Case Report

The Annals of Internal Medicine (ISSN 3064-6650)

Proton-Pump Inhibitors In PUD: A Mini Review.

Bansari Parikh[1], Shuchi Shukla[1], Dr. Jayesh Trivedi*

[1]PharmD 6th Year Interns, Sal Hospital, Ahmedabad, Gujarat
Email Id: *parikhbansari23@gmail.com*

Corresponding author

Dr. Jayesh Trivedi ,
Professor of Medicine and Medical Superintendent, SAL Institute of Medical Sciences, Ahmedabad, Gujarat.
Email : drjvtrivedi@rediffmail.com

Received Date : December 30, 2024
Accepted Date : December 31, 2024
Published Date : February 01, 2025

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ABSTRACT

Peptic ulcer disease (PUD) is a prevalent gastrointestinal disorder primarily caused by Helicobacter pylori infection and the overproduction of gastric acid. Proton pump inhibitors (PPIs), such as omeprazole, esomeprazole, and pantoprazole, are first-line treatments, offering effective acid suppression, ulcer healing, and symptom relief. Despite their effectiveness, long-term PPI use is associated with risks like nutrient deficiencies, infections, and renal complications. Recent advancements, including dual delayed-release PPIs and potassium-competitive acid blockers, provide potential improvements in treatment efficacy and safety. This review highlights the pivotal role of PPIs in PUD management and underscores the need for careful monitoring and appropriate use to mitigate adverse effects.

INTRODUCTION

Peptic ulcer disease (PUD) is a prevalent gastrointestinal condition that results from an imbalance between aggressive factors such as gastric acid and Helicobacter pylori infection, and the protective mechanisms of the gastric mucosa. The management of PUD commonly involves the use of proton pump inhibitors (PPIs), which are highly effective in reducing gastric acid secretion, promoting ulcer healing, and providing symptomatic relief. PPIs, such as omeprazole, esomeprazole, and pantoprazole, have become the mainstay of treatment for both gastric and duodenal ulcers and are particularly useful in preventing complications such as rebleeding in complicated ulcer disease [1][2].

PPIs irreversibly inhibit the H+/K+ ATPase pump in the stomach's parietal cells, significantly reducing gastric acid production. The efficacy of PPIs in treating PUD has been extensively studied, with results indicating that PPIs accelerate ulcer healing and offer superior symptomatic relief compared to other treatments [3]. In addition to their use in monotherapy, PPIs are also critical in combination regimens, particularly for eradicating H. pylori, a leading cause of PUD [4].

However, concerns about the long-term use of PPIs have emerged due to potential adverse effects, including nutrient deficiencies (e.g., vitamin B12, magnesium), increased fracture risk, and gastric atrophy [5]. Despite these risks, PPIs remain essential in managing PUD, especially in patients at high risk for complications or those who do not respond to other therapies [1]. This mini-review aims to evaluate the role of PPIs in PUD treatment, focusing on their clinical efficacy, safety considerations, and recommendations for optimal use.

DISCUSSION

What is Peptic Ulcer Disease (PUD)?

Peptic ulcer disease (PUD) is a condition characterized by localized mucosal damage in the stomach (gastric ulcer) or the proximal duodenum (duodenal ulcer), resulting from the corrosive effects of gastric acid and pepsin. The disease occurs due to an imbalance between aggressive factors, such as acid secretion and Helicobacter pylori (H. pylori) infection, and the protective mechanisms of the gastric mucosa [1,4].

PUD affects 4-10% of the global population, with declining rates in developed nations but persistently high rates in Asia, Africa, and Latin America [9]. In India, the prevalence of duodenal ulcers is higher than gastric ulcers, particularly in younger individuals, while gastric ulcers are more common in the elderly. H. pylori is implicated in over 80% of cases. [8].

Etiology and Contributing Factors

1. H. pylori Infection: The primary global cause of PUD, with virulence factors like urease and cytotoxins causing mucosal inflammation and ulceration, especially in developing nations [4].
2. NSAID Use: Chronic NSAID use inhibits cyclooxygenase enzymes, reducing prostaglandin synthesis and impairing mucosal protection [1].
3. Lifestyle Factors: Smoking, alcohol, and poor diet exacerbate PUD risk, though less significantly than H.

The Annals of Internal Medicine (ISSN 3064-6650)

pylori and NSAID use [6].

4. Hypersecretory Conditions: Zollinger-Ellison syndrome, caused by gastrin-secreting tumors, leads to excessive acid production and severe ulceration [7].
5. Other Factors: Genetic predisposition, psychological stress, and non-H. pylori infections contribute to PUD [2].

Epidemiology

PUD prevalence has decreased in developed countries due to better sanitation, reduced H. pylori transmission, and PPI use. However, it remains prevalent in developing countries with high H. pylori infection rates [1,4]. In India, H. pylori infection affects 50-90% of the population, especially in rural areas [7].

Pathophysiology

1. Aggressive Factors: Excess gastric acid and pepsin activity contribute to ulcer formation, worsened by H. pylori's effect on gastrin secretion [1, 2].
2. Impaired Mucosal Defense: Reduced mucus, bicarbonate, and blood flow weakens the mucosal barrier [7].
3. Inflammation: H. pylori and NSAIDs trigger local inflammation, leading to further mucosal injury [4].

PPI in Gastric Ulcers

Proton pump inhibitors (PPIs) are the first-line treatment for gastric ulcers, effectively suppressing gastric acid by inhibiting the H+/K+ ATPase enzyme. [8]

Omeprazole (20–40 mg daily) is commonly preferred for its availability and efficacy. Other PPIs, such as esomeprazole, pantoprazole, and rabeprazole, offer similar healing rates (~90–95% within 4–8 weeks) at standard doses. All PPIs provide comparable results, with esomeprazole offering prolonged acid suppression in severe cases. [9]

PPIs in Duodenal Ulcers

PPIs are highly effective in healing duodenal ulcers by suppressing gastric acid secretion. Standard treatment involves omeprazole (20–40 mg), esomeprazole (20–40 mg), pantoprazole (40 mg), or rabeprazole (20 mg) daily for 2–4 weeks. Healing rates are approximately 90–100%, with symptom relief often occurring within days. PPIs are superior to H2 blockers in promoting rapid healing and reducing relapse rates [10].

PPIs in H. pylori Eradication

For H. pylori-associated ulcers, PPIs are used in triple therapy to eradicate the infection and promote healing. A typical regimen includes a PPI (e.g., esomeprazole 20 mg twice daily) combined with clarithromycin and amoxicillin or metronidazole for 7–14 days. This approach improves eradication rates and significantly lowers the risk of recurrence. Quadruple therapy may be used for resistant strains, incorporating a PPI, bismuth subsalicylate, and two antibiotics [11].

PPIs in NSAID-Induced Ulcers

Chronic NSAID use impairs mucosal defense, leading to ulcers. PPIs like esomeprazole (20–40 mg daily) or pantoprazole (40 mg daily) are effective in both treatment and prevention. Studies show 80–90% healing rates within 4–8 weeks. PPIs also reduce gastrointestinal symptoms and prevent recurrence in patients requiring ongoing NSAID therapy. Co-prescription with NSAIDs is recommended for high-risk patients [12].

PPIs in Stress-Induced Ulcers

Stress-related mucosal damage in critically ill patients can result in upper gastrointestinal bleeding. PPIs are used prophylactically to suppress gastric acid secretion and reduce the risk of ulcer formation. Both intravenous and oral PPIs (e.g., pantoprazole 40 mg or esomeprazole 40 mg daily) are effective. Prophylaxis is typically recommended in patients with risk factors such as mechanical ventilation or coagulopathy [13].

Safety use of PPIs

Proton pump inhibitors (PPIs) are effective for short-term treatment of conditions like peptic ulcer disease and GERD, but prolonged use (beyond 8 weeks) may lead to risks. Long-term PPI use has been associated with nutrient deficiencies, particularly in magnesium, calcium, and vitamin B12, increasing the risk of fractures and other complications [14]. Additionally, PPIs reduce stomach acid, elevating the risk of gastrointestinal infections such as Clostridium difficile and pneumonia [15]. Prolonged PPI therapy is also linked to an increased risk of chronic kidney disease and acute kidney injury, especially in individuals with pre-existing renal conditions [16]. Furthermore, some studies suggest that long-term PPI use, particularly after H. pylori infection, may raise the risk of gastric cancer . Despite these potential risks, PPIs remain a safe and effective treatment when used appropriately, and regular reassessment of long-term therapy is essential, especially for high-risk patients.

Newer Advancements in PPIs

Recent advancements in proton pump inhibitors (PPIs) include novel formulations like dual delayed-release PPIs, such as dexlansoprazole, which offer extended acid suppression with once-daily dosing [17]. Efforts are also underway to minimize long-term side effects, including fewer drug interactions and reduced risk of nutrient deficiencies [18]. Additionally, more targeted delivery systems, such as enteric-coated PPIs, aim to improve drug stability and absorption in patients with gastric motility issues [19]. Research into PPI-resistance and

The Annals of Internal Medicine (ISSN 3064-6650)

the development of potassium-competitive acid blockers (P-CABs) are providing promising alternatives for refractory conditions [20].

CONCLUSION

In summary, proton pump inhibitors (PPIs) are fundamental in the management of peptic ulcer disease (PUD), effectively promoting ulcer healing, alleviating symptoms, and addressing complications linked to H. pylori infection, NSAID use, and stress-induced ulcers. While PPIs are generally well-tolerated, their long-term use raises concerns regarding nutrient deficiencies, gastrointestinal infections, and renal risks. Recent innovations, such as dual delayed-release formulations and potassium-competitive acid blockers, offer promising enhancements in both efficacy and safety profiles. Proper usage, combined with ongoing patient monitoring, is crucial to optimize therapeutic outcomes and minimize potential adverse effects.

Acknowledgements
We would like to thank Dr. Jayesh Trivedi, SAL Hospital, for providing us his guidance and support to conduct this review.
Conflict of Interest: Nil
Financial Support: Nil

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