International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 30, Issue 9, September 2024 **ijppr.humanjournals.com** ISSN: 2349-7203

Review of Impact of Proton Pump Inhibitors on GERD Patients

Bibitha A[1], Anjali Krishnan P[1], Shamna M A[1], Tamilselvan T[2]

[1]Master of Pharmacy Student, Department of Pharmacy Practice, Nehru College of Pharmacy, Kerala, India.

[2]Professor and Head, Department of Pharmacy Practice, Nehru College of Pharmacy, Kerala, India.

Received: 2024-09-03 Revised: 2024-09-11 Accepted: 2024-09-15

ABSTRACT

Gastroesophageal reflux disease is the term used to describe the backflow of stomach contents into the esophagus (GERD). Esophagitis and other symptoms that lower quality of life can be brought on by this condition. The most often prescribed drug for GERD is proton pump inhibitors (PPIs). It has been demonstrated to improve the quality of life for GERD patients. Proton pump inhibitors impede the proton pump, which in turn reduces acid production. Presently, PPIs that are sold commercially come in racemic mixtures of isomers S and R, such as omeprazole, pantoprazole, rabeprazole, and lansoprazole. When compared to the racemic mixture, PPIs' chiral forms exhibit better pharmacokinetic and metabolic profiles as well as higher therapeutic efficacy. The creation of esomeprazole (the omeprazole isomer), S-pantoprazole (the pantoprazole isomer), and dexrabeprazole (the rabeprazole isomer) has served as evidence of this. This study compared the effectiveness and safety of proton pump inhibitors that are currently prescribed for the treatment of GERD.

KEYWORDS: PPI, GERD, esomeprazole, pantoprazole, omeprazole, dexlansoprazole

INTRODUCTION

A very common digestive disorder, gastroesophageal reflux disease (GERD) is characterized by bothersome symptoms and complications that arise from the reflux of stomach contents into the esophagus[1,2]. Heartburn, regurgitation, dysphagia, and chest pain are among the most typical signs of GERD in an individual[3,4]. The symptoms of dyspepsia include upper abdominal bloating, postprandial fullness, early satiety, burning and pain in the epigastrium, nausea, vomiting, and belching[5]. Non-erosive reflux disease (NERD) and erosive GERD are the two forms of the disease. Acid reflux and heartburn are the clinical manifestations of NERD, while endoscopic examination can detect mucosal damage in erosive GERD[6].

First-line agents that are recommended for the short- and long-term management of GERD are proton pump inhibitors (PPIs), which are the most effective treatment option[7]. PPIs have been clinically proven to be more effective than histamine-2 receptor antagonists (H2RAs) in treating esophagitis and relieving GERD symptoms [8-10].

METHODS

This article will review the efficacy and safety of different proton pump inhibitors in GERD using the keywords in the search engines of Pubmed and google, and present a balanced view of the available data.

EFFECT OF PROTON PUMP INHIBITORS

Celebi Altay et al. evaluated the impact of 40 mg of esomeprazole, 20 mg of rabeprazole, 30 mg of lansoprazole, and 40 mg of pantoprazole on intragastric pH in patients with gastroesophageal reflux disease who are extensive metabolizers. Four treatment groups were randomly assigned to patients. On days 1 and 5, the four groups of patients—ten on esomeprazole, eleven on Rabeprazole, ten on Lansoprazole, and ten on Pantoprazole—were subjected to an efficacy analysis. The groups' mean percentage of time with intragastric Ph>4 on day 1 of PPI treatment was 54%, 58%, 60%, and 35%, respectively; on day 5, these values were 67%, 60%, 68%, and 59%, respectively. On the first day of treatment, rabeprazole, lansoprazole, and esomeprazole were found to be better than pantoprazole. They concluded that, in comparison to the other PPIs tested on the first day of treatment, pantoprazole

is a less effective proton pump inhibitor. Esomeprazole exhibited the fastest action when it came to raising the intragastric pH to over 4, with lansoprazole and rabeprazole following closely behind [11].

In a study conducted by Kerstin Rohss et al., it was determined that in patients exhibiting symptoms of gastro-oesophageal reflux, rabeprazole 20 mg, pantoprazole 40 mg, and lansoprazole 30 mg were less effective at controlling intragastric acid than omeprazole 40 mg. Patients with GERD symptoms received once-daily treatment with esomeprazole 40 mg or lansoprazole 30 mg (study A), omeprazole 20 mg (study B), pantoprazole 40 mg (study C), and rabeprazole 20 mg (study D) for five days in four randomized crossover studies. They came to the conclusion that, in patients exhibiting symptoms of GERD12, rabeprazole 20 mg, pantoprazole 40 mg, lansoprazole 30 mg, and omeprazole 20 mg all provided less acid control and did not sustain intragastric pH greater than 4 for as long[12].

After standard dosages of esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole, Miner P Jr. aimed to assess and compare intragastric pH. In 34 Helicobacter pylori-negative patients with symptoms of gastroesophageal reflux disease who were between the ages of 18 and 60, this randomized, open-label, comparative five-way crossover study assessed the 24-hour intragastric pH profile of oral esomeprazole 40 mg, lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg, and rabeprazole 20 mg once daily. The standard doses of lansoprazole, omeprazole, pantoprazole, and rabeprazole were found to be less effective in controlling gastric acid at steady state in patients exhibiting symptoms of gastroesophageal reflux disease than Esomeprazole at 40 mg once daily[13].

EFFECT ON GERD

A Randomized Placebo-Controlled N-of-1 Trial: The Impact of Proton Pump Inhibitor in the Treatment of Gastroesophageal Reflux Disease was carried out by Fernando Sierra-Arango and colleagues. A 58-year-old man with a body mass index of 26 kg/m2 who was not obese and had no history of alcohol or tobacco use was included in this study. A 40 mg dose of esomeprazole administered in the morning and at night 30 minutes before meals, or a placebo administered in the morning and at night 30 minutes before meals, were the two treatments administered to the chosen patient. There were six distinct treatment determinations examined, and twelve pairs of one-week periods totaling twenty-four weeks were conducted. A two-day washout period using alginate 10 ml every 12 hours was added to each period, for a total of 29 weeks of treatment. During the six months of the study, they discovered that the patient's GERD symptoms did not significantly improve with an increased oral esomeprazole dosage[14].

The CYP2C19 genotype was found to have a greater influence on the acid-inhibitory effect and kinetics of pantoprazole than esomeprazole[15] in a study by Hunfeld et al. The acid-inhibitory effects of rabeprazole were found to be less affected by the CYP2C19 genotype than by lansoprazole and omeprazole[16] in a study recently published by Sugimoto et al. A study on the effects of intravenous esomeprazole 40 mg versus pantoprazole 40 mg on the intragastric pH over a 24-hour period in healthy adults was carried out by Dirk Hartmann et al. Researchers discovered that esomeprazole 40 mg given intravenously produces an intragastric acid control that is both quicker and more noticeable than pantoprazole 40 mg given intravenously[17].

To investigate intragastric acidity during treatment with either pantoprazole 40 mg twice a day or esomeprazole 40 mg twice a day, S. Miehlke et al. carried out a randomized, two-way crossover study. They discovered that in comparison to pantoprazole 40 mg twice a day, esomeprazole 40 mg twice a day offers superior and more reliable intragastric acid control[18]. Their findings also hold for crossover studies, which consistently demonstrate that esomeprazole 40 mg once daily significantly reduces the production of intragastric acid at a level greater than that of omeprazole 20 and 40 mg, lansoprazole 30 mg, pantoprazole 40 mg and rabeprazole 20 mg[19-22].

According to these studies, esomeprazole 40 mg once daily produces an intragastric pH > 4 for roughly 15 hours out of every 24 hours when taken in a steady state. However, only roughly half of the subjects were able to effectively control the intragastric pH for more than 16 hours with esomeprazole at the standard dosage [23]. This may be the cause of the observation that, following 8 weeks of esomeprazole treatment, 10-15% of patients with severe erosive oesophagitis do not heal[24-27].

Johnson, D. A., and others The chosen treatment determines the response to acid suppression. Compared to all other regimens studied, esomeprazole 40 mg twice daily offered superior control of intragastric pH. On the other hand, esomeprazole 40 mg once daily outperformed lansoprazole 30 mg twice daily and was comparable to both[28]. Standard doses of rabeprazole, omeprazole, lansoprazole, and pantoprazole were found to provide fewer mean hours in a 24-hour period with pH above prespecified thresholds (between 2.0 and 6.0) in a five-way crossover study[29]. If a patient's symptoms don't improve after taking PPIs, the doctor might decide to increase the dosage instead of switching to a different drug. It is both clinically and financially successful to move from twice-daily PPIs to once-daily esomeprazole[30].

CONCLUSION

This study highlights the varied efficacy and safety profiles of different proton pump inhibitors (PPIs) in treating gastroesophageal reflux disease (GERD). The findings consistently demonstrate that esomeprazole, particularly at a dosage of 40 mg, offers superior control over intragastric pH compared to other PPIs such as pantoprazole, omeprazole, and rabeprazole. While esomeprazole shows greater efficacy in maintaining a higher intragastric pH over extended periods, some patients with severe GERD may still experience suboptimal responses, indicating a potential need for adjusted dosing or alternative treatment strategies. Ultimately, the choice of PPI and its dosing should be carefully tailored to the individual patient's needs to optimize therapeutic outcomes.

REFERENCES:

1. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut 2014;63:871-880.
2. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R, Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am J Gastroenterol 2006;101:1900-1920.
3. Simadibrata M. Dyspepsia and gastroesophageal reflux disease (GERD): Is there any correlation? Acta Med. Indones. 2009; 41: 222–7.
4. Gyawali CP, Kahrilas PJ, Savarino E et al. Modern diagnosis of GERD: the Lyon Consensus. Gut. 2018; 67: 1351–624
5. Stanghellini V. Functional dyspepsia and irritable bowel syndrome: Beyond Rome IV. Dig. Dis. 2017; 35: 14–7.
6. Yamaji Y, Isomura Y, Yoshida S, Yamada A, Hirata Y, Koike K. Randomized controlled trial comparing the efficacy of mosapride plus omeprazole combination therapy to omeprazole monotherapy in gastroesophageal reflux disease. J Dig Dis. 2014 Sep;15(9):469-76. doi: 10.1111/1751-2980.12167. PMID: 24957863.
7. Freston JW, Malagelada JR, Petersen H, et al. Critical issues AJG – March, 2001 Esomeprazole vs Omeprazole in Erosive Esophagitis 663 in the management of gastroesophageal reflux disease. Eur J Gastroenterol Hepatol 1995;7:577–86
8. Fennerty M. Medical treatment of gastroesophageal reflux in the managed care environment. Semin Gastrointest Dis 1997; 8:90–9.
9. Bell NJ, Hunt RH. Progress with proton pump inhibition. Yale J Biol Med 1992;65:649–57 (discussion 689–92).
10. Chiba N. Proton pump inhibitors in acute healing and maintenance of erosive or worse esophagitis: A systematic overview. Can J Gast
11. Çelebi A, Aydın D, Kocaman O, Konduk BT, Şentürk Ö, Hülagü S. Comparison of the effects of esomeprazole 40 mg, rabeprazole 20 mg, lansoprazole 30 mg, and pantoprazole 40 mg on intragastrıc pH in extensive metabolizer patients with gastroesophageal reflux disease. Turk J Gastroenterol. 2016 Sep;27(5):408-414. doi: 10.5152/tjg.2016.15514. PMID: 27782887.
12. Röhss K, Lind T, Wilder-Smith C. Esomeprazole 40 mg provides more effective intragastric acid control than lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg and rabeprazole 20 mg in patients with gastro-oesophageal reflux symptoms. Eur J Clin Pharmacol. 2004 Oct;60(8):531-9. doi: 10.1007/s00228-004-0804-6. Epub 2004 Sep 2. PMID: 15349707.
13. Miner P Jr, Katz PO, Chen Y, Sostek M. Gastric acid control with esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole: a five-way crossover study. Am J Gastroenterol. 2003 Dec;98(12):2616-20. doi: 10.1111/j.1572-0241.2003.08783.x. PMID: 14687806.
14. Sierra-Arango F, Castaño DM, Forero JD, Pérez-Riveros ED, Ardila Duarte G, Botero ML, Cárdenas A, De la Hoz-Valle J. A Randomized Placebo-Controlled *N*-of-1 Trial: The Effect of Proton Pump Inhibitor in the Management of Gastroesophageal Reflux Disease. Can J Gastroenterol Hepatol. 2019 Dec 12;2019:3926051. doi: 10.1155/2019/3926051. PMID: 31929980; PMCID: PMC6935808.
15. Hunfeld NG, Touw DJ, Mathot RA, van Schaik RH, Kuipers EJ. A comparison of the acid-inhibitory effects of esomeprazole and rabeprazole in relation to pharmacokinetics and CYP2C19 polymorphism. Aliment Pharmacol Ther. 2012 Apr;35(7):810-8. doi: 10.1111/j.1365-2036.2012.05014.x. Epub 2012 Feb 13. PMID: 22324425.
16. Sugimoto M, Shirai N, Nishino M, Kodaira C, Uotani T, Yamade M, Sahara S, Ichikawa H, Sugimoto K, Miyajima H, Furuta T. Rabeprazole 10 mg q.d.s. decreases 24-h intragastric acidity significantly more than rabeprazole 20 mg b.d. or 40 mg o.m., overcoming CYP2C19 genotype. Aliment Pharmacol Ther. 2012 Oct;36(7):627-34. doi: 10.1111/apt.12014. Epub 2012 Aug 10. PMID: 22882464.
17. Hartmann D, Eickhoff A, Damian U, Riemann JF, Schilling D. Effect of intravenous application of esomeprazole 40 mg versus pantoprazole 40 mg on 24-hour intragastric pH in healthy adults. Eur J Gastroenterol Hepatol. 2007 Feb;19(2):133-7. doi: 10.1097/01.meg.0000252628.57925.32. PMID: 17272998.
18. Miehlke S, Madisch A, Kirsch C, Lindner F, Kuhlisch E, Laass M, Knoth H, Morgner A, Labenz J. Intragastric acidity during treatment with esomeprazole 40 mg twice daily or pantoprazole 40 mg twice daily--a randomized, two-way crossover study. Aliment Pharmacol Ther. 2005 Apr 15;21(8):963-7. doi: 10.1111/j.1365-2036.2005.02432.x. PMID: 15813831.
19. Wilder-Smith CH, Rohss K, Nilsson-Pieschl C, et al.Esomeprazole 40 mg provides improved intragastric acidcontrol as compared with lansoprazole 30 mg andrabeprazole 20 mg in healthy volunteers. Digestion 2003;68: 184–8.

20. Rohss K, Hasselgren G, Hedenstrom H. Effect of esomeprazole40 mg vs omeprazole 40 mg on 24-hour intragastric pH inpatients with symptoms of gastroesophageal reflux disease.Dig Dis Sci 2002; 47: 954–8.
21. Hassan-Alin M, Andersson T, Niazi M, et al. Apharmacokinetic study comparing single and repeated oraldoses of 20 mg and 40 mg omeprazole and its two opticalisomers, S-omeprazole (esomeprazole) and R-omeprazole, inhealthy subjects. Eur J Clin Pharmacol 2004; 60: 779–84.
22. Wilder-Smith CH, Rohss K, Bondarov P, et al. Esomeprazole40 mg i.v. provides faster and more effective intragastricacid control than pantoprazole 40 mg i.v.: results of arandomized study. Aliment Pharmacol Ther 2004; 20:1099–104.
23. Kahrilas PJ. Review article: is stringent control of gastric pHuseful and practical in GERD. Aliment Pharmacol Ther 2004;20(Suppl. 5): 89–94
24. Kahrilas PJ, Falk GW, Johnson DA, et al. Esomeprazoleimproves healing and symptom resolution as compared withomeprazole in reflux oesophagitis patients: a randomizedcontrolled trial. Aliment Pharmacol Ther 2000; 14: 1249–58.
25. Richter JE, Kahrilas PJ, Johanson J, et al. Efficacy and safety ofesomeprazole compared with omeprazole in GERD patientswith erosive esophagitis: a randomized controlled trial. Am JGastroenterol 2001; 96: 656–65.
26. Castell DO, Kahrilas PJ, Richter JE, et al. Esomeprazole(40 mg) compared with lansoprazole (30 mg) in thetreatment of erosive esophagitis. Am J Gastroenterol 2002;97: 575–83.
27. Labenz J, Armstrong D, Lauritsen K, et al. A randomizedcomparative study of esomeprazole 40 mg versuspantoprazole 40 mg for healing erosive esophagitis: theEXPO study. Aliment Pharmacol Ther 2005 (in press).
28. Johnson DA, Stacy T, Ryan M, Wootton T, Willis J, Hornbuckle K, Brooks W, Doviak M. A comparison of esomeprazole and lansoprazole for control of intragastric pH in patients with symptoms of gastro-oesophageal reflux disease. Aliment Pharmacol Ther. 2005 Jul 15;22(2):129-34. doi: 10.1111/j.1365-2036.2005.02534.x. PMID: 16011671.
29. Katz P, Miner P, Chen Y, Roach A, Sostek M. Effects of 5marketed proton pump inhibitors on acid suppression relativeto a range of pH thresholds [abstract]. Am J Gastroenterol2004; 99: S34
30. Fass R, Thomas S, Traxler B, Sostek M. Patient reportedoutcome of heartburn improvement: doubling the protonpump inhibitor (PPI) dose in patients who failed standard dosePPI versus switching to a different PPI, Gastroenterology 2004; 126: A37

How to cite this article:
Bibitha A et al. Ijppr.Human, 2024; Vol. 30 (9): 62-65.

Conflict of Interest Statement: All authors have nothing else to disclose.