years or older, or with one or more alarm symptoms. In patients who have not been taking a PPI within one to two weeks of endoscopy, or bismuth or an antibiotic within four weeks, the rapid urease test performed on the biopsy specimen provides an accurate, inexpensive means of diagnosing *H. pylori* infection [35]. Patients who have been on these medications will require histology, with or without rapid urease testing. The health care provider can pass tiny tools through the endoscope to: Take photos of the peptic ulcer, obtain a biopsy of the lining of the stomach or small intestine. A biopsy is a procedure that involves taking a small piece of tissue for examination with a microscope by a pathologist—a health care provider who specializes in examining tissues to diagnose diseases. The patient will not feel the biopsy. The test can show the presence of *H. pylori*: Inject medications that help the blood clot, stop any bleeding with an electrical probe or special medications. Upper GI series is an x-ray exam that provides a look at the shape of the upper GI tract to help diagnose peptic ulcer disease.

Computerized Tomography Scan

Computerized tomography scans use a combination of x rays and computer technology to create images. For a CT scan, a nurse or technician may give the patient a solution to drink and an injection of a special dye, called contrast medium. CT scans require the patient to lie on a table that slides into a tunnel-shaped device that takes the x rays. An x-ray technician performs the procedure in an outpatient center or a hospital, and a radiologist interprets the images. The patient does not need anaesthesia. CT scans can help diagnose a perforated peptic ulcer.

MANAGEMENT OF PEPTIC ULCER DISEASE

Drugs used in treatment of peptic ulcer

Pharmacologic management of peptic ulcer disease continues to evolve with the introduction of diverse types of new therapeutic agents. The ideal aims of treatment of peptic ulcer disease are to relieve pain, heal the ulcer, and delay ulcer recurrence. Drug treatment of peptic ulcers is targeted at either counteracting aggressive factors or stimulating the mucosal defense. Drugs that inhibit or neutralize gastric acid secretion include histamine H₂-receptor antagonists, proton pump inhibitors, anticholinergics, prostaglandins, and antacids. H₂-receptor antagonists have become first-line drugs for treatment of uncomplicated duodenal ulcers, gastric ulcers, prevention of ulcer relapse, and mild esophagitis. The drugs used in treatment of peptic ulcer was represented in Table 1.

Table1. Drugs for peptic ulcer

TREATMENT	OPTIONS
Eradication of Helicobacter pylori	Omeprazole or Lansoprazole + Amoxicillin or Metronidazole + Clarithromycin
	Ranitidine bismuth citrate + Clarithromycin or Metronidazole + Tetracycline or Amoxicillin
	Levofloxacin + Amoxicillin +Pantoprazole
Antacids	
Systemic Antacids	Sodium bicarbonate Calcium carbonate
Non- Systemic Antacids	Magnesium hydroxide, Aluminium hydroxide Magnesium trisilicate Magnesium oxide
Histamine H2 Blockers	Ranitidine, Famotidine, Cimetidine, Nizatidine, Roxatidine, Tiotidine, Lupitidne, Metiamide, Oxmetidine and Lafutidine
Proton Pump Inhibitors	Omeprazole, Lansoprazole, Esomeprazole ,Rabeprazole, Haprazole, Timoprazole,Tenatoprazole and Pantoprazole
Anticholinergics	Pirenzepine
Mucosal Protective Agents	Sucralfate (Carafate) and Colloidal Bismuth subcitrate potassium, Bismuth subsalicylate and Carbenoxolone
Prostaglandins	Misoprostal PGE2-(Enprostil, Arbaprostil, Rioprostil)
Surgery	Duodenal ulcer: Truncal vagotomy, selective vagotomy, highly selective vagotomy, partial gastrectomy. Gastric ulcer: Partial gastrectomy with gastroduodenal or gastrojejunal anastomosis

Nutritional assessment on peptic ulcer

Nutritional recommendations for patients with peptic ulcer are described as follows: According to Marrota and Floch [36], calories distribution for patients with peptic ulcer should be normal, with values ranging from 50-60% of carbohydrates, 10-15% of proteins, and 25-30% of lipids, with total energy value sufficient to maintain or recover the nutritional status. Reis[37] suggested that calories distribution should be adjusted according to the patient's needs to normalize the nutritional status, having as recommended macronutrients a protein intake of up to 1.2 g/kg/weight/day in the acute stage (5th to 8th week) and up to 1.5 g/kg/weight/day in the recovery stage. Carbohydrates should be adjusted to the patient's needs, without disaccharides concentration, so as to avoid fermentation, and lipids without concentration of saturated fats. To accelerate the healing process, in addition to protein, there are specific micronutrients such as zinc, which is essential to maintain the immune system function, as a response to oxidative stress, and to heal wounds [38]. Selenium may reduce infection complications and improve healing [39,40]. In addition, vitamin A may be used as a supplement, but the research that supports this practice is of limited effectiveness, because very high dosages do not promote cure, and excessive intake may be toxic [41]. Allowed foods, foods that should be consumed with caution, and foods that must be avoided for peptic ulcer was represented in Table.2.

Table2. Food groups that allowed, use with caution and prohibited for peptic ulcer

FOOD GROUPS	ALLOWED & USE WITH CAUTION	PROHIBITED
Dairy	Milk, low-fat cheeses, yogurt, fermented milk	
	Use with caution: Fatty cheeses	
Oilseeds	Flaxseed, Brazilian nut, walnuts	
Oils and olive oils	Vegetable oils, olive oil	Fried foods
Fruits	Apple, papaya, melon, banana	Lemon
	Use with caution: Orange, pineapple, acerola, passion fruit	
Vegetables	Leafy dark green vegetables, carrot, beet, green bean, spinach, kale, radish, zucchini, leek	Spicy peppers (black pepper, chillies)
	Use with caution: Broccoli, cauliflower, cabbage, cucumber, onion, red pepper	
Legumes	Bean soup, lentils, chickpeas, soybean	
	Use with caution: Beans	
Meats	Lean meat (beef, pork, chicken, fish)	
	Use with caution: Fatty meats, organ meats and sausages	
Sweets	Use with caution: Concentrated sweets	Chocolate
Beverages	Natural juices	Coffee, black tea, fizzy/cola drinks
	Use with caution: Citrus/acidic fruit juices	
Other foods	Use with caution: Industrialized seasonings, spices and condiments	Mustard grain

CONCLUSION

Peptic ulcer is a disease of chronic development, characterized by an imbalance between the factors that damages the mucosa and those for its protection, resulting in a lesion of the lining of the upper digestive tract. It has been one of the most prevalent diseases in the world, and some of its complications have been the major causes of morbidity and mortality. In conventional medical treatment for ulcer, unhealthy lifestyle factors (including smoking, drinking, and stress) are left unchanged. In this review, we can concluded that the Patients should be encouraged to abstain from smoking and alcohol consumption, and smoking cessation therapy should be offered when appropriate. Patients must be made aware that a number of over the counter medications and herbal products contain NSAIDs, and that they should consult their health care provider prior to taking these medications. Additional patient education emphasizing the importance of adherence and counseling on proper administration of drug therapy is an essential component for treatment success. In addition, a balanced diet is vital in the treatment of peptic ulcer, once food can prevent, treat or even alleviate the symptoms involving this pathology. Accordingly, dietotherapy has played a key role in the prevention and treatment of Peptic ulcer, with the main purpose of recovering and protecting the gastrointestinal lining, improving digestion, relieving pain, and contributing to a satisfactory nutritional status.

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