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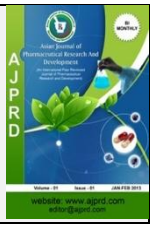

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Review Article

Peptic Ulcer Disease (PUD): An overview of the History, Risk factors, Symptoms, Diagnosis Considerations and Conventional Management

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A B S T R A C T

Gastric and duodenal ulcer (PUD), are upper gastrointestinal disorders sharing a common abnormality, too much acid and pepsin activity followed by inflammation, necrosis and ulceration of exposed mucosa. H. Pylori infection, use of NSAIDs and stress are the major risk factors that lead to the occurrence of PUD. With the introduction of proton pump inhibitors (PPIs) and antibiotics against H. Pylori resolution of symptom and rapid ulcer healing was obtained but cure of PUD has failed. However, new challenges have emerged due to increasing antibiotic resistance of H. pylori. Management of peptic ulcer needs accurate identification of the ulcerogenic cause in the individual patient for proper selection of therapy.

Keywords: PUD, Risk factors, H. Pylori, PPIs, Resistance

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INTRODUCTION:

Peptic ulcer disease (PUD) is a common disease worldwide. It occurs as a defect in the mucosa of the stomach or duodenum that exceeds the muscularis mucosa.[1,2]PUD results from an imbalance between factors that protect the mucosa of the stomach and duodenum, and factors that cause damage to it. [3,4]It presents with gastrointestinal symptoms similar to dyspepsia and can be difficult to distinguish clinically. It can have potentially serious complications such as bleeding or perforation, with a high risk of mortality.[5]Patients with gastric and duodenal ulcers present similarly. They may report epigastric or retrosternal pain, early satiety, nausea, bloating, belching, or postprandial distress. These symptoms are non-specific and may be difficult to distinguish clinically from functional dyspepsia.[6]

Risk Factors for Peptic Ulcer Disease:

Many studies suggest that H pylori infection is an important risk factor for duodenal ulcers and gastric ulcers.[7,8] Medications such as aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) cause approximately 10% of peptic ulcers.[9]Marginal ulcer is seen in approximately 5% of patients who have undergone gastric bypass surgery for obesity.[10]

Others Risk factors and causes of ulcers in the stomach and duodenum are as follows:

- Smoking and chewing [11]
- Excessive drinking of alcohol
- Selective serotonin reuptake inhibitors [12,13]
- Physiological stress associated with serious trauma and critical illness (eg, septicaemia) [14]
- Infections, mainly in immunocompromised patients, e.g., tuberculosis [15]

Rare specific factors [16]

- Crohn's disease
- Eosinophilic gastroduodenitis
- Systemic mastocytosis
- Radiation damage
- Colonisation of stomach with H. heilmannii
- Severe systemic disease
- Cameron ulcer

Symptoms of Peptic Ulcer Disease:

An ulcer may or may not have symptoms. When symptoms occur, they may include:[17]

- Burning pain in the middle or upper stomach
- Bloating
- Heartburn
- Nausea or vomiting

In severe cases, symptoms can include: [18]

- Dark or black stool
- Vomiting blood
- Weight loss
- Severe pain in the mid to upper abdomen

Though ulcers often heal on their own, you shouldn't ignore their warning signs. If not properly treated, ulcers can lead to serious health problems, including:[19]

- Bleeding
- Perforation (a hole through the wall of the stomach)
- Gastric outlet obstruction from swelling or scarring that blocks the passageway leading from the stomach to the small intestine

DIAGNOSIS CONSIDERATIONS:

Testing for H. pylori infection is essential in all patients with peptic ulcers. In most of patient's routine laboratory tests usually are not helpful. In diagnosis of suspected patients CBC count, liver function tests (LFTs), levels of amylase and lipase may be useful. The ACG guidelines recommend eradication of HPI with the use of a urea breath test, faecal antigen test, or biopsy-based testing.[20]

Endoscopic or invasive tests for H pylori include a rapid urease test, histopathology, and culture. The presence of H pylori in gastric mucosal biopsy specimens is detected by testing for the bacterial product urease. Fecal antigen testing identifies active H pylori infection by detecting the presence of H pylori antigens in stools.[21]

Three kits (i.e., CLO test, Hp-fast, Pylori Tek) are commercially available for H pylori testing, and each contains a combination of a urea substrate and a pH sensitive indicator. One or more gastric biopsy specimens are placed in the rapid urease test kit. If H pylori is present, bacterial urease converts urea to ammonia, which changes the pH, resulting in a color change.[22]

Urea breath tests detect active H pylori infection by testing for the enzymatic activity of bacterial urease. In the presence ofurease produced by H pylori, labeled carbon dioxide is produced in the stomach, absorbed into the bloodstream, diffused into the lungs, and exhaled.[23]

Histopathology, often considered the criterion standard to establish a diagnosis of H pylori infection, if the rapid urease test result is negative and a high suspicion for H pylori persists (presence of a duodenal ulcer).[24]

MANAGEMENT OF PUD:

The first effective therapy was introduced in the 1980s, and consisted of a combination of bismuth, tetracycline, and metronidazole that was given for two weeks.[25] The standard first-line therapy is a triple therapy consisting of a proton pump inhibitor (PPI) and two antibiotics, such as clarithromycin plus amoxicillin or metronidazole given for seven to 14 days.[26] However, with an increasing prevalence of antibiotic resistance, especially for clarithromycin, there has been a marked declinein the success of triple therapy over the last 10–15 years.

The recommended standard first-line therapy is either a bismuth-containing quadruple therapy for 14 days (PPI, a bismuth salt, tetracycline, and metronidazole) or a 14-day concomitant therapy for patient's intolerant of bismuth (PPI, clarithromycin, amoxicillin, and metronidazole); both regimens yield eradication rates higher than 90%.[27]

Second-line therapy is prescribed if a first-line regimen fails, and should not include metronidazole or clarithromycin.[28]Levofloxacin triple therapy (PPI, amoxicillin, and levofloxacin) for 14 days seems to be an efficacious therapy, achieving eradication rates between 74–81%.

Despite well-developed recommendations for choosing proper treatment regimens, 5–10% of patients have persistent infection. The most common reasons for the failure of two treatments are suboptimal compliance or the resistance of H. pylori to one or more antibiotics, in which case susceptibility testing is strongly recommended.[29]

Many strategies are available for the prevention of NSAID associated gastro duodenal ulcers and their complications, such as the co-therapy of NSAIDs with a PPI, H2 receptor antagonist, or misoprostol; the use of COX-2-selective NSAIDs; or their combination with a gastro protective agent.[30]The combination of COX-2-selective NSAIDs and a PPI offers the best protection against peptic ulcer complications.[31]

For refractory ulcers, the doubling of PPI dose for another six to eight weeks is often recommended, although the evidence supporting this is weak. After the exclusion of false-negative H. pylori status, unusual causes of peptic ulcer should be explored, such as malignancies, infections, Crohn's disease, vasculitis, upper abdominal radiotherapy, cocaine use, and Zollinger–Ellison syndrome.[32]

Reports are suggesting that the use of PPIs mightincrease the risk of enteric infections such as Salmonella and Campylobacter, community-acquired pneumonia [33], Clostridium difficile infections[34], and spontaneous bacterial peritonitis [35].Additionally, PPIs might increase the risk for osteoporosis and bone fractures by interfering with the ionization and solubilization of the calcium salts that are required for their absorption.[36]

There has been a dramatic increase in reports of miscellaneous, unanticipated adverse effects of PPIs over the past several years, such as myocardial infarction, stroke, acute and chronic kidney disease, and eosinophilic esophagitis.**[37]**The suppression of acid production raises gastric pH and inactivates pepsin, inhibiting peptide ingestion and degradation, and causing allergic reactions in the small intestine.[38]

CONCLUSION:

Peptic ulcer complications are serious therapeutic challenge. H. pylori, NSAIDs and stress are the important factors for the occurrence of PUD. To prevent the PUD and its complication eradication and prevention of these factors should be conducted. Management of H. pylori-associated PUD has improved during the past few decades, culminating in the widespread use of PPIs based triple therapy. However, use of remedies concerned in the aetiology of PUD, such as a NSAIDs, have also increased in recent years. PUD has declined significantly but has not extinct. Etiologies are diverse and heterogeneous and demand for selective cures for controlling PUD and diminish the complications.

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