DOI: https://doi.org/10.53350/pjmhs22169427

ORIGINAL ARTICLE

A Prospective Observational Study Combinition of Proton Pump Inhibitors with Prokinetics in Gerd

ZOBIA MUSHTAQ[1], BUSHRA ADEEL[2], TANVEER HUSSAIN[3], MAZHAR ALI[4], MUHAMMAD AYYAZ[5], IMRAN JOHER[6]
[1]*Associate Professor Pharmacology, Faisalabad Medical University, Faisalabad*
[2]*Assistant Professor, Department of pathology, Rashid Latif Medical College Lahore*
[3]*Associate Professor Gastroenterology, RMU, Rawalpindi*
[4]*Associate Professor, Department of Rehabilitation and Health Sciences, Nazir Hussain University Karachi, Pakistan*
[5]*Assistant Professor of Medicine, M. Islam Medical and Dental College, Gujranwala*
[6]*MRCP UK, Associate Professor, Department of Medicine, Sharif Medical College, Lahore*
Corresponding author: Zobia Mushtaq, Email: drzobiausman@gmail.com

ABSTRACT

Background: Gastroesophageal reflux disease (GERD), a fairly common ailment that has a negative influence on quality of life. 30- 40% of patients with GERD have an insufficient response to standard PPIs therapy. For subjects resistant to this PPI therapy, double the PPI dosage or switch to different PPIs, which may not be ideal. So, combination therapy with prokinetic agent will significantly improve GERD symptoms.

Study Design: A prospective observational study.

Place and Duration: In the Department of Medicine, Faisalabad Medical University, Faisalabad from May 2022 to July 2022.

Material and methods: 130 patients with suggestive symptoms of GERD were included to evaluate overlap between GERD and delayed gastric emptying and to forecast the necessity for therapy in combination with prokinetic drugs using the Frequency Scale for the Symptoms of GERD (FSSG) score.

Results: 17.20 ± 8.40 was the mean total score of FSSG. Of the 130 subjects, 106 (81.54%) patients have GERD symptoms with an overall FSSG score >8. 7.43 ± 4.08 was the mean reflux score, and 9.40 ± 5.30 was the mean dysmotility score. In this analysis, patients with GERD symptoms had high score of FSSG, the symptoms of dysmotility appeared to be the main symptom than acid reflux.

Conclusions: Based on this analysis results, combination therapy with prokinetic and PPIs in the subgroups of subjects with high scores of FSSG improved GERD symptoms.

Keywords: Dysmotility score, delayed gastric emptying, GERD and Reflux score.

INTRODUCTION

Gastro-esophageal reflux disease is a chronic disease that progresses when gastric reflux results in bothersome symptoms and complications[1-2]. The GERD prevalence in Pakistan varies from 9-18%, conferring to the latest research based on various research methodologies and case definitions[3]. The GERD other types include non-erosive reflux disease (NERD) and erosive esophagitis (EE)[4]. About 50% to 70% of GERD subjects have NERD with GERD and approximately 28% of GERD patients had erosive esophagitis while about 5% have Barrett's esophagus[5]. The disorders of gastrointestinal motility termed as gastroparesis is categorized by late emptying of stomach in the absenteeism of any obstruction mechanically[6]. Though gastroparesis symptoms may fluctuate in every patient, they typically consist of vomiting, nausea, bloating, early satiety, and discomfort in the upper abdomen with retention of gastric contents[7]. Proved trials recommend that many GERD patients had delaying emptying of stomach. One analysis on gastroparesis incidence among 120 cases with GERD exhibited that 41% have late emptying of stomach[8]. Though, few people like those with diabetes, might be at higher jeopardy for both situations. PPIs are the maximum operative drugs to increase gastric pH and is the main drug treatment for disorders with acidity of stomach[9]. PPIs inhibit secretion of gastric acid by deactivating the proton pumps situated in gastric lining accountable for secretion of acid[10]. Various researches have revealed that about 42% of patients with GERD report that their symptoms do not respond completely or partially to the standard PPI dosage of once a day[11]. The patients may have refractory GERD who do not respond to once-daily PPIs therapy for 4-8 weeks. The refractory GERD patients often require aggressive suppression of acid therapy or additional treatment approaches, such as temporary measures to reduce relaxation of the lower sphincter of esophagus, and if gastroparesis is suspected, concomitant prokinetic agents' administration to normalise emptying of stomach[12]. Identifying a specific subgroup of GERD patients with gastroparesis remains difficult, especially if patients have no classic gastroparesis symptoms such as nausea, bloating, early satiety and vomiting, or if these symptoms are misunderstood as linked to GERD[13]. Therefore, it is important to consider gastroparesis in all cases of GERD and allow clinicians to initiate an optimal treatment strategy that directly emphasizes both disease states. The commonly used prokinetic remedies, such as domperidone and levosulpiride, increase emptying of stomach, prevent acid or food acid retention and reflux, improve esophageal peristalsis and increase pressure in the lower esophageal sphincter. Levosulpiride and domperidone have prokinetic and antiemetic actions as they antagonize receptors of dopamine in the CNS but also in the GI tract, where dopamine inhibits motility[15]. This study was held to assess the GERD patient's symptom profile and the overlap of symptom between delayed gastric emptying and GERD to govern the scores of FSSG to determine the necessity of treatment given in combination with PPI monotherapy and prokinetic drugs.

METHODS

This questionnaire-based prospective, observational study was conducted in the Department of Medicine, Faisalabad Medical University, Faisalabad from May 2022 to July 2022. After Ethical committee approval, 130 patients were included in the study, who fulfill the inclusion and exclusion criteria.

Outpatients (male and female) 20-70 years of age with symptoms indicative of delayed gastric emptying and/ or GERD for at least 3 months were eligible for enrolment in this study.

Previous gastrointestinal cancer or serious illness (lung or liver cirrhosis, end-stage heart, any malignant neoplasm or cancer, AIDS, alcoholism), gall stones disease, pregnancy, patients on dialysis or gastric surgery, known or suspected users of illegal drugs and breastfeeding mothers were omitted from this analysis. Those who do not answer will be excepted if they decline to response the survey questionnaire.

Assessment of the FSSG score: 7 questions (questions 1, 4, 6, 7, 9, 10 and 12) in the FSSG questionnaire in Table 1 were correlated to acid reflux and five questions (questions 2, 3, 5, 8 and 11) were related to disorders of motility. For each question on the FSSG scale, 5 answer options were given: never (for score = 0), sometimes (for 1 point), sometimes (for 2 points), often (for 3 points), and always (for points). = 3). = 3) for points. points = 4). Thus, the acid / reflux symptom scores ranged from 0 to 28; The

scale of dysmotility symptoms ranges from 0 to 20. A high score of FSSG is the factors associated with PPI monotherapy failure, so GERD with increase score of FSSG needs combination PPI treatment to achieve a more satisfactory result.

All data was documented on the application form and then well-organized by descriptive statistics, accessible as proportion (%) for categorical data and mean ± SD for numerical data. The paired T test is used for statistical analysis using graph pad prism seven. P <0.05 were measured as significant statistically.

RESULTS

In total, the FSSG point questionnaire was completed by 130 patients, of which 60% were men and 40% women (70 men, 60 women). 37.2 years was the patients mean age (20-70 years old). Table-II shows patient's profile.

Table-1: shows the FSSG questionnaire

Using threshold 8 (FSSG score of 8 or higher), 108 (83.1%) of 130 patients with symptoms suggestive of GERD met GERD criteria at threshold 8. Patients with a total FSSG score of 8 or higher: GERD is more likely which requires combination therapy with PPI and prokinetics. The symptoms of the patients improved with the combination therapy having FSSG score> 8.

Table-2: shows the improvement in GERD symptoms with combination therapy of PPI and prokinetics

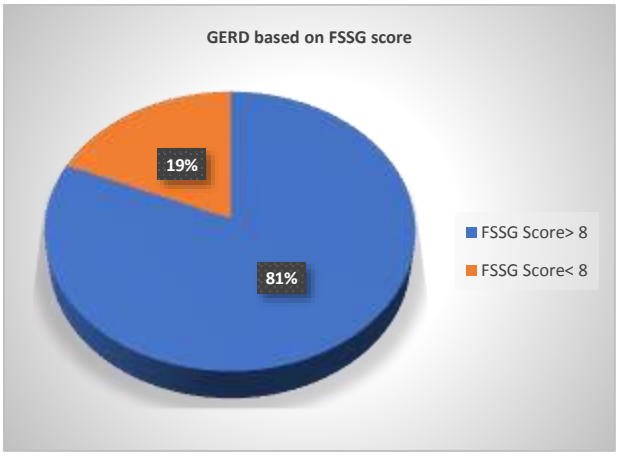
FSSG score	No of patients	GERD Symptoms improve after combination therapy
FSSG>8	108(83.1%)	101(93.5%)
FSSG<8	22(16.9%)	10(45.5%)

Among 130 examined patients, symptoms of dysmotility disorders (9.40 ± 5.30) were more frequent than symptoms of acid reflux (7.31 ± 3.89). In 130 patients, the FSSG score had an overall mean score of 17.20 ± 8.40, and 2 patients had the lowest score of 5 and a maximum overall score of 37 (seen in 1 patient).

Table-3: Patient Demographics

Sl No	Parameter	N (Mean ±S.D.)
1	Gender (Male to Female) 69:53 (56.5:43.5)	
2	Age	20-70
3	Chief complaint 1. Heartburn	106 (81.5 %)
	2. Regurgitation	95 (73.1 %)
	3. Heartburn+ Regurgitation	92 (70.8 %)
4	FSSG Score (Total)	17.20 ± 8.40 (Mean ±S.D.)
	1. Reflux Score	7.43 ± 4.08 (Mean ±S.D.)
	2. Dysmotility/ Dyspeptic score	9.40 ± 5.30 (Mean ±S.D.)

The mean reflux score (7.43 ± 4.08) accounted for 42(32.3%) of the total score of refluxes (28 total score), while the dysmotility disorders mean score was 9.40 ± 5.30, which is 64(49.2%) of the total dysmotility reflux score (20 points). The symptoms of dysmotility disorders in 118 examined patients have predominant reflux symptoms.



DISCUSSION

The association between GERD and gastroparesis is multifactorial. The delayed emptying of stomach related with gastroparesis result in protracted food retention in the stomach, which may be prone to reflux[16]. The delayed gastric emptying in this patient group is believed to be related with the advanced proximal stomach dilatation, which condenses the lower esophageal sphincter length till it becomes insufficient, as does balloon inflation shorten its lengthm of neck[17]. With a condensed sphincter and due to faulty emptying, reflux occurs with more solids and liquids in the stomach after meals[18]. In a subject with clinical signs of GERD-associated heartburn, other symptoms of gastrointestinal like nausea, vomiting and early satiety indicate that progression towards gastroparesis[19]. The existence of delayed emptying of stomach may result in an insufficient response to treatment in these patients. In addition, Ren LH et al meta-analysis in 2016, showed that therapy of combination with prokinetics and PPIs improved the individual life quality by reducing the episodes of acid reflux episodes[20]. In this study, the mean score of FSSG was moderately in height (17.20 ± 8.40). The results of this analysis are in line with the earlier studies presented by Miyamoto et al. Conferring to the study of Miyamoto et al[21]. A high score of FSSG develops to be an aspect related with the PPI monotherapy failure. Miyamoto et al. institute in their study that the group with failed monotherapy of PPI had 17.4 of mean FSSG score, and this group then received therapy in combination with PPI and prokinetics[22]. Miyamoto suggested that the pre-treatment FSSG results could be used to predict the need to add a prokinetic drugs to PPI remedy before treatment[23]. The physicians in Japan generally add a prokinetic drug to the dose of PPI, rather than doubling the PPI dose in cases refractory to monotherapy with PPI. At low pH, PPIs are not stable, the immobility will slow emptying of gastric contents, resultant in PPI retaining[24]. Grounded on these conclusions, the PPI therapy combination with prokinetics will enhance the PPI effect. Moreover, S. Ndraha et al. Confirmed comparable results in their clinical practice and found that the PPIs given in combination of with prokinetics improved the action of PPIs[25].

CONCLUSION

Patients with GERD in this analysis had a high mean score of FSSG, signifying that symptoms of dysmotility were more common than acid reflux. Grounded on these observations, treatment given in combination with prokinetic and PPIs is suggested in the

subgroups of subjects with high scores of FSSG. If the scores of FSSG are high, predominance of dysmotility is suggested, patients respond much more frequently to the combination of prokinetic and PPIs than to PPIs alone. In addition, future studies are needed to assess the improvement in score of FSSG in cases getting PPI therapy in combination with prokinetics in comparison to PPI alone.

REFERENCES

1. Sylvester CN. Current Trends in the Management of Gastroesophageal Reflux Disease:A Review. ISRN Gastroenterol. 2012:391631.
2. Kumar S, Shivalli S. Prevalence, perceptions and profile of gastroesophageal reflux disease in a rural population of north Bihar. National Journal of Community Medicine. 2014;5(2):214-18.
3. Emerson CR, Marzella N. Dexlansoprazole:Proton pump inhibitor with a dual delayed-release system. Clin Ther. 2010;32(9):1578-96.
4. Fass R, Richard WM, Henry PP. Treatment Challenges in the Management of Gastroparesis-Related GERD. Gastroenterol Hepatol. 2009;5(10 Suppl 18):4–16.
5. Carlos AP. Delayed Gastric Emptying in Patients with Abnormal Gastroesophageal Reflux. Ann Surg. 2001;234 (2):147–148.
6. Bais JE, Samsom M, Boudesteijn EAJ, van Rijk PP, Akkermans. Impact of Delayed Gastric Emptying on the Outcome of Antireflux Surgery. Ann Surg. 2001;234(2):139-146.
7. Dominguez-Munoz JE, Sobrino M. Clinical response (remission of symptoms) in erosive and non-erosive gastroesophageal reflux disease. Drugs 2005;65 Suppl 1:43-50.
8. Scarpignato C, Pelosini I. Review article:The opportunities and benefits of extended acid suppression. Aliment Pharmacol Ther. 2006;23(Suppl 2):23–34.
9. Cicalas M, Emerenziani S, Guarino MP, Ribolsi M. Proton pump inhibitor resistance, the real challenge in gastro- esophageal reflux disease. World J Gastroenterol. 2013;19 (39):6529–6535.
10. Singh H, Bala R, Kaur K. Efficacy and Tolerability of Levosulpiride, Domperidone and Metoclopramide in Patients with Non-Ulcer Functional Dyspepsia:A Comparative Analysis. J Clin Diagn Res. 2015;9(4):FC09-FC12.
11. Ren LH, Chen WX, Qian LJ, Li S, Gu M, et al. Addition of prokinetics to PPI therapy in gastroesophageal reflux disease:A meta-analysis. World J Gastroenterol. 2014;20(9):2412-2419.
12. Tutuian R. Update in the diagnosis of gastroesophageal reflux disease. J Gastrointestin Liver Dis. 2006;15(3):243-7.
13. Lawenko RMA, Lee YY. Evaluation of Gastroesophageal Reflux Disease Using the Bravo Capsule pH System. J Neurogastroenterol Motil. 2016;22:25-30.
14. Ndraha S. Frequency scale for the symptoms of GERD score for gastroesophageal reflux disease in Koja hospital. The Indonesian Journal of gastroenterology, Hepatology, and Digestive Endoscopy. 2010;11(2):75-8.
15. Miyamoto M, Haruma K, Takeuci K, Kuwabara M. Frequency scale for symptoms of gastroesophageal reflux disease predicts the need for addition of prokinetics to proton pump inhibitor therapy. J Gastroenterol Hepatol. 2008;23:746–51.
16. Indian Council of Medical Research:New Delhi. Ethical guidelines for biomedical research on human subjects (2006).
17. World Medical Association. Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. JAMA. 2013;310(20):2191-4.
18. Ndraha S. Combination of PPI with a Prokinetic Drug in Gastroesophageal Reflux Disease. Acta Med Indones. 2011;43(4):233-36.
19. Corley DA. Safety and complications of long-term proton pump inhibitor therapy: getting closer to the truth. Gastroenterology. 2019 Sep 1;157(3):604-7.
20. Foocharoen C, Chunlertrith K, Mairiang P, Mahakkanukrauh A, Suwannaroj S, Namvijit S, Wantha O, Nanagara R. Prevalence and predictors of proton pump inhibitor partial response in gastroesophageal reflux disease in systemic sclerosis: a prospective study. Scientific Reports. 2020 Jan 21;10(1):1-9.
21. Triadafilopoulos G, Zikos T, Regalia K, Sonu I, Fernandez-Becker NQ, Nguyen L, Nandwani MC, Clarke JO. Use of esophageal pH monitoring to minimize proton-pump inhibitor utilization in patients with gastroesophageal reflux symptoms. Digestive Diseases and Sciences. 2018 Oct;63(10):2673-80.
22. Zatorski H, Mosinska P, Storr M, Fichna J. Relamorelin and other ghrelin receptor agonists-future options for gastroparesis, functional dyspepsia and proton pump inhibitors-resistant non-erosive reflux disease. J Physiol Pharmacol. 2017 Dec 1;68(6):797-805.
23. Mathew JS, Nandini MR, Saraswathy GR, Subeesh V, Maheswari E. Determinants of Gastroesophageal Reflux Disease (GERD) severity and Utilization of Proton Pump Inhibitors among GERD Patients: A Cross-Sectional Study. Journal of Applied Pharmaceutical Science. 2017 Nov 30;7(11):172-6.
24. Mori H, Suzuki H. Role of acid suppression in acid-related diseases: proton pump inhibitor and potassium-competitive acid blocker. Journal of Neurogastroenterology and Motility. 2019 Jan;25(1):6.
25. Bhutto AR, Abbasi A, Chandio SA, Lolai AA, Arsalan M. Gastroesophageal reflux disease: Treatment options are beyond the proton pump inhibitors. The Professional Medical Journal. 2020 Jul 10;27(07):1401-7.