“ Peptic Ulcer Disease : A Comprehensive Review of Pathogenesis , Clinical Features and Contemporary Management”

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Abstract

Peptic Ulcer Disease (PUD) is a gastrointestinal tract disorder characterized by the erosion of the stomach and duodenum lining, caused by an imbalance between aggressive factors, including acid and pepsin, and protective factors, such as prostaglandins, blood flow, and cell regeneration. Aggressive factors, including alcohol misuse, smoking, Helicobacterpylori colonization, and the use of nonsteroidal anti-inflammatory medicines, contribute to the development of PUD. The disease can lead to severe complications, such as perforation and death, resulting in significant public health expenses and affecting a substantial portion of the population. Understanding the Etiologic and pathogenesis of PUD is crucial for the development of effective prevention and treatment strategies, reducing the burden of this disease on public health and improving patient outcomes. This study aims to provide an overview of the current knowledge on PUD, highlighting the interplay between aggressive and protective factors, and discussing the implications for diagnosis, treatment, and prevention.

Key words :Peptic ulcers, gastrointestinal tract, Diagnosis, NSAID, Helicobacter Pylori, Proton Pump Inhibitor.

Introduction

Peptic ulcers are caused by acid and pepsin, which damage the stomach and duodenum lining. PUD is brought on by an imbalance between aggressive factors including alcoholmisuse, smoking, Helicobacter pylori colonization, and the use of nonsteroidal anti-inflammatory medicines, and protective factors like prostaglandins, blood flow, and cell regeneration.[1]

A gastrointestinal tract wound that penetrates the inner, submucosal, and potentially outer muscular layers, leading to perforation and death, is referred to as a peptic ulcer (PUD). The illness raises public health expenses and affects a sizable section of the global population.Ulcers are a prevalent ailment that impacts individuals globally. Because of the unpleasant side effects, treating ulcer symptoms is bad for your health.Nowadays, ulcers are treated using a variety of herbs and secondary metabolites.[2]

Conventional dental care is widely recognized, However, the efficacy of this treatment may be diminished by drug breakdown in the gastrointestinal environment, decreased oral bioavailability, and inadequate drug transport to the target location.Following this strategy, using strategies to increase the efficacy of these conventional medications becomes appealing.The formulation's particle size should be in the nanoscale range for maximum penetration effectiveness and improved results.Consequently, the composite material is given precedence over the generated nanoparticles.Because of their improved performance over bulk materials and their tenable physical, chemical, and biological properties, nanomaterials are becoming more and more significant in innovation. It is important to take into account the size, content, shape, and origin of nanomaterials.[3]

Mucosal damage of the stomach or duodenum due to an imbalance between aggressive luminal factors and mucosal Defense mechanisms is the hallmark of peptic ulcer disease, a relatively uncommon but clinically severe disorder in children [4-5] Despite the fact that peptic ulcers are more frequently identified in adults, their prevalence in children has grown in recent decades, primarily as a result of easier access to endoscopic operations.[6-9]

There are two types of paediatric peptic ulcers: primary, which is usually linked to Helicobacter pylori infection, and secondary, which is usually brought on by systemic illness, physiological stress, or the use of medications such nonsteroidal anti-inflammatory medicines (NSAIDs).[10-12]A rare but potentially fatal surgical emergency in children, perforated peptic ulcers (PPUs) are among the possible side effects of PUD and can result in substantial morbidity and mortality if not identified and treated quickly [13-15]

Pathophysiology of ulcer

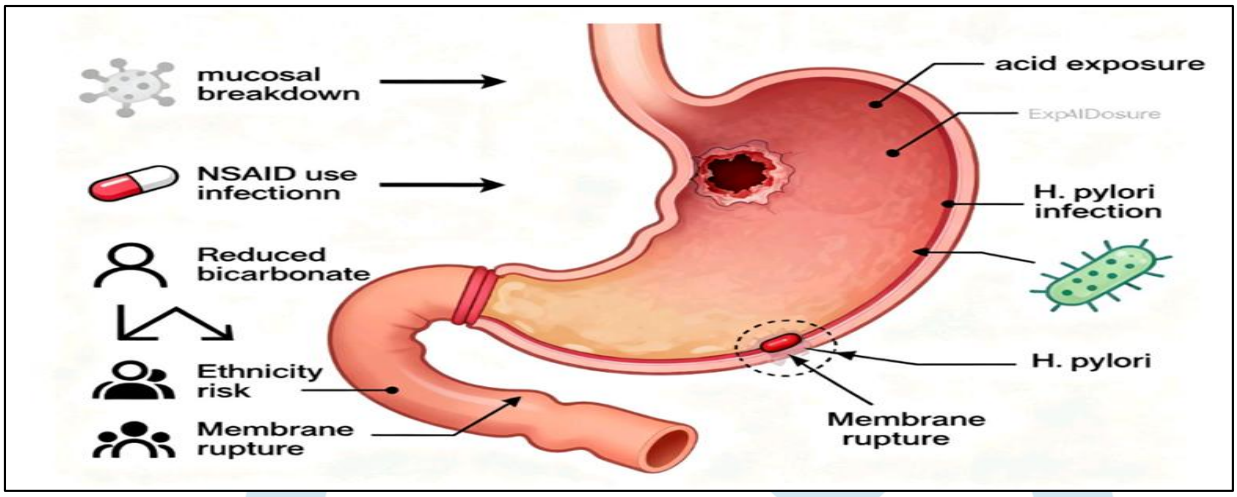

Figure1: Representative diagram of peptic ulcer Causative Factors.

An ulcer is a persistent breakdown of the mucosa or skin's outermost layer brought on by molecular death.A rupture of the body's inner lining that stops a membrane-bound organ from functioning normally is called an ulcer.Peptic ulcer disease is brought on by an imbalance between the lining of the gastrointestinal tract's protective and destructive components.NSAID use and H. pylori infection are risk factors for PUD. African-American/Hispanic ethnicity, migration from industrialized nations, and first-degree relatives with PUD. Peptic ulcers frequently result in a mucosal defect that extends to the muscle mucosa.When the mucous membrane that shields the surface is compromised, the interior layers become vulnerable to acid. Additionally, mucosal cells' capacity to secrete bicarbonate is compromised. Additionally, H pylori increases stomach acidity, stimulates metabolism, and prevents the release of bicarbonate. [18]

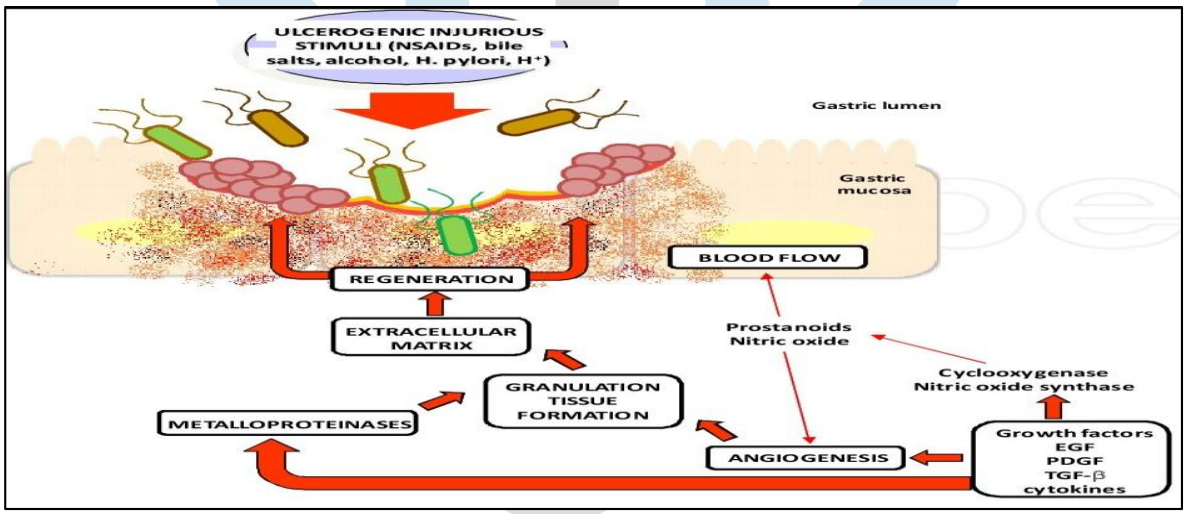

Figure 2: The main mechanism involved in the healing of gastric ulcers. EGF: epidermal growth factor; PDGF: platelet-derived growth factor; TGFβ: transforming growth factor β.

Evaluvation

The patient should be assessed for warning signs if the initial clinical presentation points to peptic ulcer disease. Bleeding is suggested by anaemia, hematemesis, melena, or home-positive stool; blockage is suggested by vomiting; malignancy is suggested by anorexia or weight loss; persistent upper abdomen pain radiating to the back indicates penetration; and severe, spreading upper abdominal pain indicates perforation. Referrals for an upper endoscopy should be made as soon as possible for patients over 55 and those with alarm signs.Compared to upper gastrointestinal barium tests, esophagogastroduodenoscopy (EGD) is more sensitive and selective for peptic ulcer disease and enables biopsy of stomach lesions[19]Individuals under the age of 55 who do not exhibit any alarm signs ought to get tested for an H. pylori infection and counselled to stop using NSAIDs, smoking, drinking, and using illegal drugs. A stool antigen test, urea breath test, endoscopic biopsy, or serum enzyme-linked immunosorbent assay (ELISA) can all be used to confirm the presence of H. pylori. The least accurate test is serum ELISA, which is only helpful for identifying the initial infection. Although less practical, the stool antigen test is quite accurate and, like the urea breath test, can be used to confirm H. pylori eradication. [19]Antsecretory medication, preferably with a proton pump inhibitor, should be given for four weeks in order to eradicate the infection if test results for H. pylori are positive.[19, 20]The radiologic or endoscopic diagnostic serves as the basis for additional treatment. Endoscopy should be recommended for patients with prolonged symptoms in order to rule out cancer and refractory ulcers.

Types of peptic ulcer

1)Gastric Ulcer: Gastric ulcers are peptic ulcers that develop in the stomach lining. They are commonly associated with factors such as Helicobacter pylori infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs)[21].

2***) Duodenal Ulcers*:** Duodenal ulcers are a form of peptic ulceration that occurs in the duodenum, the proximal portion of the small intestine. They are more prevalent than gastric ulcers and are commonly associated with *Helicobacter pylori* (H. pylori) infection and the administration of nonsteroidal anti-inflammatory drugs (NSAIDs)[22].

3)Stress Ulcers: Stress ulcers, also referred to as acute stress-related mucosal damage, typically develop in response to significant physiological stress, including major trauma, extensive burns, surgical procedures, or critical illness. These lesions are most frequently observed in the stomach and are primarily attributed to reduced mucosal perfusion and increased gastric acid secretion mediated by stress-induced hormonal changes.[23].

Causes of peptic ulcer

Although there are many different causes of PUD, the majority of the disease's genesis can be attributed to Helicobacter pylori-associated PUD and NSAID-associated PUD [24].

Typical

1. Infection with H. pylori
2. NSAIDs
3. Drugs

Infrequent

- Zollinger-Ellison syndrome;
- cancer (lung and stomach cancer, lymphomas);
- stress (head injuries, burns, and acute sickness);
- viral infection
- Crohn's disease
- Insufficiency of the arteries with radiation therapy
- Chemotherapy

1)Helicobacter Pylori-Associated PUD

The gastric epithelial cells contain the gram-negative bacillus H. pylorus. 90% of duodenal ulcers are caused by this bacterium, and 70% to 90% of stomach ulcers. A H. pylori infection is typically contracted as a child and is more common in people with lower socioeconomic level. The bacteria can cling to and inflame the stomach mucosa because of its broad range of virulence factors. This causes Achlorhydria or hypochlorhydria, which in turn causes stomach ulcers.

Helicobacter pylori virulence factors

1. Urease: This enzyme neutralizes the acidic stomach environment and converts urea into ammonia, protecting the body.
2. Toxins: CagA/VacA is linked to host tissue damage and inflammation of the stomach mucosa.
3. Flagella: Facilitates migration in the direction of the stomach epithelium by providing motility.

2)NSAID-triggered PUD

After H. pylori infection, the use of nonsteroidal anti-inflammatory medications is the second most common cause of PUD [25], Prostaglandin secretion often shields the stomach mucosa. By blocking the COX-1 enzyme, NSAIDs prevent the creation of prostaglandins, which lowers the formation of gastric mucus and bicarbonate as well as mucosal blood [26].

3)Drugs

In addition to NSAIDs, the etiology of PUD has been linked to corticosteroids, bisphosphonates, potassium chloride, and fluorouracil. Although the relationship is not linear, smoking also seems to contribute to duodenal ulcers. Alcohol can cause acidity and irritate the stomach mucosa. These circumstances result in a hypersecretory environment:

- Zollinger Ellison syndrome
- Systemic Mastocytosis
- Cystic fibrosis
- Hyperparathyroidism
- Antral G cell hyperplasia

Figure 3. Photograph of a peptic ulcer taken during an upper endoscopy. This ulcer is a "gastric ulcer" because it is located in the stomach.

Signs and symptoms

Symptoms of a peptic ulcer may include:

- Severe abdominal pain, usually epigastric ,Associated with mealtimes. Duodenal ulcers cause pain three hours after eating and can disrupt sleep.
- Bloatingand abdominal fullness.
- Waterbrash (a burst of saliva following regurgitation to neutralize acid in esophagus, especially common in gastroesophageal reflux illness).
- Symptoms include severe nausea and vomiting.
- Gastric ulcers can cause appetite reduction and weight loss
- Symptoms of duodenal ulcers include weight gain owing to pain relief via eating, as well as hematemesis (bloody vomiting) caused by ulcer bleeding or esophageal injury.
- Melena refers to tarry, foul-smelling feces caused by oxidized iron from hemoglobin
- An ulcer can cause stomach or duodenal rupture, resulting in rapid peritonitis and severe stabbing pain, [27] Immediate surgery is required.

Table 1. Tests for the Diagnosis of Peptic Ulcer

Test	Comments
EGD	Indicated in patients with evidence of bleeding, weight loss, chronicity, or persistent vomiting; those whose symptoms do not respond to medications; and those older than 55 years More than 90 percent sensitivity and specificity in diagnosing gastric and duodenal ulcers and cancers
Barium or diatrizoatemeglumine and diatrizoate sodium (Gastrografin) contrast radiography (double-contrast hypotonic duodenography)	Indicated when endoscopy is unsuitable or not feasible, or if complications such as gastric outlet obstruction suspected Diagnostic accuracy increases with extent of disease; 80 to 90 percent sensitivity in detecting duodenal ulcers
Stool antigen test	Inconvenient but accurate (sensitivity, 91 to 98 percent; specificity, 94 to 99 percent) Can be used to confirm eradication
Helicobacter pylori testing Serologic ELISA	Useful only for initial testing (sensitivity, 85 percent; specificity, 79 percent); cannot be used to confirm eradication
Endoscopic biopsy	Culture (sensitivity, 70 to 80 percent; specificity, 100 percent), histology (sensitivity, > 95 percent; specificity, 100 percent), rapid urease (CLO) test (sensitivity, 93 to 97 percent; specificity, 100 percent)
Urine-based ELISA and rapid urine test	Sensitivity, 70 to 96 percent; specificity, 77 to 85 percent Cannot be used to confirm eradication

EGD = esophagogastroduodenoscopy; ELISA= enzyme-linked immunosorbent assay; PPI= proton pump inhibitor; CLO= Campylobacter-like organism [19,20]

Diagnosis of peptic ulcer

In order to record the existence of ulcers, radiologic and/or endoscopic procedures are typically necessary. Endoscopic testing is costly and intrusive, thus it is only recommended for patients with new-onset dyspepsia who are 60 years of age or older. Younger than 60-year-old dyspepsia patients may avoid endoscopy, but they should still get noninvasive H. pylori testing and receive treatment if the results are positive. If an H. pylori test is negative, the patient should either have an endoscopy or be offered a trial of acid suppression therapy for 4–8 weeks. An upper endoscopy examination is necessary if the dyspepsia persists after an acid suppression treatment trial. The diagnosis of PUD cannot be made using standard laboratory testing. To find bleeding, hematocrit, hemoglobin, and stool guaiac tests are performed.Both endoscopic and nonendoscopic diagnostic procedures can be used to find the existence of H. pylori. Samples of stomach tissue are taken during endoscopic diagnosis, and these samples are then examined for H. pylori. The stool antigen assay, serologic testing, and the urea breath test are nonendoscopic techniques for testing for H. pylori. Compared to endoscopy, these tests are less costly and invasive.

The urea breath test is usually first line because of its excellent sensitivity and specificity and rapid turnaround time. Antibiotic or acid suppressive medication used concurrently may produce false-negative results. Additionally, the urea breath test can be used to verify that an H. pylori infection has been eradicated. Serologic testing offers a rapid (within 15 minutes) office-based evaluation of H. pylori exposure.However, it is unable to distinguish between an ongoing infection and one that has already been treated; patients may continue to test positive for years after eradication. For patients receiving recent or ongoing antibiotic or acid-suppressive medication, serologic testing is advised.
Assays for stool antigen can be helpful for both initial diagnosis and confirming the removal of H. pylori. They are less impacted by concurrent pharmaceutical use and have good sensitivity and specificity.[28]

Risk AssessmentAnd Pre-Endoscopic Managment

It is crucial to assess patients right away and start appropriate resuscitation by giving them IV fluids, oxygen, and blood transfusions when necessary. introducing UGIB. Although the effect of red blood cell transfusions on rebleeding and mortality is unknown, they are typically given once the hemoglobin level falls below 70 g/L, depending on the underlying illness and clinical presentation. The effects of red blood cell transfusions in adults with UGIB were evaluated in a Cochrane meta-analysis [29]. 126 individuals participated in three randomized or quasi-randomized trials that contrasted red blood cell transfusion with routine therapy that did not involve red blood cell transfusion.
According to these research, receiving red blood cell transfusion was linked to greater rebleeds (38% vs. 4%; 1 study) and deaths (5% vs. 0%; 2 studies). But the trials that were included had a number of methodological flaws and varied in terms of treatment plans and outcome metrics, suggesting that the meta-analysis's findings should merely serve as a catalyst for additional research rather than as definitive clinical recommendations. Data on 4441 patients with acute UGIB were gathered for a sizable recent study conducted in the UK. In comparison to patients who were not early transfused, those who received transfusion within 12 hours of presentation experienced a 28% increase in mortality (OR 1.28; 95% CI 0.94–1.74) and a twofold greater rate of rebleeding (OR 2.26; 95% CI 1.76–2.90).
Following adjustment for the extent of the bleeding using Rockall scores andhemoglobin concentrations at However, the findings might have been skewed by long-lasting variations in the case mix between individuals who received transfusions early on and those who did not [30]. It is necessary to conduct prospective research using a well-defined transfusion regimen. Meanwhile, each red blood cell transfusion's advantages and disadvantages need to be carefully considered.

Pharmacotherapy Prior to Endoscopy

Prior to endoscopy, strong doses of proton pump inhibitors (PPIs) are administered intravenously to neutralize pH and stabilize blood clots. Investigators from In 638 individuals with UGIB, Hong Kong investigated the impact of a preemptive infusion of omeprazole given as an 80 mg intravenous bolus and an 8 mg infusion every hour prior to endoscopy. In patients treated with omeprazole, they observed a substantial decrease in the requirement for endoscopic therapy (19% vs. 28%, P=0.007), more ulcers with clean base (64% vs. 47%, P=0.001), and fewer active bleeds during endoscopy (6% vs. 15%, P=0.01) [31].other significant outcome metrics,including as mortality,rebleedingand transfusion requirement,showed no change. In oeder to reduce the need for endoscopic intervention and downstage the bleeding site, pre-endoscopic PPI medication may be used, according to international standards[32].

Risk Assessment

Early risk assessment is essential for identifying individuals with the highest risk of rebleeding, determining the best time for an endoscopy, and anticipating when additional measures will be required. blood transfusions, IV fluid delivery, and hospitalization to intensive care. Numerous risk classification systems have been created for this reason. The Blatchford score and the Rockall score are two widely used scoring schemes [33,34].

The latter includes both a pre-endoscopic and a post-endoscopic section that includes the endoscopy results. Comorbidity and vital signs at presentation are taken into account by both the Blatchford and Rockall scoring systems. Compared to the Rockall score, the Blatchford score is less concerned with age and more focused on laboratory findings (hemoglobin and urea) and symptoms (melena and/or syncope).According to a recent prospective cohort study that compared the reliability and applicability of different rating systems, the Blatchford score but not the pre-endoscopic The Rockall score can be used to

predict low-risk individuals who might benefit from outpatient care and do not require therapeutic endoscopy [35]. Unfortunately, neither measure had a high positive predictive value for the necessity of endoscopic intervention. This backs efforts to create new scoring systems or modify current ones in order to achieve more accurate risk categorization.

Treatment of peptic ulcer

Relieving symptoms, repairing craters, avoiding complications, and preventing recurrences are the objectives of treatment for peptic ulcer disease. Drug treatment should be a part of medical therapy, which aims to achieve the following goals:

1) Lower stomach acidity by neutralizing or inhibiting acid release,

2) Cover ulcer craters to stop pepsin and acid from reaching the ulcer base.

3) Offer an analog of prostaglandin,

4) Eliminate environmental hazards including smoking and NSAIDs, and

5) Lessen emotional stress (in a subgroup of patients).[36]

Peptic ulcer medications

A) Inhibitors of Gastric Acid Secretion
Cimetidine, Ranitidine, Famotidine, Roxatidine, and Lafutidine are examples of H2 antihistamines.

Anticholinergic drugs: Oxyphenonium, Propantheline, and Pirenzepine.
Omeprazole, Esomeprazole, Pantoprazole, Lansoprazole, Rabeprazole, and Dexrabeprazole are examples of proton pump inhibitors.
Misoprostol, an analogue of prostaglandin

B) Neutralizers for Gastric Acid

Systemic Antacid: Sodium Citrate and Sodium Bicarbonate
nonsystemic antacids.
Magnesium hydroxide, magnesium trisilicate, and aluminum hydroxide

C) Ulcer Protectives: Colloidal Bismuth Subcitrate and Sucralfate

D) Anti-H. Pylori medications: Amoxicillin, Tetracycline, Metronidazole, Tinidazole, and Clarithromycin.

Management of ulcers linked to H. pylori

•***Uncomplicated Ulcer***: PPIs (such as omeprazole 20 mg twice daily) administered for 14 days, in conjunction with an antibiotic program to treat H. pylori, are typically sufficient to promote healing in patients with simple ulcers.[36]

•***Complicated ulcer*** - An intravenous PPI should be used as the first line of treatment for individuals with complex peptic ulcers, which include ulcers that have bleeding, perforation, penetration, or obstruction of the stomach outlet. Patients should be switched to an oral PPI at a high dose twice daily to promote healing once they are able to tolerate oral drugs (e.g., omeprazole 40 mg twice daily). After four weeks, the dosage should normally be lowered to once daily. However, if there is no sign of recurrent bleeding, people who are bleeding can have their intravenous PPI changed to a lower oral dose (such as 20 mg of omeprazole once daily) 72 hours following the endoscopy. The presence of risk factors for macrolide resistance and the existence of a penicillin allergy should inform the initial antibiotic regimen chosen to treat H. pylori.[36]

We recommend triple therapy with a proton pump inhibitor (PPI), amoxicillin (1 g twice daily), and clarithromycin (500 mg twice daily) for 14 days as initial therapy in individuals without risk factors for macrolide resistance (Grade 2B). Since metronidazole resistance is widespread and can decrease treatment efficacy, we recommend replacing amoxicillin with metronidazole only in those who are allergic to penicillin.[36]

Peptic ulcers linked to NSAIDs:

Patients with PUD should stop taking NSAIDs, including aspirin, or take them less frequently. For pain treatment, substitute medications such acetaminophen or a nonacetylatedsalicylate (such as salsalate) should be utilized whenever feasible.

Depending on the size of the ulcer, patients with NSAID-associated ulcers should get treatment for four to eight weeks with a PPI (such as omeprazole 20 to 40 mg daily). For peptic ulcer patients who must continue taking
aspirin or NSAIDs, maintenance antisecretory
PPI medication, such as omeprazole 20 mg daily, can lower the risk of ulcer recurrence or complications.

Patients undergoing long-term NSAID or aspirin therapy for osteoarthritis, rheumatoid arthritis, or cardiac protection frequently need to follow preventative regimens against PUD. To lower the risk of NSAID-induced PUD, controlled trials have assessed misoprostol, H2RAs, PPIs, and COX-2 selective inhibitors.[36]

H2-Receptor antagonists

Standard dosages of H2RAs, such as 40 mg/day of famotidine, are beneficial in avoiding duodenal ulcers caused by NSAIDs, but not gastric ulcers, which are the most common kind of ulcer linked to NSAIDs.

Ranitidine

When compared to cimetidine, this non-imidazole (which has a furan ring instead of an imidazole ring) H2 blocker has a number of advantageous properties: roughly five times as strong as cimetidine. Clinically, a longer duration of action with stronger 24-hour acid suppression is achieved due to its increased potency, even if its pharmacokinetic profile and t½ of 2-3 hours are similar to those of cimetidine.

Dosage: 300 mg at bedtime or 150 mg BD for ulcer healing; 150 mg at bedtime for maintenance. 0.1-0.25 mg/kg/hr by I.V infusion has been used for stress prevention, as has a parenteral dose of 50 mg I.M. or gradual intravenous injection every 6–8 hours (rapid intravenous injection can produce hypotension). ulceration, especially after extended surgery. 300 mg three to four times a day for Gastrinoma.[37]

Famotidine

Despite an elimination t½ of 2.5–3.5 hours, an H2 blocker with a Thiazole ring that binds firmly to H2 receptorsand has a longer duration of action. In the absence of histamine, there has been evidence of some inverse agonistic activity on H2 receptors. It has five to eight times the potency of ranitidine. There is no anti-androgenic effect.The modest dose and low affinity for cytochrome P450 result in a negligible propensity to influence drug metabolism. Famotidine has a 40–50% oral bioavailability and is eliminated by the kidney, with 70% of the unaltered form. The only side effects that have been documented include headache, lightheadedness, upset stomach, and infrequently, confusion and rash. Doses include 40 mg before bed or 20 mg BD (for healing); 20 mg before bed for maintenance; up to 480 mg daily for ZE syndrome; and 20 mg intravenously 12 hours apart or 2 mg per hour intravenous infusion.[38]

Proton Pump Inhibitors

It works better than H2RAs at lowering the risk of duodenal and stomach ulcers brought on by nonselective NSAIDs. PPIs are more well-tolerated than misoprostol, but they are just as effective. When used in prescribed dosages, all PPIs are effective.[39]

Omeprazole

Without significantly affecting pepsin, intrinsic factor, juice volume, or gastric motility, it is a potent inhibitor of gastric acid that can completely stop HCI secretion, both at rest and when triggered by food or any of the secretagogues. When the pH falls below 5, omeprazole transforms into two charged cationic forms (sulfenic acid and sulfenamide structures), which react covalently with the SH groups of the H+K+ ATPase enzyme to permanently inactivate it.particularly when one enzyme molecule interacts with two omeprazole molecules. It becomes concentrated in the acidic canaliculi after being absorbed into the bloodstream and then diffusing into the parietal cell because the charged forms produced at the acidic pH cannot diffuse back. Additionally, it forms a strong bond with the enzyme via covalent connections. Omeprazole and all other PPIs have a high degree of selectivity of action due to these characteristics and the particular localization of H+ K+ ATPase to the apical membrane of the parietal cells. Only after the synthesis of new H+K ATPase molecules (reactivation half time of 18 hours) does acid secretion resume. Additionally, it suppresses the gastrointestinal mucosal carbonic anhydrase.[37]

Pharmacokinetics: To ensure their safety, all PPIs are taken orally in enteric coated form. from the acidic gastric juice's molecular rearrangement. The pill with enteric coating or Before swallowing, granules in capsules shouldn't be crushed or broken. Verbal Because of its acid lability, omeprazole has a 50% bioavailability. When the pH of the stomach increases, a higher up to 3/4 of the proportion may be absorbed. Food lowers the bioavailability of all PPIs. They ought to be consumed on an empty stomach when just 10% of the proton pumps are functioning, then 1 an hour later.[37]

Anticholinergics

Unless there is food in the stomach to dilute the acid released, Atropinic medications decrease the volume of gastric juice without increasing its pH. Gastric secretion stimulated is less fully suppressed. Anti-muscarinic medications (Oxyphenonium, propantheline, and atropine) at effective dosages (for ulcer healing) always result in unpleasant side effects. PPIs, blockers, and introduction H2 have rendered them obsolete.[38]

Pirenzepine

In Europe, this selective M1 anticholinergic was used to treat peptic ulcers. More potent H2 blockers and PPIs have rendered it unnecessary, despite the fact that antimuscarinic side effects were less noticeable.

Systemic antacids

Sodium bicarbonate

It works instantly and dissolves in water, although its duration of action is brief. It has a strong neutralizing effect (1 g→ 12 mEq HCI), and the pH can increase above 7. But it has a number of drawbacks:

(a) Systemically absorbed: high dosages will cause alkalosis.

(b) The stomach produces CO2, which increases the risk of ulcer perforation, distention, pain, and belching.

(c) Acid rebound happens, but it normally passes quickly.

(d) Increases Na' load, which could exacerbate CHF and edema. Sod is used. Bicarbonate is only used to treat heartburn informally. It offers prompt symptom alleviation.

Additional applications include treating acidosis and alkalizing urine. Sodium citrate shares characteristics with sod. 10 mEq HCI is neutralized by 1 g of bicarbonate; CO2 is not evolved.[38]

Nonsystemic antacids

These are basic substances that are insoluble and poorly absorbed; they react in the stomach to produce the appropriate chloride salt. HCO3 is not saved for absorption; no acid-base disruption takes place as a result of the chloride salt's second reaction with intestinal bicarbonate. But tiny Magnesium hydroxide has a limited water solubility; its aqueous suspension (milk of magnesia) has a low concentration of OH ions and, hence, low alkalinity.

Absorbable levels have the same alkalinizing action as NaHCO3. Nevertheless, it is an effective antacid (1 g → 30 mEq HCI) and reacts with HCI quickly.

MAGNESIA MILK 0.4 g/5 ml suspension: 12 mEqacid is neutralized by 5 ml. In clinical application, only about 1 mEq of magnesium trisilicate is neutralized, despite the fact that 1 g can react with 10 mEq of acid.[40]

cytoprotective substance

Sucralfate
a non-absorbable, negatively charged molecule that binds to positively charged proteins in exudates to produce a complex that is sticky, viscous, and paste-like. Use is restricted, many daily doses are required, the tablets are big, and they interact with several other drugs (such as digoxin and fluoroquinolones).

Constipation, nausea, metallic taste, and the potential for aluminum toxicity in people with renal failure are some of the side effects.[41]

CONCLUSION

Peptic ulcer disease remains a frequent clinical problem in our environment predominantly affecting all age of people. As the prevalence of peptic ulcer disease increases with advancing age it is expected that this common disease will continue to have a significant global impact on health-care delivery, health economics and the quality of life of patients. The majority of people who present with dyspepsia should be examined for peptic ulcer disease. In conclusion, the management of peptic ulcer disease requires a comprehensive understanding of its pathophysiology, risk factors, treatment modalities, and preventive strategies. Peptic ulcers represent a significant health burden worldwide, with potential complications such as gastrointestinal bleeding, perforation, and obstruction, which can lead to substantial morbidity and mortality if left untreated. Therefore, timely diagnosis, appropriate treatment, and regular follow-up are paramount in optimizing patient outcomes and reducing the risk of complications.

This review article has provided insights into various aspects of peptic ulcer disease, including its etiology, pathogenesis, clinical presentation, diagnostic approaches, and treatment options. Helicobacter pylori infection and nonsteroidal anti-inflammatory drug (NSAID) use remain the leading causes of peptic ulcers, emphasizing the importance of targeted interventions, such as H. pylori eradication therapy and NSAID avoidance or co-therapy with gastroprotective agents.

Advances in diagnostic techniques, such as endoscopy, urea breath tests, and stool antigen tests, have facilitated the accurate diagnosis of peptic ulcers and associated complications, allowing for prompt initiation of appropriate treatment. Furthermore, the advent of proton pump inhibitors (PPIs), H2-receptor antagonists, and mucosal protective agents has revolutionized ulcer management by effectively suppressing gastric acid secretion, promoting ulcer healing, and preventing recurrence.

REFERENCES

1)Spósito L, Fortunato GC, Furquiim de CamargoBA, Dos San tos MA, de Souza PMC, Meneguin AB, et al. Exploiting drug delivery systems for an oral route in the peptic ulcer disease treatment," J. Drug Target., vol. 0, no. 0, pp. 1–19, 2021, doi: 10.1080/1061186X.2021.1904249.

2) Singh AK, Singh SK, Singh PP, Srivastava AK, Pandey KD, Ku mar A, et al. "Biotechnological aspects of plants metabolites in the treatment of ulcer: A new perspective," Biotechnol. Reports, vol. 18, p. e00256, 2018, doi: 10.1016/j.btre.2018.e00256.

3) Chaubey P, Mishra B, "Mannose-conjugated chitosan nanoparticles loaded with rifampicin for the treatment of visceral leishmaniasis," Carbohydr. Polym., vol. 101, no. 1, pp. 1101–1108, 2014, doi: 10.1016/j.carbpol.2013.10.044.

4) Almadi MA, Lu Y, Alali AA, Barkun AN. Peptic ulcer disease. Lancet. 2024;404(10447):68–81. https://doi.org/10.1016/s0140-6736(24)00155-7.

5) Lanas A, Chan FKL. Peptic ulcer disease. Lancet. 2017;390(10094):613–24. http s://doi.org/10.1016/s0140-6736(16)32404-7.

6)Almadi MA, Lu Y, Alali AA, Barkun AN. Peptic ulcer disease. Lancet. 2024;404(10447):68–81. https://doi.org/10.1016/s0140-6736(24)00155-7.

7)Lanas A, Chan FKL. Peptic ulcer disease. Lancet. 2017;390(10094):613–24. http s://doi.org/10.1016/s0140-6736(16)32404-7.

8)Abbasi-Kangevari M, Ahmadi N, Fattahi N, Rezaei N, Malekpour MR, Ghamari SH et al. Quality of care of peptic ulcer disease worldwide: A systematic analy sis for the global burden of disease study 1990–2019. Chu DT, editor. PLOS ONE. 2022;17(8):e0271284. https://doi.org/10.1371/journal.pone.0271284

9)Groenen MJ, Kuipers EJ, Hansen BE, Ouwendijk RJT. Incidence of duodenal ulcers and gastric ulcers in a Western population: back to where it started. Can J Gastroenterol. 2009;23(9):604–8. https://doi.org/10.1155/2009/181059

10) Urs AN, Narula P, Thomson M. Peptic ulcer disease. Paediatr Child Health. 2014;24(11):485–90. https://doi.org/10.1016/j.paed.2014.06.003.

11) Ecevit CO, Ozgenç F, Yuksekkaya HA, Unal F, Arikan C, Yagci RV. Peptic ulcer disease in children: an uncommon disorder with subtle symptomatology. Turk J Gastroenterol. 2012;23(6):666–9. https://doi.org/10.4318/tjg.2012.0562.

12) Yadav S, Gupta V, El Kohly A, Al Fadhli W. Perforated duodenal ulcer: A rare complication of deferasirox in children. Indian J Pharmacol. 2013;45(3):293. ht tps://doi.org/10.4103/0253-7613.111901.

13) Munoz Abraham AS, Osei H, Martino A, Kazmi S, Saxena S, Fitzpatrick CM, et al. Incidence and outcomes of perforated peptic ulcers in children: analysis of the Kid's inpatient database and report of two cases treated by laparoscopic omental patch repair. J LaparoendoscAdvSurg Tech. 2019;29(2):248–55. http s://doi.org/10.1089/ lap.2018.0186.

14) Søreide K, Thorsen K, Harrison EM, Bingener J, Møller MH, Ohene-Yeboah M, et al. Perforated peptic ulcer. Lancet. 2015;386(10000):1288–98. https://doi.or g/10.1016/s0140-6736(15)00276-7.

15) Alhaj Saleh A, Esquivel EC, Lung JT, Eaton BC, Bruns BR, Barmparas G, et al. Laparoscopic omental patch for perforated peptic ulcer disease reduces length of stay and complications, compared to open surgery: A SWSC multi center study. Am J Surg. 2019;218(6):1060–4. https://doi.org/10.1016/j.amjsur g.2019.09.002.

16) Ivanova N, Gugleva V, Dobreva M, Pehlivanov I, Stefanov S, Andonova V, et al. Pathophysiology of Gastric Ulcer Develop ment and Healing: Molecular Mechanisms and Novel Therapeu tic Options," Intech, vol. I, no. tourism, pp. 114–142, 2016.

17) Snowden FM, "Emerging and reemerging diseases: a historical perspective. (Special Issue: Immunology of emerging infections.)," Immunol. Rev., vol. 225, pp. 9–26, 2008.

18) Hasnath Siddique DRA, "Prevalence of Peptic Ulcer Disease among the Patients with Abdominal Pain Attending the Depart ment Of Medicine in Dhaka Medical College Hospital, Bangla des et. al, " IOSR J. Dent. Med. Sci., vol. 13, no. 1, pp. 05–20, 2014, doi: 10.9790/0853-13190520.

19) Talley NJ, Vakil NB, Moayyedi P. American Gastroenterological Association technical review on the evaluation of dyspepsia. Gastroenterology 2005;129:1756-80.

20) University of Michigan Health System. Peptic ulcer disease. Accessed May 4, 2007, at: http://www.cme.med.umich.edu/pdf/guideline/PUD05.pdf.

21) Malfertheiner, P., Megraud, F., O'Morain, C. A., Gisbert, J. P., Kuipers, E. J., Axon, A. T., ... & Graham, D. Y. (2017). Management of Helicobacter pylori infection—the Maastricht V/Florence Consensus Report. Gut, 66(1), 6-30.

22) Moayyedi, P., Lacy, B. E., Andrews, C. N., Enns, R. A., Howden, C. W., Vakil, N., ... & Quigley, E. M. M. (2017). ACG and CAG Clinical Guideline: Management of Dyspepsia. The American Journal of Gastroenterology, 112(7), 988-1013.

23) Cook, D., Heyland, D., Griffith, L., Cook, R., Marshall, J., Pagliarello, J., & Canadian Critical Care Trials Group. (1999). Risk factors for clinically important upper gastrointestinal bleeding in patients requiring mechanical ventilation. Critical Care Medicine, 27(12), 2812-2817.

24) Narayanan M, Reddy KM, Marsicano E. Peptic Ulcer Disease pylori infection. Mo and Helicobacter Med. 2018 Jun;115(3):219-224.

25) Lanas Á, Carrera-Lasfuentes P, Arguedas Y, García S, Bujanda L, Calvet X, Ponce J, Perez Aísa Á, Castro M, Muñoz M, Sostres C, García-Rodríguez LA. Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. ClinGastroenterolHepatol. 2015 May;13(5):906 12.e2

26) Huang JQ, Sridhar S, Hunt RH. Role of Helicobacter pylori infection and non steroidal anti-inflammatory drugs in peptic ulcer disease: a meta-analysis. Lancet. 2002 Jan 05;359(9300):14-22.

27) Bhat S . SRB's Manual of Surgery. 2013: 364.

28) Jaswanth et al., UPI j. pharm. med. health sci, 5(1), 2022: 19-26

29)Jairath V, Hearnshaw S, Brunskill SJ, et al.: Red cell transfusion for the management of upper gastrointestinal haemorrhage. Cochrane Database Syst Rev. 2010:CD006613.

30)Hearnshaw SA, Logan RF, Palmer KR, et al. Outcomes following early red blood cell transfusion in acute upper gastrointestinal bleeding. Aliment PharmacolTher. 2010;32:215–24.

31) Lau JY, Leung WK, Wu JC, et al. Omeprazole before endoscopy in patients with gastrointestinal bleeding. N Engl J Med. 2007;356:1631–40.

32)Barkun AN, Bardou M, Kuipers EJ, et al.: International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2010, 152:101–113. This paper published by an international consensus group is of outstanding importance because it provides widely endorsed consensus recommendations on the management of patients with non-variceal upper gastrointestinal bleeding. Similarly important is alike consensus of the Asia-Pacific Working Group which allows for the specific needs of resource-limited countries and ethnic differences in the Asia-Pacific region [29]

33) Rockall TA, Logan RF, Devlin HB, et al. Risk assessment after acute upper gastrointestinal haemorrhage. Gut. 1996;38:316–21.

34) Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. Lancet. 2000;356:1318–21.

35) Pang SH, Ching JY, Lau JY, et al. Comparing the Blatchford and pre-endoscopic Rockall score in predicting the need for endo scopic therapy in patients with upper GI hemorrhage. GastrointestEndosc. 2010;71:1134–40.

36)Mechu Narayanan, MD, Kavya M. Reddy, MD & Elizabeth Marsicano, MD, Peptic Ulcer Disease andHelicobacter pylori infection, 2018.

37) Tara V. Shanbhag, SmitaShenoy, Pharmacology for Medical Graduates, Third, 2015.

38) KD Tripathi, Essentials of Medical Pharmacology, 5 th edition Jaydeep brothers medical publishers, the health science publisher, New Delhi,

39) Lucija Kuna 1, JelenaJakab 2,3, Robert Smolic 2,4,5, Nikola Raguz-Lucic 1, AleksandarVcev 2,5 and Martina Smolic 1,4,* Peptic Ulcer Disease: A Brief Review Of Conventional Therapy And Herbal Treatment Options,Journal Of Clinical Medicine, 2019.

40) R.S. Satoskar, Nirmala N. Rege, Raakhi K. Tripathi S.D. Bhandarkar, Pharmacology and Pharmacoterapeutics. popularprakashan, 2017; 25. ISBN: 978-81-312-4886-7

41) Park JY, Dunbar KB, Mitui M, Arnold CA, Lam-Himlin DM, Valasek MA, et al. Helicobacter pylori Clarithromycin Resistance and Treatment Failure Are Common in the USA. Dig Dis Sci, 2016; 61: 2373-2380.