

AN OVERVIEW OF RECENT ADVANCEMENTS IN DISEASE MANAGEMENT PROGRAM OF ULCER

**Dr. Shobhit Prakash Srivastava¹, Arvind Kumar Srivastava²,
Hriday Shankar Chaurasia³, Suman Jaiswal⁴, Surya Prabhakar Singh⁵**

¹ Dr. M. C. Saxena college of Pharmacy, 171, Barawankala, Mall Road, IIM Rd, Dubagga, Lucknow, affiliated to APJAKTU, Lucknow, Uttar Pradesh, India.

² Department of Pharmaceutical Chemistry, United Institute of Pharmacy, affiliated to APJAKTU, UP, India

³ Jyotiraditya Institute of Pharmacy, JD Shikha Gram, Pratapgarh, UP, India.

⁴ Department of Pharmacology, United Institute of Pharmacy, affiliated to APJAKTU, UP, India

⁵ Department of Pharmaceutics, United Institute of Pharmacy, affiliated to APJAKTU, UP, India

Corresponding Author:

Arvind Kumar Srivastava

Address: Department of Pharmaceutical Chemistry, United Institute of Pharmacy, affiliated to APJAKTU, UP, India

e-mail id: arvind.org@live.com

ABSTRACT

Peptic ulcers are defined by erosions on the mucosa of the gastrointestinal system that can reach the muscular layer. Their origin is multifaceted, occurring when the balance of offensive and protective components in the mucosa is disrupted. Peptic ulcers are a global health concern that affects millions of individuals and has a high recurrence rate. *Helicobacter pylori* infection and the use of nonsteroidal anti-inflammatory medicines (NSAIDs) are two of the most major risk factors for the development of peptic ulcers. As a result, novel supplementary treatment options are required to avoid ulcer formation and recurrence. Conventional therapies for peptic ulcers, such as proton pump inhibitors (PPIs) and histamine-2 (H₂) receptor antagonists, have shown side effects, relapses, and numerous medication combinations. therefore, this review presents, pharmacological and non-pharmacological treatment methods have been listed for effective treatment of different types of ulcers such as, acupuncture, electrical stimulation/modulation, antacids, Pyroloplasty and SPV, H. pylori-Induced PUD Treatment, standard therapy, triple drug therapy.

Keywords: *Helicobacter pylori*, gastrointestinal, Pyroloplasty, acupuncture, Peptic ulcers.

Introduction

Peptic ulcer disease (PUD) is defined as the breach of the protective barrier of the stomach and duodenum's epithelial mucosa, which is accompanied by an inflammatory process and ulcer development. Ulcers range from superficial epithelium injury to deeper erosions, which result in organ hemorrhage and perforation. (1.) (2). PUD (incidence of 0.1-0.3% per year) affects around 5-10% of the global population and varies by age, gender, and geographic area. (3). Epidemiological statistics for this disease and its consequences indicate significant heterogeneity in incidence and prevalence. A peptic ulcer is a local hole or excavation on the stomach's surface with a mucosal break of 5 mm or bigger, caused by the sloughing of inflammatory necrotic tissue.(4)

Historical aspect

For the last century, stomach acid secretion has been a source of discussion, with a focus on both molecular and cellular mechanisms involved. Gastric juice was chemically examined, and William Prout (5) isolated hydrochloric acid (HCL) for the first time in 1824. After James Black discovered the histamine (H₂) receptor in 1971, antagonists became accessible for the treatment of peptic ulcers (6). The discovery of proton-pump inhibitors in 1989 altered the management of peptic ulcers by blocking the final phase of acid generation in the stomach lumen (7).

The earliest description of a perforated peptic ulcer was made in 1670 by Princess Henrietta of England (8). Barry Marshall and Robin Warren discovered *H. pylori* as the cause of peptic ulcers in the late twentieth century,(9) for which they were awarded the Nobel Prize in 2005.

Epidemiology

The incidence and prevalence of PUD vary depending on the presence of *Helicobacter pylori*. Higher rates are seen in countries with higher *H. pylori* infection (10, 11). The annual incidence of PUD in *H. pylori*-infected persons is around 1%, which is 6- to 10-fold greater than in uninfected individuals. A comprehensive evaluation of seven research from industrialized nations found that the population-based one-year prevalence of PUD ranged between 0.1 and 1.5 percent based on physician diagnosis and 0.1 to 0.19 percent based on hospitalization data. A research in the United States found a 2% endoscopic point prevalence for peptic ulcers in asymptomatic, *H. pylori*-positive people. Other investigations, in apparently asymptomatic people whose *H. pylori* status was unknown, revealed endoscopic point prevalences ranging from 1 to 6%.

Ulcer prevalence rises with age for both duodenal ulcers (DUs) and stomach ulcers (GUs), however the incidence of simple PUD plateaus with age, but the incidence of severe PUD rises. DUs happen two decades sooner than GUs, especially in men (12).

About 4.6 million Americans suffer from peptic ulcer illness each year, and 10% of the country's population is thought to have had duodenal ulcer symptoms at some point. 90% of duodenal ulcers and 70%–90% of stomach ulcers are caused by *H. pylori* infection. As people age, the percentage of those with peptic ulcer disease and *H. pylori* infection rises steadily.

The incidence of peptic ulcer disease has changed from being more common in men to being equally common in women. For men, the lifetime prevalence is roughly 11%–14%, and for women, it is 8–11%. When it comes to ulcer occurrence, age trends show that older women have higher rates and younger men have dropping rates, especially for duodenal ulcers.

The yearly incidence rates of peptic ulcer disease were determined to be 0.03-0.17% based on hospitalization data and 0.10-0.19% based on physician diagnosis after a thorough review of PubMed, EMBASE, and the Cochrane library. Based on hospitalization statistics, the 1-year prevalence was 0.10-0.19%, while the prevalence based on physician diagnosis was 0.12-1.50%. Most studies found that the incidence or prevalence of peptic ulcer disease decreased over time.

The main factors influencing the prevalence of peptic ulcer disease in other nations are its correlation with the two main causes of the condition, H pylori and NSAIDs. Spain had the greatest yearly incidence of total peptic ulcer illness (141.8/100,000 people), whereas the United Kingdom had the lowest (23.9/100,000 people), according to a 2018 systematic MEDLINE and PubMed review. South Korea had the greatest yearly incidence of perforated peptic ulcer illness (4.4/100,000 persons), while the United Kingdom had the lowest incidence (2.2/100,000 persons). (13)

Etiology: Peptic ulcer disease (PUD) has various causes; however, Helicobacter pylori-associated PUD and NSAID-associated PUD account for the majority of the disease etiology.

Causes of Peptic Ulcer Disease

1. H. pylori infection
2. NSAIDs
3. Medications
4. Zollinger-Ellison syndrome
5. Malignancy (gastric/lung cancer, lymphomas)
6. Stress (Acute illness, burns, head injury)
7. Viral infection
8. Vascular insufficiency
9. Radiation therapy
10. Crohn disease
11. Chemotherapy

Pathophysiology

Under normal circumstances, the mucus-bicarbonate barrier, neutral pH, and ongoing epithelial cell renewal preserve the integrity of the duodenum and stomach mucosa [14]. PGE2 stimulates mucus production, cell division, and H₂CO₃ release, supporting a crucial function in mucosa preservation. An important distinguishing characteristic of gastric homeostasis is adequate blood flow. In order to ensure that nutrients and oxygen are delivered to the stomach mucosa and that harmful metabolites are removed, NO and PGs are responsible for maintaining the proper perfusion to prevent tissue damage [15].

Helicobacter pylori infection and the use of NSAIDs are common risk factors that precede PUD and gastritis. Less common risk factors include, among other things, radiation therapy, Crohn's disease, severe sickness, alcoholism, smoking, cocaine, and autoimmune issues [16].

Helicobacter pylori: The duodenal side is better informed about the mechanisms by which the HP promotes the progression of PU than the gastric side [17]. H. pylori causes epithelial cell deterioration and destruction as well as an inflammatory response including neutrophils, lymphocytes, plasma cells, and macrophages inside the mucosal layer.

With little to no inflammation in the corpus, gastritis frequently gets worse in the antrum. H. pylori testing should be done on all patients who developed peptic ulcers [14]. The type of peptic ulcer that develops can be determined by sequencing hypo- or hyperchlorhydria in inflammation associated with H pylori infection [18, 19, 20].

NSAIDs induced ulcer: NSAIDs cause harm to the stomach and duodenal mucosa through two main mechanisms. On the one hand, these drugs act like weak, non-ionized acids that easily enter the mucous layer and the epithelial cells. The unique and very necessary result is the ability of the cyclooxygenase inhibitory enzyme to lower the intracellular prostaglandin content. Due to their intramucosal vasodilator effect, which preserves blood flow, they are important in preserving the integrity of the gastroduodenal mucosa function. They also stimulate local production of mucus and H₂CO₃, which promotes cell turnover and epithelization [21, 22]. NSAIDs are widely used to reduce pain and inflammation in a range of circumstances; nevertheless, some users report gastrointestinal adverse effects. Distinctive advance a lower degree of topical injury known as NSAID gastropathy, which manifests as mucosal erosions and hemorrhages. These numerous little erosions can be detected throughout the body, however they are typically found in the antrum [23]. Although there are both systemic and local ways whereby NSAIDs harm the gastroduodenal mucosa, the primary mechanism is thought to be the systemic suppression of prostaglandins generated from constitutively expressed cyclooxygenase 1 (COX-1). Decreased mucosal PG values are associated with reduced generation of mucus and H₂CO₃, inhibition of cell proliferation, and deescalated mucosal blood flow—all of which are essential for maintaining the integrity of the mucosa. NSAIDs cause mucosal damage to the cell by disabling mitochondrial oxidative phosphorylation and destroying mucus phospholipids or the cell membrane [24–27].

Stress and diet: Stress caused by significant health issues, such as those requiring treatment in an intensive care unit, is widely recognized as a precursor to peptic ulcers, sometimes known as stress ulcers [28]. Caffeine and coffee are widely believed to cause or worsen pain, although they don't seem to have as much of an impact [29]. Missing meals allows stomach acid to directly affect the lining of the stomach, creating irritation that ultimately leads to gastric ulcers. Abdominal pain that worsens with meals is a precursor to gastric ulcers [30].

Smoking and alcohol: Smoking and alcohol consumption are risk factors. Prolonged alcohol use disrupts stomach mucosal barriers by inhibiting COX 1 receptor enzymes, which reduce the release of prostaglandins that are cytoprotective. Smoking cigarettes causes the amount of circulating epidermal growth factor to decrease and increases the release of free radicals in the stomach mucosa [31].

TYPES OF ULCER

Peptic Ulcer

Peptic ulcer is a general word that refers to ulcers of the digestive tract in the stomach or duodenum. Previously, it was thought that stress and spicy foods caused this type of ulcer. However, current study has revealed that these are only the exacerbating variables. The causal agent is an infection with the bacterium H. pylori or a response to certain medications, such as nonsteroidal anti-inflammatory drugs. Peptic ulcer symptoms include weight loss, decreased appetite, bloating, nausea, and vomiting, as well as dark feces, which suggest gastrointestinal bleeding.

Aphthous Ulcers

Mouth ulcers are sores that form on the mouth's inner lining. Mouth ulcers are widespread and generally caused by trauma, such as ill-fitting dentures, shattered teeth, or fillings. Some of the most frequent causes of oral ulcers or sores are anemia, measles, viral infection, oral candidiasis, persistent infections, throat cancer, mouth cancer, and vitamin B deficiency. Aphthous minor is one of the most prevalent oral ulcerative illnesses, affecting around 15-20% of the global population. In certain communities, the incidence has been found to be as high as 50-66%, with North America being particularly frequent. Smokers had a reduced incidence of aphthous ulcers compared to nonsmokers. (32) (33)

Duodenal ulcers (DU)

DU is most frequent in young people and affects men more than women. "Kissing ulcers" can form on both the anterior and posterior borders of the duodenum. Patients with DU create more acids, especially at nighttime.

Gastric ulcers (GU): Gastric ulcers (GU) are more frequent in older adults, especially females. Although GU patients have normal or even reduced acid production, ulcers can form even in the absence of acid.

Stress ulcers (SU): Stress ulcers (SU) are stomach or duodenal ulcers that develop after a severe sickness or trauma, necessitating extensive treatment. Stress-related ulcers have a somewhat different etiology than typical peptic ulcers that include acid and mucosal ischemia.

NSAID induced ulcers

NSAIDs such as aspirin and indomethacin are known to cause stomach ulcers. Chronic NSAID users had a 2%-4% chance of having a symptomatic ulcer, GI bleeding, or perforation.

Recurrent oral ulceration.

Recurrent painful fibrin-covered ulcers are a frequent and problematic issue, especially in children and the elderly. It might be linked to vitamin B group deficits, iron insufficiency, or other dietary sensitivities. (34).

Name/Type	Cause/causative agent	Part affected	Major symptoms	Treatment
Peptic ulcer	H. Pyroli or allergens	digestive tract in the stomach or the duodenum	weight loss, poor appetite, bloating, nausea, and vomit and black stools that indicate gastrointestinal bleeding	Proton pump inhibitors (PPIs); H2-receptor antagonists; Antacids; Antibiotics
Aphthous Ulcers	Trauma :ill-fitting dentures, fractured teeth, or fillings, Anemia, measles,	Inner mouth linings	burning or tingling sensation, red bump, painful sores, Problems	Topical anesthetics, such as benzocaine; A doxycycline capsule of 100 mg in 10 mL of water

	viral infection, oral candidiasis, chronic infections, throat cancer, mouth cancer and vitamin B deficiency (35)		with chewing or tooth brushing	administered as a mouth rinse; or tetracycline 500 mg plus nicotinamide 500 mg administered 4 times daily
Duodenal ulcers	Helicobacter pylori (H. pylori); Nonsteroidal anti-inflammatory drugs (NSAIDs); Zollinger-Ellison syndrome, malignancy, vascular insufficiency, Smoking, alcohol, stress	Duodenum, parts of stomach	dull or burning pain, Feeling full, Burping, nausea, vomiting, not feeling hungry, losing weight without trying, bloody or black stool, vomiting blood (36)	Proton pump inhibitors (PPIs); H2-receptor antagonists; Antacids; Antibiotics
Gastric ulcers	Helicobacter pylori (H. pylori); Nonsteroidal anti-inflammatory drugs (NSAIDs)	Stomach	Sharp burning pain, nausea, Indigestion, heartburn, acid reflux, bloating, abdominal fullness, weight loss, and fatigue, Blood in vomit or stool	Proton pump inhibitors (PPIs); H2-receptor antagonists; Antacids; Antibiotics; Epinephrine injection
Stress ulcers	Stress/ Trauma	Stomach	shock, sepsis, trauma or other conditions and are found in patients with chronic illnesses	Medications; Enteral nutrition; Endoscopy; Angiography; Surgical treatment; Antibiotics
NSAIDS induced ulcers	Aspirin, indomethacin; Reduced prostaglandin secretion; Gastric epithelium irritation;	Gastrointestinal tract	burning pain in the abdomen; Feeling full or bloated after eating; Nausea and vomiting;	Selective COX-2 inhibitor monotherapy; Prostaglandin analogs; Proton pump inhibitors (PPIs); H2-receptor

	Reduced mucus production; Reduced blood flow		Indigestion; Belching; Loss of appetite; Weight loss (37)	antagonists; Antacids; Antibiotics
Recurrent oral ulceration	Genetic predisposition; Vitamin B12 deficiency; Trauma; Infections; Medications; Food intolerance; Stress; Immune system disorders	Lips; Cheeks; Tongue; Floor of the mouth; Back of the roof of the mouth; Around the tonsil area	pain or burning, followed in 1 to 2 days by a canker sore (38)	Topical agents; Mouthwashes; Systemic medications; Light therapy; Rinsing

Management of PUD

In patients with PUD, *Helicobacter pylori* should be eradicated. The goals of care are to alleviate ulcer pain, heal the ulcer, prevent ulcer recurrence, decrease ulcer-related complications, and eliminate *H. pylori* in *H. pylori*-positive patients.

Recent improvements in the treatment of Peptic Ulcer Disease (PUD) demonstrate a move toward more nuanced and individualized approaches. Traditional methods to *Helicobacter pylori* (*H. pylori*) eradication have developed, with customized regimens that recognize the varied landscape of antibiotic resistance (39). This move aims to improve treatment results and counteract the declining efficacy of traditional medicines. Vonoprazan, a new acid suppressor, is a significant advance. Vonoprazan, which inhibits stomach H⁺/K⁺-ATPase, has the potential to eradicate clarithromycin-resistant *H. pylori* strains. However, long-term use of acid suppressants, whether classic or new, brings possible adverse effects, including hypergastrinemia, pneumonia, bacterial overgrowth, and *C. difficile* infection, needing careful consideration in treatment planning. (40).

In the preventative area, current research into an *H. pylori* vaccination gives optimism for a groundbreaking discovery. While still in research, this vaccine has the potential to serve as a primary preventative tool, reducing the prevalence of *H. pylori* infection and its consequences (41). Furthermore, the search for new therapeutic routes has led to the study of natural compounds, including monoterpenes obtained from medicinal plants. These chemicals, with varied chemical compositions, possess anti-ulcer, healing, and antibacterial properties, position (42)

I. Non-pharmacologic Treatment

Eliminate or reduce psychological stress, reduce use of nonselective NSAIDs (including aspirin), use alternatives for pain relief such as acetaminophen or COX-2 selective inhibitors, quit smoking, restrict beverages and foods that antecedent dyspepsia or exacerbate ulcer symptoms, such as caffeine, spicy foods, alcohol, and emergency surgery for some patients with bleeding, perforation, or obstruction. (43).

a) Acupuncture

Acupuncture is being employed as a non-pharmacological therapy for peptic ulcers. Acupuncture is traditionally performed by penetrating the skin with solid metallic needles and then manually manipulating the needle (e.g., twisting, elevating, and thrusting). Acupuncture sites can also be stimulated with electro-acupuncture, which involves delivering electrical currents through an inserted needle to a specific acupuncture point at a set frequency and intensity. Compared to conventional acupuncture, electro-acupuncture offers a more objective, quantitative type of acupuncture.(44)

b) Electrical Stimulation/Modulation

Transcutaneous electrical stimulation of acupuncture sites, also known as transcutaneous electrical acustimulation (TEA), is a modern variation of electro-acupuncture that has been employed in the treatment of FD. TEA employs electrodes placed on the skin's surface to provide electrical stimulation. Electrodes on the skin's surface restrict the depth of penetration of electrical current. Compared to electro-acupuncture and traditional acupuncture, TEA is less intrusive, may be self-administered by the patient, and can be performed more frequently.(45,46.)

II. Pharmacological Treatment**a) Antacids:**

Transcutaneous electrical stimulation of acupuncture sites, also known as transcutaneous electrical acustimulation (TEA), is a modern variation of electro-acupuncture that has been employed in the treatment of FD. TEA employs electrodes placed on the skin's surface to provide electrical stimulation. Electrodes on the skin's surface restrict the depth of penetration of electrical current. Compared to electro-acupuncture and traditional acupuncture, TEA is less intrusive, may be self-administered by the patient, and can be performed more frequently.

b) Pyroloplasty and SPV:

Between 1964 and 1982, 1407 duodenal ulcers and 308 gastric ulcers were found at the Munich surgical clinic, with selective proximal vagotomy (SPV) and non-resulting technique, Pyroloplasty of function and shape, either open or submucous, and, when needed, ulcer excision. 11 days, 45 days, and yearly examinations with biopsy and endoscopy from the antrum and fundus, as well as preoperative and postoperative results, were accomplished over a period of 5-7 years. Reduction in basal acid production by 90% clinically demonstrated in 89% of patients, a 21% reduction in mucosal diameter postoperatively, 75% maximum acid output, and an increase in chief cell despite continuous chief cell. In 90% of patients, pain is relieved, weight is increased by 75%, dumping is 1.8%, diarrhea is 2%, recurrence in DU and GU is 7.3%, and death is 0.5%. Pyroloplasty and SPV can raise GU by up to 16% and DU by 10% in the stomach antrum, respectively. 7% have preoperative maximal GC, and stomach surgery has grown significantly in recent years. In GU or DU, no inflammation occurred prior to surgery, although it was found in fundus ventriculi. Instead of morphological alteration following a single therapy SPV with Pyroloplasty, acid secretion has been reduced for years. For four years, the recurrence probability of DU and GU was just 24%. It is not necessary to have pharmacological interaction. The SPV complication rate is zero (47).

c) **Anti-secretory Drugs and Other Interventions**

Antisecretory medications, particularly PPIs, are the cornerstone of medical therapy for PUD. These medications inhibit acid production, providing symptom relief and aiding in the healing process. Management may include calcium supplements to reduce the risk of bone fractures associated with long-term PPI usage. NSAID-induced PUD requires the withdrawal or dosage decrease of NSAIDs, and prostaglandin analogues such as misoprostol may be used as prophylactic (48).

d) **H. pylori-Induced PUD Treatment**

The first-line therapy for H. pylori-induced ulcers is a triple regimen that includes two antibiotics and a PPI. Antibiotic selection takes antimicrobial resistance into account. If the first treatment fails, a quadruple therapy with bismuth and other antibiotics is initiated. (49).

- **Standard Triple Therapy**

A 7- to 10-day triple treatment regimen including a PPI, amoxicillin 1 g, and clarithromycin 500 mg twice daily has long been the first-line therapy for Helicobacter pylori eradication. The first line of treatment for H. pylori eradication is a PPI, clarithromycin, and amoxicillin or metronidazole (for PCN-allergic individuals) for 7 to 14 days. PPI-based triple therapy for 10 to 14 days: PPI once/bid + clarithromycin 500 mg bid + amoxicillin 1 g bid or metronidazole 500 mg bid; primary management of choice for eradicating H. pylori; metronidazole should be substituted for amoxicillin only in penicillin (PCN) allergic individuals because metronidazole resistance is common. PPI should be taken 30-60 minutes before a meal, along with the two antibiotics.

The regimens include: (a) PPI in regular dosage + clarithromycin 500 mg + amoxicillin 1000 mg, each given twice daily; (b) PPI in standard dose + clarithromycin 500 mg + metronidazole 400 mg, each given twice daily. (c) Ranitidine bismuth citrate (RBC) 400 mg + clarithromycin 500 mg + amoxicillin 1000 mg, twice daily; (d) RBC 400 mg + clarithromycin 500 + metronidazole 400 mg, twice daily. Each of the foregoing regimens should be administered for seven days (50). Rifabutin triple treatment includes PPI (normal dosage twice daily), amoxicillin (1 g twice daily), and rifabutin (150-300 mg/day) for 10 days. (51)

- **Sequential Therapy**

Sequential treatment is another type of quadruple therapy that involves a 5-day dual therapy with a PPI and amoxicillin, followed by a 5-day triple therapy with a PPI, clarithromycin, and tinidazole or metronidazole. Hybrid quadruple treatments comprise 10-14 days of dual therapy with PPI and amoxicillin and 7 days of clarithromycin and metronidazole.

Sequential therapy: PPI (normal dosage twice daily) + amoxicillin (1 g twice daily) for 5 days, then PPI (standard dose twice daily) + clarithromycin (500mg twice daily) + tinidazole (500mg twice daily) for 5 days. Levofloxacin triple therapy: PPI (normal dosage twice daily), amoxicillin (1g twice daily), and levofloxacin (500mg twice daily) for ten days. (52) (53)

- **Bismuth-Based Quadruple Therapy**

This is the conventional quadruple regimen, which includes a bismuth salt (subsalicylate 525 mg or subnitrate potassium 420 mg), metronidazole 250 mg, and tetracycline 375 to 500 mg, all used four times daily, in addition to a PPI administered twice a day. The regimen is typically administered for 10 to 14 days. The standard first-line treatment is either a bismuth-

containing quadruple therapy (PPI, a bismuth salt, tetracycline, and metronidazole) or a nonbismuth-based quadruple concomitant therapy (PPI, clarithromycin, amoxicillin, and metronidazole) for 14 days; both regimens have an extermination rate of more than 90%. Quadruple therapy: PPI or H2RA once or twice daily with bismuth subsalicylate 525 mg qid + metronidazole 250-500 mg qid + tetracycline 500 mg qid is an alternate first-line eradication therapy for PCN allergic patients and is sometimes retained as a second-line therapy following treatment failure with the PPI-based regimen. All drugs, except PPI, should be taken with meals and before bedtime for 10 days (54).

- **Levofloxacin-Based Triple Therapy**

This 10-day treatment includes a PPI, 1 g of amoxicillin twice daily, and 500 mg of levofloxacin once daily. It should be reserved for second-line treatment and is better tolerated than bismuth-based quadruple therapy (55)

- e) **Endoscopy and endoscopic therapy**

Dual treatment, which includes adrenaline/epinephrine infiltration and either thermal coagulation with a bipolar probe or mechanical haemostasis with endoclips, is still considered the best endoscopic therapy by major standards (56). Three key recent breakthroughs in endoscopy include Doppler probe-guided lesion evaluation and therapy, big over-the-scope clips, and haemostatic powders.

Doppler probe examination to identify substantial artery signals in the ulcer base has been documented many years ago. Doppler probe evaluation is more accurate than conventional endoscopic score in predicting rebleeding risks (57), and a randomized experiment found that Doppler probe-guided therapy lowers rebleeding and subsequent intervention when compared to standard treatment. Doppler analysis revealed that many oozing ulcers (Forrest 1b) are not connected with considerable arterial flow into the ulcer (only 46.7% displayed a positive Doppler signal) and had a lower rebleeding rate than previously thought. The incidence of Doppler-positive arterial flow in oozing ulcers is really much lower than the prevalence of positive Doppler signals for active arterial bleeding (100%), non-bleeding visible vessels (Forrest 2a, 90.7%), and those with adhering clot (Forrest 2b, 68.4%). (58)

Haemostatic powders occupy a similar role. There are currently many powders commercially pushed in various geographical places, the first of which is Hemospray (Cook Medical, Bloomington, IN, USA), but others are also available, but they have not yet been FDA-approved for usage in the US. These are patented mineral formulations that, when sprayed into a bleeding spot via a cannula put into the channel of an endoscope, cause fast haemostasis. The powder works as both a physical barrier when in contact with moisture and a potent procoagulant by concentrating clotting components at the point of application.(59).(60)

- f) **Surgical Interventions**

The following surgeries are performed for ulcers with varied localizations:

1. Pyloroplasty is recommended for ulcers in the antral region that are aggravated by severe stenosis of the pyloric sphincter or scarring of the gatekeeper. The procedure entails longitudinally opening the bacciform section, excision of the gatekeeper region, and suturing the ends transversely or longitudinally in the shape of an open T or an inverted U, reinforced by a circular myotomy.

2. In the absence of significant post-ulcer scar alterations, it is recommended to exclude the Magen-Den Fa and build an adhesive pyloroplasty for gastro-jejunal anastomosis ulcers that are refractory to conservative care. After opening the bacciform part, a jejunum is mobilized from the mesentery, the wound is sutured longitudinally, the Magen-Den channel is sutured in such a way that the festering channel is sutured antiperistaltic, and the two layers of suturing are sewn between the rows of sections with the jejunum of the looped loop. Following transplant healing, tension builds, preventing the formation of a new ulcer. In certain circumstances, a similar procedure is performed on the afferent jejunum in conjunction with anastomosis between the afferent and recurrent jejuna. This approach has some contraindications and is not appropriate for all individuals. Palliative surgeries are expected to give way to more drastic ones as blood flow to the stomach improves in the future, due to advances in plastic surgery. (61) (62)

Treatment	Comment	Options
		Omeprazole (Prilosec) 20 mg two times daily or lansoprazole (Prevacid) 30 mg two times daily plus amoxicillin 1 g two times daily or metronidazole (Flagyl) 500 mg two times daily (if allergic to penicillin) plus clarithromycin (Biaxin) 500 mg two times daily (63)
	Treatment duration is 10 to 14 days (although courses lasting one to seven days have been reported to have comparable effectiveness (64, 65)	Ranitidine bismuth citrate (Tritec)* 400 mg two times daily plus clarithromycin 500 mg two times daily or metronidazole 500 mg two times daily plus tetracycline 500 mg two times daily or amoxicillin 1 g two times daily Levofloxacin (Levaquin) 500 mg daily
Eradication of Helicobacter pylori	Eradication rates 80 to 90 percent or higher (66, 67)	Levofloxacin (Levaquin) 500 mg daily plus amoxicillin 1 g two times daily plus pantoprazole (Protonix) 40 mg two times daily Bismuth subsalicylate (Pepto-Bismol) 525 mg (two tablets) four times daily

		plus metronidazole 250 mg four times daily plus tetracycline 500 mg four times daily plus H2 blocker for 28 days or proton pump inhibitor for 14 days
Histamine H2 blockers	70 to 80 percent healing in duodenal ulcer after four weeks, 87 to 94 percent after eight weeks (68)	Ranitidine (Zantac) 150 mg two times daily or 300 mg at night Famotidine (Pepcid) 20 mg two times daily or 40 mg at night Cimetidine (Tagamet) 400 mg two times daily or 800 mg at night
Proton pump inhibitors	Treatment duration is four weeks for duodenal ulcer and eight weeks for gastric ulcer 80 to 100 percent healing (69)	Omeprazole 20 mg daily Lansoprazole 15 mg daily Rabeprazole (Aciphex) 20 mg daily Pantoprazole 40 mg daily
Sucralfate (Carafate)	Treatment duration is four weeks blockers Effectiveness similar to H2 (70)	1 g four times daily
Surgery	Rarely needed	Duodenal ulcer: truncal vagotomy, selective vagotomy, highly selective vagotomy, partial gastrectomy (71, 72)

Conclusion:

Peptic ulcer disease was once quite widespread; however, it is now less prevalent in high-income nations. It is frequently linked to H.pylori infection or prolonged use of NSAIDs. In the event of H.pylori infection, we often utilize triple or quadruple therapy: a PPI and two antibiotics with or without bismuth sulfate. In the case of NSAIDs, PPI can be added with them or discontinued. The complication of peptic ulcer illness is exceedingly hazardous and prevalent, and it requires immediate care, either surgical or medicinal, to save the patient's life.

A combination of non-pharmacological and pharmacological treatments, including traditional anti-gastric ulcer medications, may have a synergistic impact against H. pylori and gastric ulcer disease, improving patient outcomes.

With just a few human investigations, it is recommended that more clinical trials with bigger sample sizes be conducted to determine the effectiveness and safety of medicinal plants with antiulcer activity. It would also be good to conduct research to examine and clarify the mechanisms of action of medicinal plants used to cure or prevent peptic ulcers.

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