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Comparative Study of Proton Pump Inhibitors versus H2 Blockers in Peptic Ulcer Disease Management

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Abstract

Introduction: Peptic ulcer disease (PUD) is one of the common GI disorders where the disorder requires good acid suppression to mitigate the symptoms and heal the mucosa. Proton pump inhibitors (PPIs) and H2 receptor antagonists (H2RAs) are known broadly used treatments, and their preferable clinical performances need additional research.

Objective: In order to compare efficacy of PPIs and H2RAs in the treatment of PUD in respect to symptom relief, ulcer healing and prevention.

Methodology: This comparative study was carried out at Hayatabad Medical Complex, Peshawar and a 12 months period was taken in this study. Out of a total of 210 patients with endoscopically confirmed PUD, Patients were randomly assigned to two groups; the large control group designated (A) PPIs (n=105) and the other large group designated (B) H2RAs (n=105). Demographics, type of ulcer, presence of *Helicobacter pylori*, symptom scores (GSRS), healed outcomes and recurrence were data collected. The statistical analysis was performed in SPSS version 26 and chi-square and t-tests were used, the value $p < 0.05$ was taken to be statistically significant.

Results: There were no differences in baseline characteristic between groups ($p > 0.05$). At 6 weeks, the percentage of patients with reports of symptom relief was much greater in the PPI group (mean GSRS reduction: 9.6 vs. 7.2; $p < 0.001$). PPIs had a higher proportion of ulcer healing (89.5 % vs. 72.4%; p = 0. 002). The rate of recurrence at 3 months was lower in the PPI group (4.8% vs. 16.2%; p 0.006). Adverse effects were minimal and comparable in the study groups.

Conclusion: PPIs are much more effective over H2RAs in the treatment of PUD providing improved symptom control, greater rates of healing and reduced recurrence.

Keywords: Peptic Ulcer, Proton Pump Inhibitors, Histamine H2 Antagonists, *Helicobacter pylori*, Ulcer Healing, Gastrointestinal Symptoms

Introduction

Peptic ulcer disease (PUD) is one of the common diseases of the gastrointestinal tract, which is associated with the loss of mucosa, most commonly in the lowest part of the stomach or proximal duodenum, and more frequently leading to the manifestation of such symptoms as epigastric pain, bloating, nausea, and the presence of gastrointestinal bleeding in more serious manifestations [1]. The most common causes of PUD are an infection with *Helicobacter pylori*, regular administration of non-steroidal anti-inflammatory drugs (NSAIDs), smoking, alcohol consumption, and stress [2]. These alterations impair the systemic equilibrium between the aggressive gastric secretions which is mainly hydrochloric acid and pepsin proteins with the protective systems of the mucosal lining [3]. Treatment of PUD is dependent therefore on mechanisms that inhibit the secretion of gastric acid and enhance healing of the mucosa [4].

The backbone of pharmacologic therapy of PUD is 2 large categories of acid-suppressing medications proton pump inhibitors (PPIs) and histamine-2 receptor blockers (H2 blockers) [5]. H2 blockers play a role in blocking histamine at H2 receptors of the gastric parietal cells competitively and they cause a moderate decrease in acid production [6]. Even after widespread use since 1970s

their effectiveness is negatively impacted by the emergence of toleration and ceiling effect in the acid quenching process [7].

Encompassing omeprazole, esomeprazole, and pantoprazole, the latest and stronger type of acid-suppressive drug are called proton pump inhibitors. PPIs cause permanent blockage of the H+/K+ ATPase enzyme system in the secretory membrane of gastric parietal cells that has a dramatic and persistent effect of gastric acid secretion [8]. These medicines were proven to be more effective as a prompts of ulcers healing, symptoms alleviation and ulcer recurrence, especially in *H. pylori* related and nonsteroidal-induced ulcers through numerous clinical trials [9]. Nevertheless, the long-term use of PPIs has been linked to such possible adverse outcomes as fractures, renal disease, and infections, including Clostridioides difficile [10].

Whereas several comparative studies are available, selection of the PPIs or H2 blockers in the everyday practice of clinical use still depend on other factors such as drug cost, drug availability, tolerability of the drugs to a particular patient and the preference of the clinician [11]. Moreover, the majority of comparative studies are either older or limited to a particular region or none of them represents changing trends related to resistance and efficacy in various healthcare environments [12].

The recent regional-specific comparative data assessing the effectiveness of PPIs versus H 2 blockers in the treatment of the peptic ulcer disease in the Pakistani population is still meager. Consequently, this research set out to determine the efficacy and safety of proton pump inhibitor compared to H2 blockers in treatment of peptic ulcer disease.

Materials and Methods

PUD is one of the common diseases of the gastrointestinal tract, which is associated with the loss of mucosa, most commonly in the lowest part of the stomach or proximal duodenum, and more frequently leading to the manifestation of such symptoms as epigastric pain, bloating, nausea, and the presence of gastrointestinal bleeding in more serious manifestations [1]. The most common causes of PUD are an infection with *Helicobacter pylori*, regular administration of NSAIDs, smoking, alcohol consumption, and stress [2]. These alterations impair the systemic equilibrium between the aggressive gastric secretions which is mainly hydrochloric acid and pepsin proteins with the protective systems of the mucosal lining [3]. Treatment of PUD is dependent therefore on mechanisms that inhibit the secretion of gastric acid and enhance healing of the mucosa [4].

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Results

PUD patients were recruited and divided into two equal groups at random: 105 patients received a proton pump inhibitor (PPI), while the remaining 105 were treated with an H2 receptor antagonist (H2RA). As shown in Table 1, the two groups' baseline clinical and demographic traits were statistically similar. The PPI group's mean age was 45.3 ± 12.8 years, while the H2RA group's was 46.1 ± 13.5 years ($p = 0.68$). Male participants made up 56.2% of the H2RA group and 59.0% of the PPI group ($p = 0.67$). There were no statistically significant differences ($p > 0.05$) in the two groups' body mass index (BMI), smoking status, or NSAID use. Furthermore, 67.6% of the PPI group and 65.7% of the H2RA group had *Helicobacter pylori* infection ($p = 0.77$). These non-significant differences confirm the success of randomization and establish baseline homogeneity, thereby strengthening the validity of subsequent treatment comparisons.

Table 1: Baseline demographic and clinical characteristics

Variable	Group A (PPIs, n=105)	Group B (H2RAs, n=105)	Test Value	p-value
Mean Age (years)	45.3 ± 12.8	46.1 ± 13.5	t = 0.41	0.68
Male Gender (%)	62 (59.0%)	59 (56.2%)	χ^2 = 0.16	0.67
BMI (kg/m²)	24.6 ± 3.2	24.2 ± 3.5	t = 0.83	0.41
Smokers (%)	28 (26.7%)	25 (23.8%)	χ^2 = 0.22	0.63
NSAID Use (%)	36 (34.3%)	39 (37.1%)	χ^2 = 0.19	0.67
H. pylori Positive (%)	71 (67.6%)	69 (65.7%)	χ^2 = 0.09	0.77

The distribution of ulcer characteristics between the two treatment groups was comparable. Duodenal ulcers were the most prevalent kind in both groups, as shown in Figure 1, occurring in 70.5% of patients in the H2RA group and 68.6% of patients in the PPI group (χ^2 = 0.09, p = 0.76). Most ulcers were small in size (<1 cm), found in 63.8% of Group A and 61.0% of Group B (χ^2 = 0.16, p = 0.69), while large ulcers (≥1 cm) were present in 36.2% and 39.0% of patients, respectively. Single ulcers were predominant in both groups, seen in 81.0% of PPI-treated and 78.1% of H2RA-treated patients (χ^2 = 0.26, p = 0.61). Multiple ulcers were slightly more frequent in Group B (21.9%) compared to Group A (19.0%), but this difference was not statistically tested. None of the comparisons showed significant p-values, indicating that ulcer type, size, and number were evenly distributed between the two groups. This supports that any differences in treatment outcomes are unlikely due to baseline ulcer characteristics.

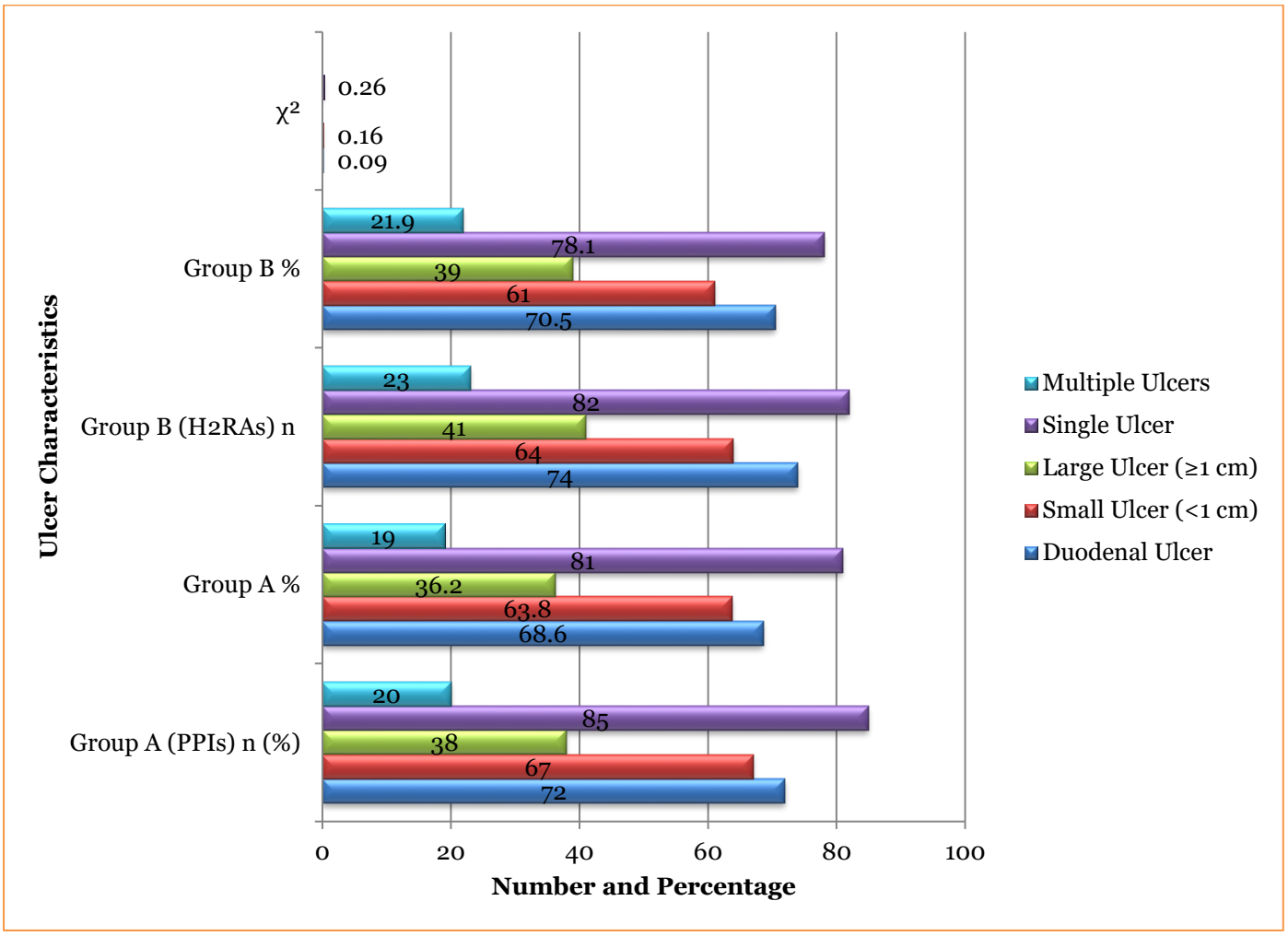

Figure 1: Ulcer type, location, and characteristics

As shown in Table 3, patients receiving PPIs experienced significantly greater symptom relief at 6 weeks than those receiving H2 blockers (t = 6.23, p < 0.001). This effect persisted across all subgroups, including *H. pylori* status and ulcer type. Patients who tested positive for *H. pylori* showed the biggest change (t = 6.30, p < 0.001). Even among *H. pylori*-negative cases, symptom relief was significantly better with PPIs (t = 2.99, p = 0.004). These consistent findings across strata underscore the superior symptom control

associated with PPI therapy. The GSRS score reduction further validates PPIs as a more effective class for symptomatic management of PUD. All differences were statistically significant, indicating a robust treatment effect.

Table 3: Symptom relief based on GSRS scores (by Subgroups)

Subgroup / Variable	Group A (PPIs)	Group B (H2RAs)	Test Value	p-value
Overall GSRS Score Reduction	9.6 ± 2.9	7.2 ± 2.6	t = 6.23	<0.001
GSRS (*H. pylori* Positive)	10.2 ± 2.5	7.6 ± 2.3	t = 6.30	<0.001
GSRS (*H. pylori* Negative)	8.7 ± 3.1	6.6 ± 2.8	t = 2.99	0.004
GSRS (Duodenal Ulcer)	9.9 ± 2.6	7.5 ± 2.4	t = 5.72	<0.001
GSRS (Gastric Ulcer)	8.8 ± 3.2	6.8 ± 2.9	t = 2.77	0.008

Table 4 shows that the PPI group had significantly improved endoscopic healing at 6 weeks (χ^2 = 9.50, p = 0.002). In *H. pylori*-positive patients, 91.5% showed complete healing with PPIs versus 72.5% with H2 blockers (χ^2 = 8.78, p = 0.003). Healing differences were also significant for duodenal ulcers (χ^2 = 9.21, p = 0.002), but not for gastric ulcers (p = 0.12). The difference in healing rates among patients who tested negative for *H. pylori* was also not statistically significant (p = 0.16). These findings suggest that while PPIs provide superior healing overall, their benefit is especially evident in duodenal ulcers and *H. pylori*-positive patients. The lack of significant improvement in gastric ulcer healing indicates that therapeutic response may vary by ulcer subtype.

Table 4: Ulcer healing outcome at 6 weeks (by subgroups)

Subgroup / Outcome	Group A (PPIs)	Group B (H2RAs)	Test Value	p-value
Total Healed (%)	94 (89.5%)	76 (72.4%)	χ^2 = 9.50	0.002
Healed (*H. pylori* Positive)	65/71 (91.5%)	50/69 (72.5%)	χ^2 = 8.78	0.003
Healed (*H. pylori* Negative)	29/34 (85.3%)	26/36 (72.2%)	χ^2 = 2.00	0.16
Healed (Duodenal Ulcers)	66/72 (91.7%)	54/74 (73.0%)	χ^2 = 9.21	0.002
Healed (Gastric Ulcers)	28/33 (84.8%)	22/31 (71.0%)	χ^2 = 2.42	0.12

As shown in Figure 2, adverse events were recorded more frequently in the H2RA group than in the PPI group, but the difference was not statistically significant (23.8% vs. 14.3%; χ^2 = 2.95, p = 0.08). The most common side effects in both groups were mild nausea (13.3% vs. 8.6%), headache (10.5% vs. 5.7%), and constipation (6.7% vs. 3.8%), all of which were self-limiting and did not require treatment discontinuation. At three months, however, the PPI group experienced a considerably lower rate of ulcer recurrence (4.8%) than the H2RA group (16.2%), with a statistically significant difference (χ^2 = 7.52, p = 0.006).This suggests superior long-term mucosal protection with PPIs, likely due to their sustained acid suppression even after the cessation of therapy. While both drugs were generally well tolerated, the marked reduction in recurrence associated with PPI use may justify their preferential use in patients at high risk for ulcer relapse or complications.

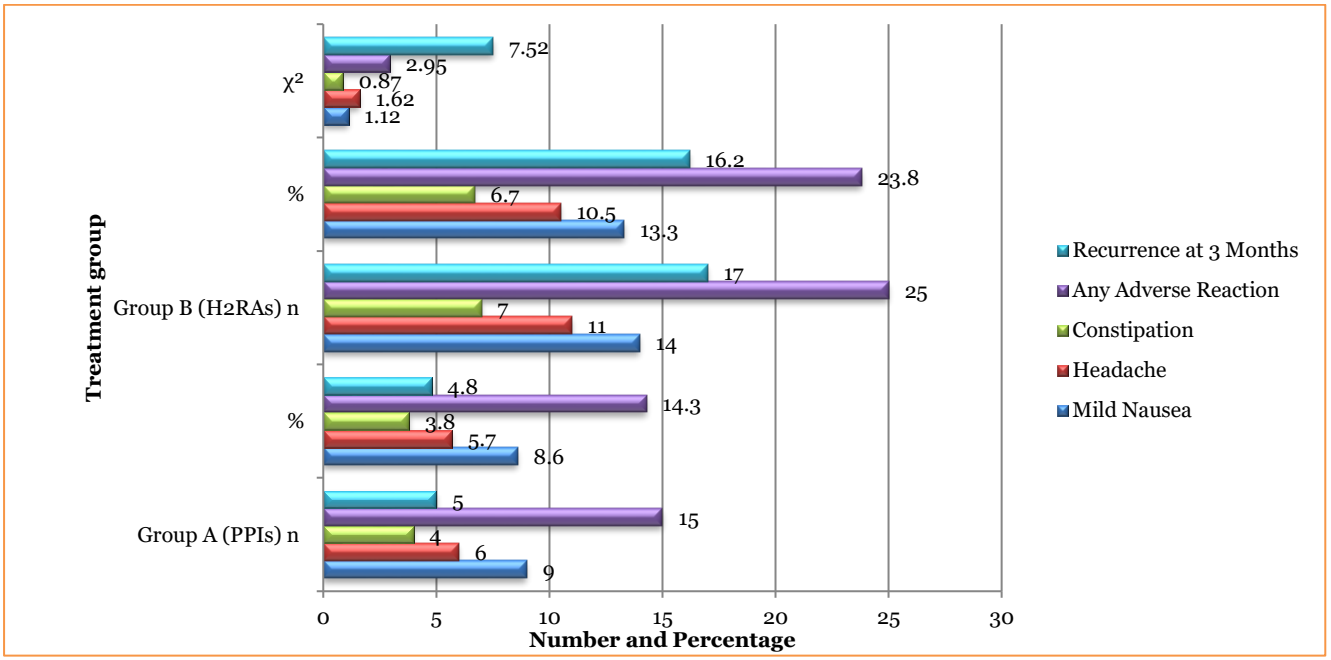

Figure 2: Adverse events and recurrence rates

Discussion

A comparative test of effectiveness of proton pump inhibitors (PPIs) and H 2 receptor antagonists (H 2RAs) in the treatment of PUD was carried out in 210 patients. The findings proved that PPIs worked much better in comparison to H2RAs regarding symptom remission, ulcer healing, and a decreased recurrence rate. Although the two groups contained similar baseline data and ulcer patterns, the PPI group recorded substantially improved results at the 6-week mark, with a larger percentage of symptom resolutions and mucosal healing. Moreover, the patients treated with PPIs showed a significant reduction in the rate of recurrence during the 3-month follow-up. While both drugs were generally well tolerated, the reduction in adverse events observed with PPI use did not reach statistical significance ($p = 0.08$) and thus should be interpreted with caution. Nonetheless, the significantly lower recurrence rate supports the clinical utility of PPIs in high-risk patients. This highlights their therapeutic advantage, particularly in those prone to relapse, although safety comparisons between the two agents require further validation in larger, long-term studies.

Compared against the current literature, the results of this trial are similar to the reported results previously and in support of PPIs use in the suppression of acids and healing ulcers [17]. Several clinical trials and observational studies have established that PPIs provide faster and more complete acid inhibition than H2RAs, which translates into superior ulcer resolution and improved patient-reported symptom scores [18]. The enhanced healing effect of PPIs, especially in *Helicobacter pylori*-positive patients, has also been repeatedly validated in international guidelines and meta-analyses [19]. In terms of safety, both PPIs and H2RAs are well-tolerated, but PPIs are often preferred for long-term management due to their prolonged duration of action and sustained mucosal protection [20]. Furthermore, the recurrence rate observed in this study for the H2RA group reflects the limitation of their short-acting acid control, particularly in high-risk ulcer patients [21].

Additional comparisons with previous studies reveal similar patterns in the superiority of PPIs across different populations and healthcare settings [22]. PPIs have consistently shown higher eradication rates of *H. pylori*-associated ulcers when used in combination therapies, along with quicker symptom resolution and reduced ulcer-related complications [23]. In patients with duodenal ulcers, PPIs demonstrate higher mucosal healing rates than H2RAs, a trend reflected in this study as well [24]. Furthermore, studies have shown that ulcer recurrence is significantly reduced with PPI maintenance therapy, especially in NSAID-associated ulcers, due to their ability to suppress both basal and stimulated acid secretion effectively [25]. This study reinforces these findings and highlights the clinical advantages of PPIs, especially in patients at risk of recurrence or complications.

Limitations and future suggestions

There are numerous limitations to this study in spite of the good findings. To begin with, it had a 3-month follow-up period that could have failed to capture long-term issues. Second, one tertiary care facility was involved in the study only, limiting its generalizability to broader populations such as rural or under-resourced communities. Third, subjective measures were used to assess patient compliance with treatment, relying primarily on verbal confirmation. Furthermore, endoscopic assessments were only done at baseline and at 6 weeks, so any possible mid-course changes could not be traced. Cost-effectiveness should be considered in future studies, especially those in regions with scarce resources. A multicenter design and longer follow-up duration are also recommended for broader analysis. Clinical recommendations can be strengthened by studying the role of *H. pylori* eradication in preventing ulcer recurrence and by incorporating quality-of-life indicators in future study.

Conclusion

This study revealed that in the management of the peptic ulcer disease proton pump inhibitors (PPIs) are significantly more effective in comparison to H2 receptor antagonists (H2RAs). PPI treated patients showed superior rates of ulcer healing, low rates of recurrence in follow up and improvement of symptoms. Regardless of the similarity of the safety profile of the two groups of therapy, there is a clear therapeutic advantage of PPIs in terms of prolonged acid inhibition. Based on these findings, PPIs must be adopted in the first-line therapy of peptic ulcer disease patients particularly when they are infected with *Helicobacter pylori* or carry high risks of relapse.

Conflict of interest

Nil.

Author Contributions

All authors have contributed to drafting the manuscript, reviewed the final version to be published, and agreed to be accountable for all aspects of the work. The concept and design were contributed by MS and UM; data acquisition, analysis, or interpretation was carried out by RA and SA; critical review for important intellectual content was performed by MS, UM and AQ; and supervision was provided by UM.

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