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Comparative Efficacy of Proton Pump Inhibitors and H2-Receptor Antagonists in Managing GERD: A Double-Blind Randomized Controlled Trial

By

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Abstract

Gastroesophageal reflux disease (GERD) is a chronic condition resulting from the reflux of gastric contents into the esophagus, leading to symptoms such as heartburn and regurgitation. While proton pump inhibitors (PPIs) and H2-receptor antagonists (H2RAs) are commonly used pharmacologic options, comparative data on their efficacy remains variable across populations. This double-blind randomized controlled trial aimed to assess the relative effectiveness of PPIs versus H2RAs in managing symptomatic GERD. A total of 180 patients diagnosed with GERD based on clinical symptoms and endoscopic findings were randomized into two groups: Group A received a standard dose of omeprazole 20 mg once daily, while Group B received ranitidine 150 mg twice daily, for 8 weeks. Primary endpoints included symptom resolution (heartburn and regurgitation) measured using a validated GERD questionnaire, while secondary endpoints included endoscopic mucosal healing and quality-of-life improvement. At 8 weeks, Group A showed significantly greater symptom relief (82.2% vs. 58.9%, $p < 0.001$), higher rates of mucosal healing (78.9% vs. 54.4%, $p = 0.002$), and improved quality-of-life scores ($p = 0.004$). These findings suggest superior efficacy of PPIs over H2RAs in managing GERD, supporting the continued use of PPIs as first-line therapy in moderate to severe cases.

Keywords: GERD, proton pump inhibitors, H2-receptor antagonists, randomized controlled trial

Introduction

Gastroesophageal reflux disease (GERD) is one of the most prevalent gastrointestinal disorders globally, affecting approximately 10% to 20% of the adult population in Western countries and an increasing number in developing nations. It is characterized by the reflux of gastric contents into the esophagus, leading to troublesome symptoms such as heartburn, acid regurgitation, and in some cases, esophagitis and Barrett's esophagus. Chronic GERD can significantly impair quality of life and lead to complications if not managed effectively.1-5

Pharmacological therapy remains the cornerstone of GERD management, with proton pump inhibitors (PPIs) and H2-receptor antagonists (H2RAs) being the most widely used agents. PPIs, by irreversibly inhibiting the H+/K+ ATPase enzyme in gastric parietal cells, offer potent and prolonged acid suppression. In contrast, H2RAs block histamine-induced gastric acid secretion by antagonizing H2 receptors on parietal

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cells, resulting in moderate acid suppression. While both drug classes are effective, PPIs are generally considered superior in healing erosive esophagitis and controlling symptoms. However, concerns regarding long-term PPI use, such as nutrient malabsorption, bone fractures, and infections, have led some practitioners to consider H2RAs as a safer alternative, particularly for milder cases.6-7

The literature offers varying conclusions regarding the comparative efficacy of these agents, especially in patients with non-erosive reflux disease (NERD) versus those with erosive esophagitis. Some meta-analyses suggest a clear advantage for PPIs, while others report similar efficacy in mild to moderate disease. Additionally, real-world data reflecting local population responses and tolerability profiles are limited, particularly in developing healthcare settings. This gap necessitates rigorously designed randomized controlled trials that account for clinical, endoscopic, and patient-reported outcomes.8-10

This study was conducted to provide high-level evidence through a double-blind randomized controlled trial comparing the short-term efficacy of a commonly prescribed PPI (omeprazole) with an H2RA (ranitidine) in managing GERD. The primary objective was to evaluate symptom resolution rates, while secondary outcomes included mucosal healing assessed via endoscopy and quality-of-life changes as measured by a standardized GERD-specific questionnaire.

Methodology

This double-blind randomized controlled trial was conducted at a tertiary care gastroenterology center over a 12-month period following approval by the institutional ethics committee. A total of 180 adult patients aged 18 to 65 years with clinically and endoscopically confirmed GERD were enrolled. Inclusion criteria included typical symptoms of GERD (heartburn and/or regurgitation at least twice per week) and either non-erosive reflux disease or grade A-C erosive esophagitis based on the Los Angeles classification. Exclusion criteria included prior long-term use of acid-suppressive therapy, history of upper gastrointestinal surgery, pregnancy, concurrent peptic ulcer disease, gastrointestinal malignancy, or significant comorbidities.

Sample size was calculated using Epi Info 7.2, setting power at 80% and alpha at 0.05, anticipating a 20% difference in symptom resolution rates between the groups, resulting in 90 patients per group. Participants were randomized using a computer-generated sequence into two groups. Group A received omeprazole 20 mg once daily, and Group B received ranitidine 150 mg twice daily. Both medications were identically encapsulated to maintain blinding. Treatment duration was 8 weeks.

Patients were evaluated at baseline, 4 weeks, and 8 weeks. Symptom severity and frequency were assessed using the GERD Health-Related Quality of Life (GERD-HRQL) questionnaire. Endoscopic evaluation was repeated at 8 weeks to assess mucosal healing. Adverse events and compliance were monitored throughout the study. Statistical analysis was performed using SPSS v26.0. Continuous variables were analyzed using Student's t-test, and categorical variables using chi-square test. A p-value < 0.05 was considered statistically significant.

Results

Out of 180 enrolled patients, 172 completed the study (Group A: 86, Group B: 86). Baseline demographic and clinical characteristics were comparable between the two groups.

Table 1: Baseline Characteristics

Variable	Group A (Omeprazole)	Group B (Ranitidine)	p-value
Age (years)	41.2 ± 10.3	42.1 ± 9.8	0.491
Male/Female	48/38	46/40	0.761
Symptom duration (months)	14.3 ± 5.2	13.8 ± 6.1	0.582

Table 2: Primary and Secondary Outcomes at 8 Weeks

Outcome	Group A (n=86)	Group B (n=86)	p-value
Symptom resolution (%)	82.2%	58.9%	<0.001
Mucosal healing (%)	78.9%	54.4%	0.002
Mean GERD-HRQL score improvement	18.5 ± 4.3	13.1 ± 3.7	0.004

Table 3: Adverse Events

Adverse Event	Group A (n=86)	Group B (n=86)	p-value
Headache	9 (10.4%)	6 (6.9%)	0.421
Nausea	5 (5.8%)	7 (8.1%)	0.538
Constipation	4 (4.6%)	3 (3.4%)	0.695

Discussion

This randomized controlled trial demonstrates the superior efficacy of omeprazole, a proton pump inhibitor, over ranitidine, an H2-receptor antagonist, in the management of GERD symptoms, mucosal healing, and quality-of-life improvement over an 8-week period. The findings are consistent with mechanistic evidence suggesting that PPIs provide more profound and sustained acid suppression than H2RAs.11-13

The symptom resolution rate of over 82% with omeprazole in this study corroborates earlier findings and further supports its role as a first-line therapeutic agent for GERD. In contrast, ranitidine, although effective in milder cases, showed significantly lower efficacy in symptom control and mucosal healing. This is likely due to its shorter duration of action and

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susceptibility to tachyphylaxis, a known limitation of H2RAs.14-17

The higher mucosal healing rate in the PPI group is clinically important, given that healing of esophagitis correlates with long-term symptom relief and prevention of complications such as strictures or Barrett's esophagus. Moreover, improvements in GERD-HRQL scores further highlight the real-world impact of effective acid suppression on daily functioning and well-being.18-20

While adverse events were mild and comparable between groups, the long-term safety of PPIs continues to be a topic of discussion. In this trial, the short duration limited assessment of rare but serious side effects. Therefore, periodic review of PPI necessity, especially in maintenance therapy, remains advisable.

This study adds to the body of evidence reinforcing the position of PPIs in the treatment hierarchy of GERD, especially in patients with moderate to severe symptoms or endoscopic esophagitis. It also highlights the need for individualized treatment strategies, considering both efficacy and safety profiles.

Conclusion

In this double-blind randomized controlled trial, omeprazole demonstrated significantly superior efficacy compared to ranitidine in symptom relief, mucosal healing, and quality-of-life improvement among GERD patients over 8 weeks. These findings affirm the role of PPIs as the preferred first-line therapy in managing GERD, while underscoring the limited utility of H2RAs in more symptomatic cases.

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