

# Effectiveness, Safety, and Tolerability of Esomeprazole and Domperidone in Gastroesophageal Reflux Disease

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## ABSTRACT

**Objective:** The purpose of this study was to examine the clinical efficacy, tolerability, and safety of Esomeprazole 20 mg + sustained release (SR) Domperidone 30mg delivered once daily in adult patients for the symptomatic alleviation of dyspepsia associated with GERD.

**Study Design:** Prospective Study

**Place and Duration:** PIMS Hospital Islamabad. Dec 2021- May 2022

**Methods:** Total 97 patients of both genders had symptomatic dyspepsia associated with GERD were presented in this study. Patients were aged between 20-75 years. Informed written consent of all the patients were taken for detailed demographics. Patients were given a fixed-dose combination of Esomeprazole 20 mg and sustained-release (SR) Domperidone 30 mg once day for two weeks. Treatment efficacy was determined by whether or not patients' symptoms improved and whether or not they were happy with the care they received. Physical tests determined the level of safety and tolerability. SPSS 22.0 was used to analyze all data.

**Results:** Among 97 patients, 56 (57.7%) patients were males and 41 (42.3%) were female patients. Mean age of the patients was 38.22±16.49 years. 52 (53.6%) patients were from urban areas and 58 (59.8%) patients were literate. Most common symptoms were heart burn, epigastric pain, acid regurgitation and belching among all cases. Post-treatment, we found significantly reduction in severity of symptoms among all cases with p value <0.002. Frequency of satisfaction rate among all cases was 91 (93.8%). Adverse events were found only in 8 (8.2%) patients.

**Conclusion:** According to the results of this study, a combination of sustained-release (SR) domperidone 30 mg and fixed-dose esomeprazole 20 mg may be an effective and well-tolerated therapy option for the management of symptomatic relief of dyspepsia associated with GERD in adult patients.

**Keywords:** Domperidone, Esomeprazole, Dyspepsia, GERD, Outcomes

## INTRODUCTION

Disease of the oesophagus and stomach (GERD) occurs when stomach acid backs up into the oesophagus and causes discomfort. As the prevalence of GERD rises, it becomes a serious public health concern. It's linked to reduced living standards and a hefty financial hit. The frequency of GERD was estimated to be 13.9% worldwide in a recent meta-analysis, however it varied widely between geographic areas (12.8% in America and Caribbean to 19.5% in North America) and national boundaries (4.1&percent; in China to 22&percent; in Turkey). Approximately 1.03 billion individuals suffer with GERD [1], as reported by the United Nations in their 2017 Review of World Population Prospects. According to research conducted by Ho et al. (1994) [2,] the incidence of GERD symptoms in the multiethnic Asian country of Singapore was 1.6%. Similar authorship from 2001 found a 10.6% rise in heartburn cases [3]. Similarly, one research found that between 1992 and 2001, the prevalence of endoscopic esophagitis in Singapore rose from 3.9% to 9.8%. The lower esophageal sphincter (LES) is the primary site of dysfunction in gastroesophageal reflux, but other physiological and pathologic variables can also play a role. The most typical reason is something called transitory relaxation of the lower esophageal sphincter sphincter, which is a brief period of suppression of the lower esophageal sphincter sphincter tension that happens independently of swallowing. Patients with gastroesophageal reflux disease (GERD) see an increase in their frequency after eating. Delays in stomach emptying can also be caused by other reasons such as a low LES pressure, abdominal swelling, oesophageal blockage, or all three [4]. Acid regurgitation and heartburn (a burning ache in the lower chest that can spread to the oesophagus) are the hallmark symptoms of gastroesophageal reflux disease (GERD) (the perception of stomach content present in the hypopharynx or mouth). Some of the more unusual signs and symptoms include globus, chest discomfort, dysphagia, cough, throat problems, and belching [5]. Oesophagitis, Barrett's oesophagus, and esophageal cancer are all forms of tissue

damage that can result from chronic acid reflux. Both oesophageal (heartburn, regurgitation) and extra-oesophageal symptoms can be brought on by reflux. Symptoms of GERD outside of the oesophagus, such as a persistent cough, asthma, laryngitis, tooth erosions, and gingivitis, are widespread but less well-known. When the typical symptoms of GERD are absent, it may be due to extra-oesophageal involvement [6]. In 2004, researchers Rajendra and Alahuddin [7] observed that 9.7% of Malaysian patients experienced monthly heartburn symptoms and 6% experienced weekly symptoms. Oesophagitis can be seen on endoscopy only in around 20% to 40% of people with GERD symptoms [8].

In patients with GERD, dysmotility and prolonged gastric emptying might cause PPIs to remain in the stomach for an extended period of time, potentially resulting in a poor acid suppression. Getting reaching the small intestine quickly is helpful because of this. Prokinetic drugs improve esophageal peristalsis, stomach emptying, and stool motility by raising pressure on the lower esophageal sphincter. By blocking the H<sup>+</sup>/K<sup>+</sup>-adenosine molecular mechanisms underlying in the proton pump of stomach parietal cells, omeprazole is a very potent inhibitor of gastric acid production. Dopamine is naturally produced in the gut, and blocking its effects with domperidone speeds up GI peristalsis and triggers prolactin production; it's a prokinetic. [9] There were no significant changes in the pharmacokinetics of omeprazole or domperidone when taken together. [10] Co-administration of a proton pump inhibitor (PPI) with a prokinetic drug is an appealing, reasonable, and highly successful therapeutic option for individuals with gastroesophageal reflux disease (GERD). It has been widely utilised in the past, and it has been shown to have therapeutic value for people with GERD. [11]

Since the release of prilosec in 1989, studies have demonstrated that PPIs are significantly more successful than H2RAs (such as ranitidine and cimetidine) in resolving esophagitis and GERD symptoms. All those who have more severe cases of reflux esophagitis are now prescribed PPIs as their first line of treatment, and increasingly so do patients with milder kinds of

esophagitis, especially those who do not react to alternative medicines. PPIs are the best medications for maintaining remission from GERD, since they allow for virtually all patients to remain in remission at optimal dosing. These medicines, as a group, have a stellar safety record. [12,13]

**MATERIAL AND METHODS**

This prospective study was conducted at PIMS Hospital Islamabad and comprised of 97 patients. Informed written consent of all the patients were taken for detailed demographics. Patients <20 years of age, severe medical illness and those did not provide any written consent were excluded from this study.

Patients were aged between 20-75 years. Included patients had symptomatic dyspepsia associated with GERD. Patients were given a fixed-dose combination of Esomeprazole 20 mg and sustained-release (SR) Domperidone 30 mg once day for two weeks. Treatment efficacy was determined by whether or not patients' symptoms improved and whether or not they were happy with the care they received. Physical tests determined the level of safety and tolerability. SPSS 22.0 was used to analyze all data. Frequencies and percentage was used for categorical variables while mean standard deviation as used for data presentation.

**RESULTS**

Among 97 patients, 56 (57.7%) patients were males and 41 (42.3%) were female patients. Mean age of the patients was 38.22±16.49 years. 52 (53.6%) patients were from urban areas and 58 (59.8%) patients were literate.(table 1)

Table-1: Baseline characteristics of enrolled cases

Variables	Frequency	Percentage
Mean age (years)	38.22±16.49	
Gender		
Male	56	57.7
Female	41	42.3
Area Of Living		
Rural	45	46.4
Urban	52	53.6
Literacy		
Yes	58	59.8
No	39	40.2

Most common symptoms were heart burn, epigastric pain, acid regurgitation and belching among all cases.(figure-1)

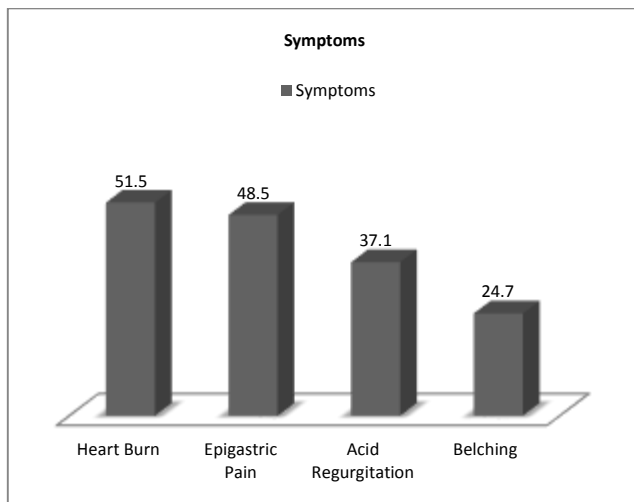


Figure-1: Symptoms among all cases

Post-treatment, we found significantly reduction in severity of symptoms among all cases with p value <0.002.(table-2)

Table-2: Post-treatment efficacy among all cases

Variables	Before Treatment Severity	After Treatment Severity
Diseases		
Heart Burn	3.10±7.24	0.4±1.05
Epigastric Pain	3.9±6.15	0.9±0.22
Acid Regurgitation	3.7±5.23	0.2±2.32
Belching	3.2±2.11	0.36±1.23

Frequency of satisfaction rate among all cases was 91 (93.8%).(figure 2)

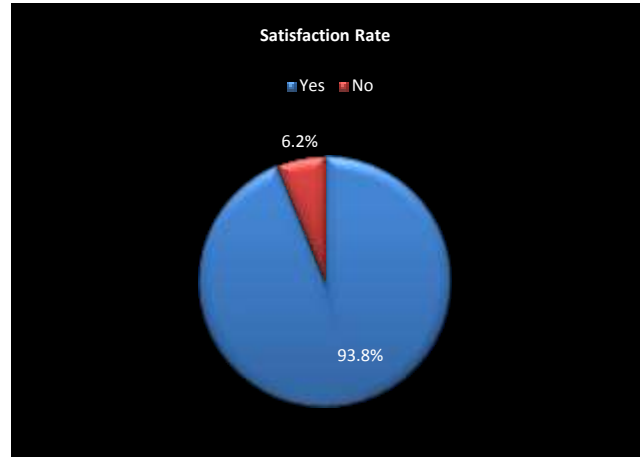


Figure-2: Satisfaction rate among all cases

Adverse events were found only in 8 (8.2%) patients. (table 3)

Table-3: Frequency of adverse effects among all cases

Variables	Frequency	Percentage
Side Effects		
Yes	8	8.2
No	89	91.8
Types of Side effect		
Nausea	3	3.1
Constipation	2	2.1
Drowsiness	2	2.1
Headache	1	1.03

**DISCUSSION**

The pathophysiology of GERD is complex and multifaceted. Since the 1960s, LES dysfunction has been regarded as a continuum along with GERD. Symptomatic yet non-erosive GERD is brought on by insignificant malfunction, like momentary LES relaxations (NERD). Severe dysphagia patients may develop Barrett's oesophagus or erosive oesophagitis (BE). Hiatus hernia and inadequate oesophageal motility are important variables in this continuum, which shows a pathological deterioration in LES function. Predisposing variables and pathophysiology that diverge from this paradigm are present in a large number of GERD patients. While having an aberrant sensory processing, patients with acid hypersensitivity might have a normal LES. Although heartburn and regurgitation are the primary symptoms of GERD, studies have shown that up to 50% of patients may also experience other dysmotility symptoms, such as nausea, early satiety, and epigastric discomfort or fullness. To enhance the patient's quality of life and lower the costs connected with acid-related illnesses, symptoms must be resolved. [14,15]

In current study 97 patients were presented. Among 97 patients, 56 (57.7%) patients were males and 41 (42.3%) were female patients. Mean age of the patients was 38.22±16.49 years. 52 (53.6%) patients were from urban areas and 58 (59.8%) patients were literate. Prior studies presented same results to our study.[16,17] Domperidone had been selected as the prokinetic

medication. While having good clinical efficacy, it does not pass the blood-brain barrier like metoclopramide does, has less SEs[18], a reduced cardiovascular risk, and fewer SEs. In patients with gastroparesis, domperidone and erythromycin both improved the symptom score more than other prokinetics. [19] Omeprazole 40 mg is clearly superior to Proton pump inhibitor 20 mg in controlling intragastric pH, as previously mentioned. So, for the therapy of GERD patients, we have chosen an omeprazole dose of 40 mg. [20]

In current study, we found significantly reduction in severity of symptoms among all cases with p value <0.002. The mean score for heartburn was significantly reduced by 88%, and the mean score for epigastric discomfort was significantly reduced by 84% at the conclusion of the treatment. At the conclusion of the trial, there was a considerable decline in the average score for acid regurgitation (85%). The mean score of belching also showed a statistically significant reduction of 89% after therapy. To treat endoscopically declared reflux acid reflux disease, omeprazole or in mixture with qasp was more effective than zantac alone or specialized form alone, and the mixture of omeprazole and specialized form was more efficient than ranitidine plus cisapride in preserving remission at 12 months of treatment. [20] When comparing cimetidine alone to cimetidine and metoclopramide, combination treatment was found to be superior in the management of GERD symptoms. [21] The combo of omeprazole 20 mg once daily and cisapride 5 mg thrice day was more effective than omeprazole 20 mg orally daily in curing class II esophagitis when provided for 8 weeks, according to another research. [22]

In current study, adverse events were found only in 8 (8.2%) patients. Most common side effects were nausea, constipation, headache and drowsiness. Fixed-dose combination therapy with 20 mg of esomeprazole and 30 mg of domperidone sustained-release (SR) was well tolerated.

## CONCLUSION

According to the results of this study, a combination of sustained-release (SR) domperidone 30 mg and fixed-dose esomeprazole 20 mg may be an effective and well-tolerated therapy option for the management of symptomatic relief of dyspepsia associated with GERD in adult patients.

## REFERENCES

- 1 Nirwan, J.S.; Hasan, S.S.; Babar, Z.-U.-D.; Conway, B.R.; Ghori, M.U. Global prevalence and risk factors of gastro-oesophageal reflux disease (GORD): Systematic review with meta-analysis. *Sci. Rep.* 2020, 10, 5814.
- 2 Ho, K.Y.; Kang, J.Y.; Seow, A. Prevalence of gastrointestinal symptoms in a multiracial Asian population, with particular reference to reflux-type symptoms. *Am. J. Gastroenterol.* 1998, 93, 1816–1822.
- 3 Ho, K.Y.; Chan, Y.H.; Kang, J.Y. Increasing trend of reflux esophagitis and decreasing trend of *Helicobacter pylori* infection in patients from a multiethnic Asian country. *Am. J. Gastroenterol.* 2005, 100, 1923–1928. [CrossRef]

- 4 DeVault, K.R.; Castell, D.O. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Am. J. Gastroenterol.* 2005, 100, 190–200.
- 5 Talley, N.J.; Zand Irani, M. Optimal management of severe symptomatic gastroesophageal reflux disease. *J. Intern. Med.* 2021, 289, 162–178.
- 6 Durazzo, M.; Lupi, G.; Cicerchia, F.; Ferro, A.; Barutta, F.; Beccuti, G.; Gruden, G.; Pellicano, R. Extra-esophageal presentation of gastroesophageal reflux disease: 2020 update. *J. Clin. Med.* 2020, 9, 2559.
- 7 Rajendra, S.; Alahuddin, S. Racial differences in the prevalence of heartburn. *Aliment. Pharmacol. Ther.* 2004, 19, 375–376.
- 8 Kumar, D.; Vinod, K.; Razavi, M. Gastroesophageal reflux disease: A Review of Superior Effects of Proton Pump Inhibitors and Prokinetic agents as a Combination Therapy versus Monotherapy. *Management* 2011, 705, 701–705.
- 9 Lowe RC. Medical management of gastroesophageal reflux disease. PART 1 Oral cavity, pharynx and esophagus—review [published online ahead of print May 16, 2006].
- 10 Zhang YF, Chen XY, Dai XJ, et al. Influence of omeprazole on pharmacokinetics of domperidone given as free base and maleate salt in healthy Chinese patients. *Acta Pharmacol Sin.* 2007;28:1243–1246.
- 11 Abbasiazaria M, Panahib Y, Mortazavic SA, et al. Effect of a combination of omeprazole plus sustained release Baclofen versus omeprazole alone on symptoms of patients with gastroesophageal reflux disease (GERD). *Iran J Pharm Res.* 2014;13:1221–1226.
- 12 Pignon JP, Poynard T, Naveau S, et al. Treatment of gastroesophageal reflux: Analysis of randomized double-blind trials. *Gastroenterol. Clin. Biol.* 1987 Oct.; 11(10): 668-680.
- 13 Klinkenberg-knol EC, Festen HP and Meuwissen SG. Pharmacological management of gastroesophageal reflux disease. *Drugs*, 1995 May; 49(5): 695-710.
- 14 Ramakrishna a and kaz PO. Pharmacologic management of gastroesophageal reflux disease. *Curr. Treat. Options Gastroenterol.* 2002 Aug; 5(4): 301-310
- 15 Klinkenberg-knol EC, Festen HP and Meuwissen SG. Pharmacological management of gastroesophageal reflux disease. *Drugs*, 1995 May; 49(5): 695-710.
- 16 Zamani, N.F.; Sjahid, A.S.; Tuan Kamauzaman, T.H.; Lee, Y.Y.; Islam, M.A. Efficacy and Safety of Domperidone in Combination with Proton Pump Inhibitors in Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. *J. Clin. Med.* 2022, 11, 5268
- 17 Vedamanickam, Dr. R. et al. "EVALUATION OF THE EFFICACY, TOLERABILITY AND SAFETY OF A COMBINATION OF ESOMEPRAZOLE AND DOMPERIDONE IN GERD." (2016).
- 18 Champion MC, Hartnett M, Yen M. Domperidone, a new dopamine antagonist. *CMAJ.* 1986;135:457–461
- 19 Sturm A, Holtmann G, Goebell H, Gerken G. Prokinetics in patients with gastroparesis: a systematic analysis. *Digestion.*
- 20 Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol.* 2013;108:308-328.
- 21 Vigenieri s, Termini R, Leandro G, Badalmenti S, Pantalena M, Savarino V, Di Mario F, Battaglia G, Meal GS, Pilotto A, et al. A comparison of five maintenance therapies for reflux esophagitis. *N.*
- 22 Lieberman DA and Keeffe EB. Treatment of severe reflux esophagitis with cimetidine and metoclopramide. *Ann. Intern- Med.* 1986 Jan.; 104(1): 21-26.