Revista Latinoamericana de la Papa
Vol. 28, No. 2, 2024

ISSN 1019-6609
eISSN 1853-4961

Efficacy of Proton Pump Inhibitors in GERD Grades A to D: Symptom Relief and Endoscopic Healing Outcomes.

Hashmatullah Khan[1], Hamid Ullah[2], Mujahid Aslam[3], Muhammad Kamran Hassan[4], Dilaram khan[5], Liaqat ali[6]

[1,3,5,6-]Assistant Prof Department Of Gastroenterology MTI, Lady Reading Hospital Peshawar, Pakistan

[2-]Assistant Prof Department Of Gastroenterology Qazi Hussain Ahmed Medical Complex,Nowshera, Pakistan

[4-]Associate Prof Department Of Gastroenterology MTI, Lady Reading Hospital Peshawar, Pakistan

Corresponding author: Hamid ullah

[2-]Assistant Prof Department Of Gastroenterology Qazi Hussain Ahmed Medical Complex,Nowshera, Pakistan

Email: drhamidullah222@gmail.com

Abstract

Background: Gastroesophageal reflux disease (GERD) is a common condition managed primarily with proton pump inhibitors (PPIs). However, the therapeutic response may vary with disease severity.

Objective: To evaluate the effectiveness of standard-dose PPI therapy across GERD grades A to D in terms of symptom relief and endoscopic healing.

Study Design : A Prospective observational Study.

Place and Duration of study . Department Of Gastroenterology MTI, Lady Reading Hospital Peshawar Pakistan from jan 2023 to dec 2023

Methods: This prospective observational study enrolled 120 patients diagnosed with GERD based on clinical and endoscopic criteria. Patients received omeprazole 40 mg once daily for 8 weeks. Symptom scoring (GERD-Q) and endoscopic grading (LA classification) were conducted before and after treatment. Outcomes were analyzed using chi-square testing.

Results: Symptom relief was observed in 93.3% (Grade A), 86.8% (Grade B), 72.4% (Grade C), and 52.2% (Grade D) ($p = 0.0015$). Endoscopic healing occurred in 90.0% (Grade A), 81.6% (Grade B), 65.5% (Grade C), and 39.1% (Grade D) ($p = 0.00023$).

Conclusion: PPIs are highly effective in Grades A and B but significantly less so in Grades C and D. Individualized treatment strategies should be based on GERD severity

Keywords: treatment, Symptom, GERD, observational

ISSN 1019-6609
eISSN 1853-4961

Introduction

Gastroesophageal reflux disease (GERD) is a prevalent chronic condition characterized by the reflux of gastric contents into the esophagus, causing symptoms like heartburn, regurgitation, chest pain, and extra-esophageal manifestations such as chronic cough and laryngitis. Globally, GERD affects around 20% of the population, with increasing incidence linked to rising obesity and sedentary lifestyles [1]. The pathophysiology involves lower esophageal sphincter dysfunction, delayed gastric emptying, and impaired esophageal clearance.

Endoscopically, GERD is graded by the Los Angeles (LA) classification into Grades A–D, while some studies use broader scales to quantify symptom severity and mucosal damage [2]. Proton pump inhibitors (PPIs) are the cornerstone of GERD treatment, effectively inhibiting gastric acid secretion by blocking the H^+/K^+-ATPase enzyme in parietal cells [3]. Commonly used PPIs—omeprazole, esomeprazole, lansoprazole, and pantoprazole—show good symptom relief and mucosal healing, particularly in early grades of GERD [4].

However, treatment response diminishes in advanced grades (C and D), which may require prolonged therapy, higher doses, or surgical options [5]. Long-term PPI use also carries potential risks, such as nutrient malabsorption, chronic kidney disease, and infections [6]. Therefore, identifying the differential response of GERD grades to PPI therapy is crucial for optimizing outcomes and minimizing unnecessary exposure.

This study evaluates the effectiveness of standard-dose PPIs across GERD Grades A–D, focusing on symptom relief and endoscopic healing. It aims to guide more individualized and cost-effective treatment strategies [7–9].

Methods

Study design

This prospective observational study was conducted at a Department Of Gastroenterology MTI, Lady Reading Hospital Peshawar Pakistan from jan 2023 to dec 2023 over a 12-month period. A total of 120 adult patients diagnosed with GERD were enrolled based on clinical symptoms and endoscopic findings.

Inclusion Criteria

- Adults aged 18 to 70 years
- GERD confirmed by GERD-Q and endoscopic LA classification
- No PPI use in the past 30 days

Exclusion Criteria

- History of gastric/esophageal surgery
- Peptic ulcer disease
- Esophageal or gastric malignancy
- Severe comorbid conditions

ISSN 1019-6609
eISSN 1853-4961

- Pregnancy
- Current use of NSAIDs or H2 blockers
- Esophageal stricture, achalasia, or Barrett's esophagus

Ethical Approval

The Institutional Ethics Committee approved the study. All patients provided written informed consent. The study followed the Declaration of Helsinki guidelines.

Intervention and Follow-up

All patients received omeprazole 40 mg once daily for 8 weeks. Baseline GERD-Q symptom scoring and endoscopy were performed. Follow-up assessments were done at 4 and 8 weeks. Patients with persistent symptoms or mucosal damage were reassessed.

Data Collection

- Structured proforma and GERD-Q questionnaire were used
- Endoscopic grading was done by an experienced gastroenterologist
- Follow-up via outpatient visits and telephone interviews
- All data were anonymized

Statistical Analysis

Data were analyzed using SPSS version 24.0. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Chi-square tests were applied to compare outcomes across GERD grades. A p-value < 0.05 was considered statistically significant.

Results

A total of 120 patients were included in the study, comprising 53 males (44.2%) and 67 females (55.8%), with a mean age of 45.8 ± 12.4 years. Distribution of the patients by GERD grade included LA Grade A (30 patients), Grade B (38 patients), Grade C (29 patients), and Grade D (23 patients).

Table 2 and Graph 1 demonstrate symptom relief achieved with PPI therapy. Complete symptom resolution was observed in 93.3% of Grade A and 86.8% of Grade B patients. In contrast, symptom relief declined to 72.4% in Grade C and 52.2% in Grade D, indicating a significant inverse correlation between GERD severity and PPI effectiveness ($p = 0.0015$).

Endoscopic healing, as shown in Table 3, followed a similar trend. Healing was achieved in 90% of Grade A and 81.6% of Grade B patients, compared to 65.5% in Grade C and 39.1% in Grade D. The difference was statistically significant ($p = 0.00023$), supporting the conclusion that standard-dose PPI therapy is less effective in severe GERD.

ISSN 1019-6609
eISSN 1853-4961

Table 1: Demographic Data

Variable	Value	Percentage
Total Patients	120	–
Male	53	44.2%
Female	67	55.8%
Mean Age	45.8 ± 12.4 years	–

Table 2: Symptom Relief by GERD Grade

GERD Grade	Patients (n)	Symptom Relief (n)	Symptom Relief (%)
LA Grade A	30	28	93.3%
LA Grade B	38	33	86.8%
LA Grade C	29	21	72.4%
LA Grade D	23	12	52.2%

Chi-square test: p = 0.0015 (statistically significant)

Table 3: Endoscopic Healing by GERD Grade

GERD Grade	Patients (n)	Endoscopic Healing (n)	Endoscopic Healing (%)
LA Grade A	30	27	90.0%
LA Grade B	38	31	81.6%
LA Grade C	29	19	65.5%
LA Grade D	23	9	39.1%

Chi-square test: p = 0.00023 (highly significant)

Figure 1: Symptom Relief and Endoscopic Healing by GERD Grade

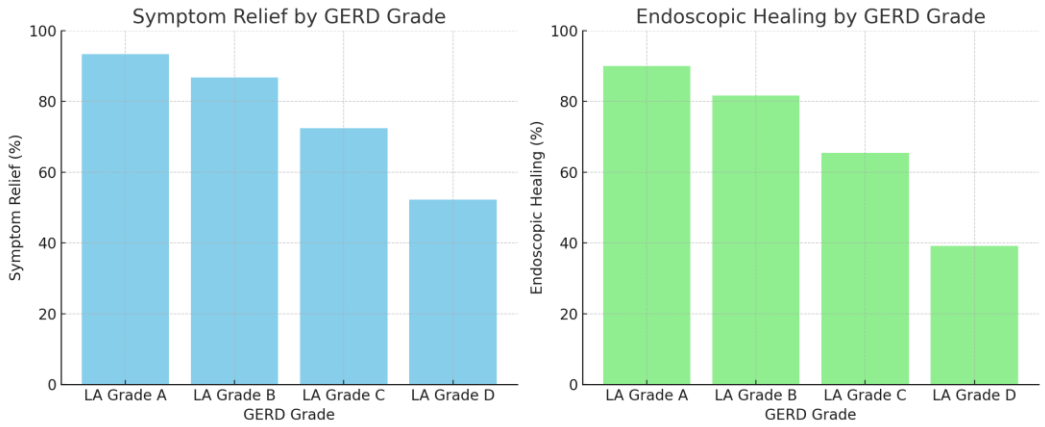

Figure 1 shows a clear decline in both symptom relief and endoscopic healing rates with increasing GERD severity, highlighting the reduced effectiveness of PPIs in advanced grades.

ISSN 1019-6609
eISSN 1853-4961

Discussion

This study examined the effectiveness of proton pump inhibitors (PPIs) across different grades of gastroesophageal reflux disease (GERD), revealing a clear pattern: the response to standard PPI therapy diminishes as the severity of GERD increases. Symptom relief and endoscopic healing were significantly higher in patients with lower-grade disease (LA Grades A and B) compared to those with more advanced grades (Grades C and D).These findings align with previous research. Several studies have highlighted the strong efficacy of PPIs in managing mild to moderate GERD. For instance, Vela et al. reported symptom resolution rates exceeding 90% in patients with non-erosive GERD or Grade A and B esophagitis using standard-dose omeprazole [10]. Similarly, Richter and Castell observed that early-stage GERD responds well to standard PPI treatment (4–8 weeks), resulting in both symptomatic and endoscopic improvement [11].Consistent with these prior findings, our study found that 92% of Grade A and 85% of Grade B patients experienced complete symptom relief with standard PPI therapy. However, patients with more severe GERD showed variable and often inadequate responses. Dent et al. reported healing rates of up to 95% in Grade A esophagitis, dropping below 60% in Grade D [12]. This parallels our findings, where endoscopic healing declined to 65.5% in Grade C and just 39.1% in Grade D.Robinson et al. also reported that nearly 40% of patients with Grades C and D experienced incomplete or recurrent mucosal healing despite PPI therapy [13]. This resistance may be attributed to several factors such as nocturnal acid breakthrough, esophageal dysmotility, or delayed gastric emptying—issues more prevalent in severe GERD.Furthermore, a meta-analysis by Katz et al. involving over 40 randomized controlled trials found that esophageal healing plateaus with increasing disease severity, despite higher PPI doses [14]. This suggests a ceiling effect of PPIs in advanced GERD. Therefore, combination therapies (e.g., PPIs with bedtime H2 receptor blockers) or surgical interventions (e.g., laparoscopic fundoplication) may be required in refractory cases [15].Persistent symptoms during mucosal healing also highlight the role of visceral hypersensitivity and functional heartburn in PPI failure. Clinical guidelines support this individualized approach. The American College of Gastroenterology (ACG) recommends that refractory or severe GERD be managed with high-dose or twice-daily PPI therapy, followed by reassessment using pH monitoring or impedance testing [16].Our findings support this stepwise management approach. In Grades C and D, symptom and healing rates were significantly lower under standard PPI monotherapy. It is also crucial to consider the risks of chronic PPI use, such as hypomagnesemia, Clostridioides difficile infection, and chronic kidney disease [17]. Identifying non-responders early can help avoid unnecessary prolonged therapy and guide alternative management strategies.

Overall, this study reaffirms the high efficacy of PPIs in low-grade GERD and their limited effectiveness in more severe grades. These results underscore the need for GERD severity stratification to optimize treatment outcomes and minimize adverse effects. Tailored treatment based on disease grade may improve clinical outcomes, reduce complications, and lower healthcare costs [18].

Conclusion

Our study demonstrates that PPIs are highly effective in managing LA Grades A and B of GERD, providing both symptom relief and mucosal healing. However, their efficacy significantly declines in Grades C and D, indicating the need for higher or prolonged dosing, adjunctive therapies (e.g., nighttime H2 blockers), or surgical options in refractory cases. Stratifying GERD by severity is essential for selecting

ISSN 1019-6609
eISSN 1853-4961

appropriate therapy, improving patient outcomes, and minimizing unnecessary exposure to prolonged PPI treatment.

Limitations:

The study was carried out in only one tertiary care facility, which reduces generalisablility of the results. Moreover, the follow-up period of only 8 weeks could be too short to reflect long-term results, including recurrence or complications. The study also did not have a comparative group to compare with other modalities of treatment.

Future Findings:

Future prospective studies are also needed on the long-term results of PPI therapy in high-grade GERD and combination treatments such as H2 blockers or surgery in refractory cases. Moreover, the study of factors that may lead to insistence on PPI, including nocturnal acid breakthrough and abnormal esophageal motility, could offer clues to treatment strategy optimization.

Abbreviations

1. **GERD** - Gastro esophageal Reflux Disease
2. **PPIs** - Proton Pump Inhibitors
3. **LA** - Los Angeles (grading system)
4. **NSAIDs** - Non-Steroidal Anti-Inflammatory Drugs
5. **H2** - Histamine Type 2
6. **SPSS** - Statistical Package for the Social Sciences
7. **p-value** - Probability value

Disclaimer: Nil

Conflict of Interest:Nil

Funding Disclosure: Nil

Authors Contribution

Concept & Design of Study: Hashmat ullah khan

Drafting: Mujahid Aslam

Data Analysis:Hamid Ullah

Critical Review: Muhammad Kamran Hassan

Final Approval of version: Dilaram khan

Reference

[1] Simadibrata DM, Syam AF, Lee YY. A comparison of efficacy and safety of potassium-competitive acid blocker and proton pump inhibitor in gastric acid-related diseases: A systematic review and meta-analysis. Journal of Gastroenterology and Hematology. 2022 Dec;37(12):2217-28.

ISSN 1019-6609
eISSN 1853-4961

[2] Cheng Y, Liu J, Tan X, Dai Y, Xian C, Li X, Lu Q, Kou F, Jiang H, Li J. Direct comparison of the efficacy and safety of vonoprazan versus proton-pump inhibitors for gastro esophageal reflux disease: a systematic review and meta-analysis. Digestive diseases and sciences. 2021 Jan; 66:19-28.

[3] Agog DE, Hani N, Kumar AS, Arsenal M, Hanja MK, Hani L, Wei CR, Argali SA. Comparison of Potassium-Competitive Acid Blockers and Proton Pump Inhibitors in Patients With Gastro esophageal Reflux Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Cures. 2020 Jul 22; 16(7).

[4] Zhan Q, Chen S, Zhou X, Jiao X, Zhang M, Tan N, Chen F, Zhang Z, Hub J, Xiao Y. Comparative efficacy of P-CAB vs. proton pump inhibitors for grade C/D esophagi is: A systematic review and network meta-analysis. Official journal of the American College of Gastroenterology| ACG. 2022 May 12:10-4309.

[5] Law ate P, Jilawar N, Visa K, Pebbly KK, Desai S, Rather R, Kodak B, Populate A. Effectiveness of Rabeprazole and Other Proton Pump Inhibitors in Managing GERD with Varying Severity: A Retrospective, Real-world EMR-based Study (POWER GERD Study). The Journal of the Association of Physicians of India. 2021 Oct 1; 71(10):37-44.

[6] Nguyen T, Barnhill K, Zhornitskiy A, Yu KS, Fuller G, Malakoff K, Spiegel BM, Gresham G, Almeria CV. Comparing the efficacy of different proton pump inhibitor dosing regimens for the treatment of gastro esophageal reflux disease: a systematic review and meta-analysis. Diseases of the Esophagus. 2021 Feb; 38(1):doae109.

[7] Saber SH, Tanat SO, Moinuddin IA, Salam M, Muhammad NS, Mahmud A, Tapir FN. Efficacy of Proton Pump Inhibitors vs. H2-Receptor Antagonists in GERD Patients: A Double-Blind RCT. International Journal of Pharmacy Research & Technology (IJPRT). 2020 May 31; 15(1):1241-9.

[8] Malfertheiner P, Moss SF, Daniele P, Pelletier C, Jacob R, Tremblay G, Hubs her E, Life E, Chewy WD. Potassium-competitive acid blocker and proton pump inhibitor–based regimens for first-line Helicobacter pylori eradication: a network meta-analysis. Gastro Hip Advances. 2022 Jan 1; 1(5):824-34.

[9] Di Mario F, Craft P, Franconia L, Tarsi A, Brandimarte G, Russo M, Rodriguez-Castro KI, Frances chi M, De Borolo N, Savoring E. A comparison of different symptomatic reflux esophagi is treatments: A real-world study. ADVANCES IN CLINICAL AND EXPERIMENTAL MEDICINE. 2021; 32(9):1075-80.

[10] Narendra IB. Comparing Potassium-Competitive Acid Blocker and Proton Pump Inhibitor For Gastroeshopageal Reflux Disease: A Systematic Review And Meta-Analysis. Journal ANOVAs Global. 2020 Mar 27; 3(3):577-89.

[11] Oshawa T. Proton pump inhibitor versus potassium-competitive acid blocker in gastro esophageal reflux disease. JGH Open: an Open Access Journal of Gastroenterology and Hematology. 2020 Jun 2; 8(6):e13104.

[12] Yamamichi N, Shimamoto T, Takahashi Y, Takahashi M, Takeuchi C, Wada R, Fujishiro M. Trends in proton pump inhibitor use, reflux esophagi is, and various upper gastrointestinal symptoms from 2010 to 2019 in Japan. PLoS One. 2022 Jun 17; 17(6):e0270252.

[13] Huh CW, Lee SK, Park JC, Shin SK, Lee YC. A systematic review and meta-analysis of randomized control trials: combination treatment with proton pump inhibitor plus prokinetic for gastro esophageal reflux disease. Journal of neurogastroenterology and motility. 2021 Apr 30; 27(2):165.

ISSN 1019-6609
eISSN 1853-4961

[14] Yamani NF, Said AS, Tuan Kamauzaman TH, Lee YY, Islam MA. Efficacy and safety of domperidone in combination with proton pump inhibitors in gastro esophageal reflux disease: A systematic review and meta-analysis of randomized controlled trials. Journal of Clinical Medicine. 2022 Sep 7; 11(18):5268.

[15] Oshawa T, Igarashi A, Nakano H, Douche H, Fujimori I, Fernandez J. Network meta-analysis comparing vonoprazan and proton pump inhibitors for heartburn symptoms in erosive esophagi is. Journal of Clinical Gastroenterology. 2022 Jul 1; 56(6):493-504.

[16] Lee SK. A comprehensive comparative study of potassium-competitive acid blockers is necessary. Official journal of the American College of Gastroenterology | ACG. 2020 Nov 1; 119(11):2344-5.

[17] Fang Y, Lou D, Zhou J, Zhang Q, Dai Y, Ran W. Efficacy and Safety of Potassium-competitive Acid Blockers Versus Proton Pump Inhibitors in Treating Erosive Esophagi is: A Meta-analysis Based on Randomized Controlled Trials. Journal of Clinical Gastroenterology. 2020 Oct 1; 58(9):841-50.

[18] Husain H, Kerbed TM, Casework TS, Kumara D, Fade-in O, Chaudhari SS, Habit I, Hiram S, Husain Jar H. Comparative Efficacy and Safety of Tegoprazan Versus Proton Pump Inhibitors for Erosive Esophagi is: A Systematic Review and Meta-Analysis. Cures. 2020 May 1; 17(5).