PEPTIC ULCER DISEASE
CAUSES, TREATMENT AND PREVENTION
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Upper gastrointestinal (GI) disorders encompassed variety of condition that can cause gastric discomfort, including non ulcer dyspepsia, peptic ulcer disease (PUD), and gastroesophageal reflux disease (GERD). The incidence of PUD varies with type of ulcer (gastric or duodenal), geographic location, gender, age and variety of environmental factor. Three factors stand out as being the most important to the development of PUD: bacterial GI infection with *Helicobacter pylori* (*H.*pylori*), ingestion of non steroidal anti-inflammatory drugs (NSAIDs), and cigarette smoking. It is estimated that up to 90% of peptic ulcer, in the absence of NSAID exposure, are associated with *H. pylori* infection.

Causes and Risk factors:

1- *Helicobacter pylori* (*H.*pylori*):
*H. pylori* infection is the predominant cause of peptic ulcer disease. *H. pylori*, a Gram-negative flagellate bacterium that infects the stomach of more than half of the global population, is regarded as the leading cause of chronic gastritis, peptic ulcer disease, and even gastric adenocarcinoma in some individuals.

2- Non-steroidal anti-inflammatory drugs (NSAIDs):
*H. pylori* and NSAIDs are the major causes of gastro duodenal ulcer disease. It is now well established that the point prevalence of peptic ulcer disease in patients receiving conventional nonsteroidal anti-inflammatory drug therapy ranges between 10 and 30%, representing a 10- to 30-fold increase over that found in the general population. In addition, by inhibiting cyclooxygenase, NSAIDs inhibit the formation of prostaglandins and their protective cyclooxygenase-2–mediated effects. NSAIDs were the most common risk factor in patients without *H. pylori* infection. Coexisting *H. pylori* infection increases the likelihood and intensity of NSAID-induced damage. Proton pump inhibitors and misoprostol (Cytotec) minimize the ulcerogenic potential of NSAIDs and reduce NSAID-related ulcer recurrence.

3- Cigarette smoking and nicotine:
Smoking and chronic nicotine treatment stimulates basal acid output which is more pronounced in the smokers having duodenal ulcer. This increased gastric acid secretion is mediated through the stimulation of H2-receptor by histamine released after mast cell degranulation and due to the increase of the functional parietal cell volume or secretory capacity in smokers.

4- Caffeine:
Even though coffee is not considered to be responsible for development of peptic ulcer, it may, however, prolong its healing by increasing acidity of gastric content. Coffee may damage gastroduodenal mucosa in habitual coffee drinkers.

5- Age:
Duodenal ulcers: More common between ages 25-55 years old. Gastric ulcer: usually does not occur before age 40, peaks between 55-65 years of age.
6- Gender:
Peptic ulcer disease affects 10% of men and 4% of women at some time in their lives. Gastric ulcers are more common in women.

7- Diseases that cause an increase in acid production, such as Zollinger-Ellison syndrome (ZES):
The ZES, is characterized by peptic ulcers of the upper gastrointestinal tract refractory to medical therapy, diarrhea and severe gastric acid hypersecretion associated with non-beta islet cell tumors of the pancreas.

8- Severe stress:
Many people believe that stress causes ulcers. It is not clear if this is true. While critically ill patients who are on a breathing machine, trauma, burns, surgery, and acute organ failure are at risk of so-called “stress ulceration,” everyday stress at work or home doesn't appear to cause peptic ulcers

Management of PUD:
Strategies used for treatment of PUD are summarized into:
I. Drugs for lowering acid concentration
II. Protective drugs
III. Eradication of H.pylori
IV. Surgery
I. Drugs for lowering acid concentration:

a. Proton pump inhibitors
They provide superior acid suppression, healing rates, and symptom relief and are recommended as initial therapy for most patients. Many proton pump inhibitors are now available for the treatment of acid-related disorders (omeprazole, lansoprazole, rabeprazole, pantoprazole, tenatoprazole and esomeprazole).

b. Histamine (H2) blockers:
The H2 blockers suppressed the normal circadian rhythm of intragastric acidity, which rises in the evening until the middle of the night and then drops in the morning.
Cimetidine (TAGAMET), ranitidine (ZANTAC), famotidine (PEPCID), and nizatidine (AXID) are less potent than proton pump inhibitors but still suppress 24-hour gastric acid secretion by about 70%. These drugs can be given by oral in intermittent intravenous boluses or by continuous intravenous infusion. Anticholinergic agents such as atropine suppress acid secretion by a different mechanism, but may have a synergistic effect when given in combination with H2 receptor antagonists. Famotidine is approximately 20 to 50 times more potent at inhibiting gastric acid secretion than cimetidine and 8 times more potent than ranitidine on a weight basis.

c. Acid neutralization (Antacids):
Antacids do not effectively heal ulcers but they do relieve symptoms of ulcers by neutralizing stomach acidity and thereby raising the pH level in the stomach. It is no longer common to find antacids used as sole therapy. However, antacids can interact with many different prescription drugs (eg; tetracycline), so a pharmacist should be consulted about possible drug-drug interactions before antacids are taken.
Sodium bicarbonate (baking soda) and calcium carbonate, the strongest antacids, may be taken occasionally for fast, short-term relief. However, because they are absorbed by the bloodstream, continual use of these drugs may make the blood too alkaline (alkalosis), resulting in nausea, headache, and weakness. Therefore, these antacids generally should not be used in large amounts for more than a few days. These products also contain a lot of salt and should not be used by people who need to follow a low-sodium diet or who have heart failure or high blood pressure.

Aluminum hydroxide is a slowly acting, relatively safe, and commonly used antacid. However, aluminum may bind with phosphate in the digestive tract, thereby depleting the body of calcium, reducing phosphate levels in the blood, and cause weakness and a loss of appetite and constipation. Magnesium hydroxide is a rapidly acting, and more effective antacid than aluminum hydroxide. This antacid acts fast and neutralizes acids effectively. Many antacids contain both magnesium hydroxide and aluminum hydroxide to minimize diarrhea.
II. Protective drugs:

a. Sucralfate:
Sucralfate is a unique therapeutic agent used for an acute and chronic treatment of deofenal ulcer treatment of gastric ulcer and prevention of stress ulceration. It is a complex polyaluminum hydroxide salt of sucrose sulfate which exerts its effect via coating and protection of the gastric mucosa. Use of sucralfate should be avoided in patients with compromised renal function to avoid aluminum accumulation and poisoning.

b. Prostaglandin E1 analogues:
NSAIDs impair prostaglandin-dependent gastric mucosal protective mechanisms. Misoprostol, prostaglandin E1 analogues, is effective for ulcers associated with the use of NSAIDs but is often poorly tolerated because of diarrhea and abdominal pain.

III. Eradication of H. pylori:
The recommended duration of therapy for eradication is 10 to 14 days; Treatment of peptic ulcers in patients who are H. pylori positive should include antimicrobial therapy to eradicate the infection; one recommended regimen is the combination of a proton-pump inhibitor (lansoprazole 30 mg or omeprazole 20 mg), clarithromycin 500 mg, and amoxicillin 1 g, each twice daily for 7-14 days. Quadruple therapy is still the most effective for Helicobacter pylori. Tetracycline, amoxicillin, imidazoles (predominantly metronidazole and tinidazole), and a few selected macrolides (in particular clarithromycin, sometimes azithromycin) are probably the drugs most widely used for H. pylori eradication therapy.

Failures are in particular related to insufficient therapy adherence, often because of side effects, and to the presence of antimicrobial resistance. Such resistance is common in patients who have had previous antibiotic treatment, including failed eradication therapies.

IV. Surgery:
Surgery is indicated in patients who are intolerant of medications or do not comply with medication regimes, and those at high risk of complications (e.g., transplant recipients, patients dependent on steroids or NSAIDs, those with giant gastric or duodenal ulcer, those with ulcers that fail to heal with adequate treatment). Surgery should also be considered for patients who have a relapse during maintenance treatment or who have had multiple courses of medications.

Complications of PUD:
About 25% of patients with peptic ulcer disease have a serious complication such as hemorrhage, perforation, or gastric outlet obstruction. Silent ulcers and complications are more common in older patients and in patients taking NSAIDs

Prevention of peptic ulcers:
The most important way to prevent any disease – including peptic ulcer disease – is to maintain a generally healthy lifestyle, which includes the following:

- Get plenty of rest and decrease your consumption of caffeine, nicotine, alcohol and anti-inflammatory medicines. Prophylactic regimens that have been shown to dramatically reduce the risk of NSAID-induced gastric and duodenal ulcers include the use of a prostaglandin analogue or a PPI.
- Stop smoking. Heavy smokers are more likely to develop duodenal ulcers. Smoking also slows healing.
- Avoid eating foods that irritate stomach, especially fatty and spicy foods, and rather choose foods with high fiber content. High-fiber foods, but can also greatly reduce risk of developing a duodenal ulcer. Fiber is believed to enhance the secretion of mucin, which protects the duodenal lining.

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