e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(8); 1449-1453

Original Research Article

A Randomized Control Study Comparing the Safety and Effectiveness of Pantoprazole Alone Versus Pantoprazole plus Amitriptyline in Patients with Functional Dyspepsia

Kundan Kumar Jha[1], Sameer Kumar[2]

[1]Associate Professor, Department of Pharmacology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

[2]Professor and HOD, Department of Pharmacology, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

Received: 01-05-2026 / Revised: 15-06-2026 / Accepted: 21-07-2026

Corresponding author: Dr. Kundan Kumar Jha

Conflict of interest: Nil

Abstract

Background: Patients with ulcer-like symptoms who do not have overt gastroduodenal ulcers are referred to as having functional dyspepsia. Postprandial distress syndrome (PDS), epigastric pain syndrome (EPS), and functional dyspepsia can be further classified according to the existence of meal-related symptoms. Postprandial fullness, early satiation, burning or discomfort in the epigastrus, and the absence of structural illness symptoms are some of its characteristics. When treating patients with functional dyspepsia, pantoprazole by itself is compared to pantoprazole plus amitriptyline.

Methods: In order to compare the safety and effectiveness of pantoprazole with pantoprazole plus amitriptyline in patients with functional dyspepsia, this randomized, prospective, open label, comparative interventional study was carried out in the Department of Pharmacology with other related departments that admitted patients with functional dyspepsia at Bhagwan Mahavir Institute of Medical Sciences, Pawapuri Nalanda, Bihar from August 2024 to July 2025. Follow-up was carried out four weeks after the start of treatment.

Results: A total of 142 cases were divided into two groups: Group 1 (pantoprazole alone, n = 68) and Group 2 (pantoprazole + amitriptyline, n = 74). The Glasgow dyspepsia severity score (GDSS) (4.26±1.14 versus 3.3±1.37, p=0.002), short form leads dyspepsia questionnaire (SF-LDQ) (4 [3-5] versus 3 [2-4], p=0.005), and visual analogue pain score (VAS) (1 [1-2] versus 1 [0-1], p=0.009).

Conclusion: With no serious safety issues, the combination of pantoprazole and amitriptyline improved functional dyspepsia symptoms more effectively than pantoprazole alone.

Keywords: Amitriptyline, Glassgow dyspepsia severity score, Pantoprazole, Visual analog scale.

DOI: 10.25258/ijcpr.18.8.216

Introduction

A wide range of symptoms, from postprandial fullness to early satiety and epigastric pain, are associated with dyspepsia. Dyspepsia affects 20–30% of people worldwide. It is more common in women and is marginally greater in the Western population. Although the exact frequency of dyspepsia in India is unknown, some studies suggest that between 7.6 and 49% of Indians suffer from it.

Rome IV is the result of the Rome committee's repeated, increasingly precise definitions of dyspepsia.[1] By omitting individuals with heartburn and acid regurgitation, these classifications have aimed to reduce the inclusion of gastro-esophageal reflux disease in those with dyspepsia.[2] Functional gastrointestinal diseases (FGIDs) are classified by the Rome Foundation mostly on the basis of symptoms, not physiological criteria.[3] Disorders of the gut-brain connection are known as functional gastrointestinal (GI) disorders. It is a collection of conditions categorized by GI symptoms associated with any combination of the following: changes in gut microbiota, immunological and mucosal function, motility disruption, visceral hypersensitivity, and central nervous system (CNS) processing.[4]

Patients with ulcer-like symptoms who do not have overt gastric or duodenal ulcers are referred to as having functional dyspepsia. Postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS) are two subtypes of functional dyspepsia. based on the existence of meal-related symptoms.

Postprandial fullness, early satiation, burning or discomfort in the epigastrus, and the absence of structural illness symptoms are some of its characteristics.[5] Approximately one-third of the normal people surveyed in the International Gastroenterology Surveillance Study (DIGEST), which included over 5500 participants, reported having dyspeptic symptoms, including acute dyspepsia in 6.5% of instances and chronic dyspepsia in 22.5% of cases. The social impact of their symptoms is only significant enough for 10 to 25 percent of people to seek medical attention.[6] In the long run, only 20% of people with functional dyspepsia achieve symptom freedom.[6, 7]

The idea that functional dyspepsia is an idiopathic condition is evolving. Acute intestinal inflammation may be a factor in the development of functional dyspepsia following acute infectious gastroenteritis.

To make a clinical diagnosis and start treatment, a normal history of persistent problematic early satiety and postprandial fullness is sufficient; nevertheless, gastroscopy is frequently needed.

Endoscopy should be prompted by any of the following red flag symptoms: escalating dysphagia or odynophagia, iron deficiency anemia, vomiting, bleeding, unexpected weight loss, new onset in older age, or a family history of upper gastrointestinal cancer. Otherwise, it seems sense to use a breath or stool antigen test to check for H. pylori infection and treat those who test positive.[6]

The goal of treatment is to improve quality of life, social functioning, and symptoms. A recent small RCT of aerobic exercise in addition to conventional care showed a substantial advantage on dyspepsia symptoms when compared with conventional management alone, despite the lack of evidence that lifestyle modifications enhance symptoms.[8]

Pantoprazole, a proton pump inhibitor, was the traditional treatment for acid reflux illness. The combination treatment of pantoprazole and amitriptyline, a tricyclic antidepressant, was found to be more effective than pantoprazole alone because functional dyspepsia involves gut-brain contact.

Material and Methods

This randomized, prospective, open label, comparative interventional study was carried out in the Department of Pharmacology with other related departments that admitted patients with functional dyspepsia at Bhagwan Mahavir Institute of Medical Sciences, Pawapuri Nalanda, and Bihar from August 2024 to July 2025.

This study included all consenting adult patients between the ages of 18 and 75, regardless of gender, who had no upper gastrointestinal endoscopic evidence of structural disease that could account for their symptoms.

Patients with cirrhosis, chronic kidney disease, chronic heart failure, coronary artery disease, and amitriptyline contraindications, such as prostatic disease, glaucoma, history of seizures, retention of urine, or use of similar drugs within the previous two weeks, were excluded from this study, as were pregnant and lactating women, active alcohol consumers, patients allergic to or with known contraindications to any of the study drugs.

Every patient with uninvestigated dyspepsia who visited the gastroenterology outpatient department had abdominal ultrasonography (USG) and upper GI endoscopy (UGIE). Before being diagnosed with functional dyspepsia, patients were tested for H. pylori using either a stool antigen test or a histological evaluation of a stomach antrum biopsy. Patients who met the criteria for functional dyspepsia and showed no signs of any structural disease or organic dyspepsia were added to the trial after carefully reading and comprehending the patient information leaflet about the study and its associated features.

Following the participants' written informed consent, computer-generated random numbers were used to assign them to either group A or B.

Prior to starting treatment, the following tests were performed: baseline haemoglobin (Hb), total leukocyte count (TLC), fasting blood sugar (FBS), serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), serum urea, serum creatinine, and serum electrolytes. These tests were then repeated after four weeks of treatment.

For four weeks, individuals in group A took 40 mg of pantoprazole orally with water half an hour before breakfast (BBF).

For four weeks, the participants in group B took pantoprazole 40 mg BBF + amitriptyline 10 mg orally with water at bedtime (hs).

On the day following the start of therapy, patients were called to ask about any discomfort or adverse effects.

Microsoft Excel was used to tabulate the data and analyze it for a number of criteria. The statistical package for social sciences (SPSS) software, manufactured by IBM in Chicago, USA, version 25.0, was used for the final analysis once the data entry was completed in the Microsoft Excel spreadsheet. Mean±standard deviation (mean±SD) was used to display quantitative data. The two groups' continuous variables were compared using the Student's t-test. The qualitative data between the two groups was compared using Chi square or

Fisher's exact probability test. A P value of less than 0.05 was considered statistically significant.

Results

The study comprised 142 people between the ages of 18 and 75 who showed no signs of structural disease. They were split into two groups at random: For four weeks, participants in the pantoprazole group (n=68) received 40 mg of pantoprazole orally 30 minutes prior to breakfast (BBF). For four weeks, participants in the pantoprazole plus amitriptyline group (n = 74) received 40 mg of pantoprazole and 10 mg of BBF + amitriptyline orally at bedtime (hs). In this investigation, the baseline and demographic features of both groups were comparable. There was no significant difference (p=0.605) between the mean±standard deviation (SD) age of 45.38±15.31 in the pantoprazole only group and 47.27±15.26 in the pantoprazole plus amitriptyline group. The gender distribution of the pantoprazole only group and the pantoprazole plus amitriptyline group in our study was similar (female: 52.94% against 59.46%, male: 47.06% versus 40.54%) (p=0.58). (Table 1)

Table 1: Gender-wise distribution of patients between two groups

Gender	Pantoprazole only group (n=68) (%)	Pantoprazole plus amitriptyline group (n=74)(%)	Total (%)	P value
Female	36 (52.94%)	44 (59.46%)	80 (56.34)	0.58†
Male	32 (47.06%)	30 (40.54%)	62 (43.66%)	
Total	68 (100%)	74 (100%)	142 (100%)	

†Chi square test

The distribution of patients by gender between two groups is shown in Table 1, where all patients in both groups had WNL ECGs, normal UGIEs, and negative H. pylori tests.

The pantoprazole plus amitriptyline group's mean±SD of improvement (%) was 66.51±11.72, which was substantially higher than the pantoprazole only group's (58.28±8.91) (p value=0.001).

The two groups' baseline laboratory values were similar, including hemoglobin (Hb), total leukocyte count (TLC), fasting blood sugar (FBS), serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), serum urea, serum creatinine, and serum electrolytes. Haemoglobin (Hb), total leukocyte count (TLC), fasting blood sugar (FBS), serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), serum urea, serum creatinine, and serum electrolytes were all similar before and after treatment. This finding implies that both medications are safe for the target demographic. [Tables 2-4]

Table 2: Comparison of haemoglobin and TLC levels between two groups

Blood parameters	Pantoprazole only group (n=68)	Pantoprazole plus amitriptyline group (n=74)	Total	P value
Haemoglobin(g/dl)				
Mean±SD	12.62±1.47	12.15±1.36	12.38±1.42	0.167‡
Median(25^{th}-75^{th}percentile)	12.8(12-13.6)	12.4(11.2-13)	12.6(11.3-13.4)	
Range	9.4-15.2	9.4-14.6	9.4-15.2	
Total leucocyte count (cells/mm³)				
Mean±SD	6691.18±814.4	6683.78±819.73	6687.32±811.34	
Median(25^{th}-75^{th}percentile)	6600(6250-7000)	6500(6200-7000)	6600(6200-7000)	0.97‡
Range	5100-10000	5100-10000	5100-10000	

‡Independent t test

Table 3: Comparison of fasting blood sugar (mg/dl) between two groups

Fasting blood sugar (mg/dl)	Pantoprazole only group (n=68)	Pantoprazole plus amitriptyline group (n=74)	Total	P value
Mean±SD	83.68±8.55	83.24±8.8	83.45±8.62	0.834‡
Median (25^{th}-75^{th}percentile)	84(78-90)	84(78-90)	84(78-90)	
Range	70-98	69-98	69-98	

‡Independent t test

Table 4: Comparison of LFT and RFT parameters between two groups

Parameters	Pantoprazole Only group (n=68)	Pantoprazole plus amitriptyline group (n=74)	Total	P value
SGOT (IU/l)				
Mean±SD	26.68±10.43	27.14±10.23	26.92±10.26	0.852‡
Median (25^{th}-75^{th}percentile)	25.5(18-32.75)	26(18-34)	26(18-34)	
Range	14-49	14-49	14-49	
SGPT (IU/l)				
Mean±SD	20.65±8.4	20.38±7.71	20.51±7.99	0.889‡
Median (25^{th}-75^{th}percentile)	18(14-27.75)	20(12-27)	18(13-27)	
Range	10-42	10-37	10-42	
Serum urea (mg/dl)				
Mean±SD	16.24±5.66	15.95±5.25	16.08±5.41	0.824‡
Median (25^{th}-75^{th}percentile)	16.5(12-21.5)	15(12-20)	15(12-20)	
Range	6-25	6-25	6-25	
Serum creatinine (mg/dl)				
Mean±SD	0.73±0.17	0.73±0.15	0.73±0.16	0.982‡
Median (25^{th}-75^{th}percentile)	0.72(0.62-0.868)	0.72(0.62-0.89)	0.72(0.62-0.89)	
Range	0.4-1.06	0.4-1.06	0.4-1.06	

‡Independent ttest

Prior to starting therapy, both groups in our study had similar GDSS scores (9.44±2.13 versus 9.41±2.03, p=0.943). After therapy, however, there was a significant difference in GDSS between the two groups (4.26±1.14 versus 3.3±1.37, p=0.002), with the pantoprazole plus amitriptyline group having a much lower GDSS. Following treatment, GDSS significantly decreased in each group (p<0.0001 for both groups).

Prior to treatment, the SF-LDQ scores of the two groups in our study were similar (10 [7.25-14] versus 9 [8-12], p=0.481). After therapy, however, there was a significant difference in SF-LDQ between the two groups (4 [3-5] versus 3 [2-4], p=0.005), with the pantoprazole plus amitriptyline group having a significantly lower score. Following therapy, SF-LDQ significantly decreased in each group (p<0.0001 for both groups).

Prior to therapy, both groups in our study had similar VAS scores (4 [4-5] versus 4 [4-4], p=0.157). Following therapy, there was a significant difference between the two groups' VAS scores (1 [1-2] versus 1 [0-1], p=0.0009), with the pantoprazole plus amitriptyline group having considerably lower values. Following therapy, VAS scores significantly decreased within each group (p<0.0001 for both groups).

Discussion

With a p value of 0.001 indicating strong statistical significance, the pantoprazole plus amitriptyline group's mean improvement in dyspepsia severity as judged by GDSS was substantially larger (66.51±11.72) than the pantoprazole-only group's (58.28±8.91). This is consistent with other research, such as the randomized controlled trial by Liu et al., which found that in comparable patient populations, amitriptyline had a greater response rate (53%) than pantoprazole (38%).[9] The findings of this study lend credence to the theory that better treatment outcomes for functional dyspepsia can be achieved by combining a proton pump inhibitor with an antidepressant. The findings' validity is strengthened by the fact that demographic factors, such as age and gender distribution, were similar between the two groups. This suggests that therapy, rather than demographic disparities, is most likely the cause of observed differences in outcomes. The gender distribution did not differ substantially (p=0.58), and the mean age was similar for both groups (45.38±15.31 for pantoprazole only and 47.27±15.26 for the combination group).

Liu et al. conducted a randomized controlled trial (RCT) in 2021 to compare amitriptyline with pantoprazole for the treatment of functional dyspepsia. There was no significant difference between the mean ages of the amitriptyline plus pantoprazole group (41±11.50) and the pantoprazole group (41.29±10.84) (p=0.964).[9]

Because baseline laboratory indicators were similar after therapy, both treatment regimens had an acceptable safety profile. This observation is in line with research showing that pantoprazole and other proton pump inhibitors are generally safe and well-tolerated. The safety of this combination therapy is further supported by the fact that amitriptyline and pantoprazole have been demonstrated to be safe and effective in treating gastroesophageal reflux disease (GERD) linked to anxiety.[10]

The results of this study are in line with earlier studies that emphasized the advantages of taking multiple drugs to treat functional dyspepsia. For example, the experiment conducted by Liu et al.

confirmed that amitriptyline is more effective when combined with pantoprazole.[10]

The effectiveness of a fixed-dose combination (FDC) of itopride [a prokinetic (PK) drug] and rabeprazole in the treatment of FD was demonstrated by Ghosh and associates [Ghosh et al. 2008]. With 93% of patients having an excellent or good response to treatment, the data showed that the majority of patients experienced symptom relief.[11] Furthermore, research has demonstrated that pantoprazole's pharmacokinetic characteristics maximize its effectiveness when taken in the morning, which may further improve symptom alleviation when used with amitriptyline.[11] This implies that enhancing treatment outcomes for patients with functional dyspepsia may depend critically on timing and combination therapy. Tricyclic antidepressants, such as amitriptyline, have been shown in earlier research to be effective in treating functional dyspepsia. The effects on visceral hypersensitivity, gastric accommodation, and cerebral pain modulation are among the suggested mechanisms; these are probably caused by amitriptyline's antagonistic actions on serotonin, histamine, and norepinephrine receptors. These results aid in the interpretation of the better symptomatic improvement observed in the current trial when pantoprazole and amitriptyline were combined as opposed to pantoprazole alone. Research has shown that functional dyspepsia is connected with a substantial financial burden and a reduced quality of life, underscoring the need for efficient treatment options such as the combination medication this study examined. It has also been demonstrated that improving quality of life and lowering healthcare utilization can be achieved by developing an efficient doctor-patient connection and a shared understanding in the therapy of functional dyspepsia.

Conclusion

With no serious safety issues, the combination of pantoprazole and amitriptyline improved functional dyspepsia symptoms more effectively than pantoprazole alone. These results imply that the combination therapy should be taken into consideration as a first-line treatment option for patients with functional dyspepsia; nevertheless, more validation in bigger studies is required.

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