

## Original Research Article

# COMPARISON OF EFFICACY OF PANTOPRAZOLE WITH OR WITHOUT DOMPERIDONE IN THE MANAGEMENT OF REFLUX DISEASE

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## ABSTRACT

**Background:** Reflux disease is a condition caused by regurgitation of stomach contents or acid into the esophagus and characterized by heartburn. Prokinetics promotes the anterograde movement in the gastrointestinal tract by increasing the lower esophageal sphincter pressure and enhancing peristalsis. The objective of the study was to compare the efficacy of pantoprazole with or without domperidone in the management of reflux disease by comparing the magnitude of change in Reflux Symptom Index score.

**Materials and Methods:** A randomized controlled trial was conducted among 97 patients presenting with Reflux disease to the Department of Otorhinolaryngology, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi. The study was done over a period of 1 (one) year from January 2019 to December 2019, after obtaining ethical approval from the institutional ethics committee.

**Results:** The mean age of the study population in Group 1 was 31.56±11.08 years, Group 2 was 34.73±10.49 years, Group 3 was 33.70±12.03 years and Group 4 was 38.14±9.20 years. The most common presenting symptom was heartburn in 98% (95) patients. On comparison of change in Reflux Symptom Index scores of different components at week 10, for the symptoms of hoarseness or change in voice improvement was statistically significant with p value <0.01 and heartburn or dyspepsia with statistically significant p value <0.01.

**Conclusion:** Reflux disease treated with the drug combination of pantoprazole with domperidone taken before sleep is most efficacious in improving the symptoms of reflux disease based on the Reflux Symptom Index score compared before and after treatment.

**Keywords:** Reflux disease, Heartburn, Pantoprazole, Domperidone, Reflux Symptom Index score.

## INTRODUCTION

Reflux disease is a condition caused by regurgitation of stomach contents or acid into the esophagus and characterized by heartburn. Reflux disease is of two types i.e. Gastroesophageal Reflux Disease (GERD) and Laryngopharyngeal Reflux Disease (LPRD). Gastroesophageal reflux disease is a condition where reflux of gastric contents causes symptoms or

complications such as heartburn or acid indigestion impairing the quality of life or leading to mucosal damage or complications.<sup>[1]</sup> Laryngopharyngeal reflux disease is a condition of reflux of gastric contents into the larynx, pharynx, and upper aerodigestive tract via esophagus and mainly presents with symptoms like globus pharyngeus, clearing of throat, persistent cough and change in voice.<sup>[2]</sup> The symptoms of reflux disease can be classified as typical (heartburn, regurgitation) and

atypical (hoarseness, chest pain, dyspepsia, nausea). GERD usually manifests during night time and on lying down position whereas LPRD manifests during daytime and in the upright position.<sup>[3]</sup> Gastroesophageal reflux is considered normal physiologically if the exposure time is less than 5% in 24 hours.<sup>[4]</sup>

Prokinetics promotes the anterograde movement through the gastrointestinal tract by increasing the lower esophageal sphincter pressure and thus enhancing peristalsis.<sup>[5]</sup> Domperidone is a gastropromotkinetic agent which helps to treat dyspepsia by increasing the gastric emptying and preventing the reflux of gastric contents.<sup>[6]</sup> The beneficial effect of a combination of proton pump inhibitors with prokinetic is due to their synergistic activity of decreasing the acid production, improving the function of the lower esophageal sphincter, improving the motility of the esophagus, increasing the activity of gastric emptying and hence a better therapeutic response.<sup>[7]</sup>

## MATERIALS AND METHODS

**Study design:** A randomized controlled trial was conducted in the Department of Otorhinolaryngology, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi over a period of 1 (one) year from January 2019 to December 2019. The objective of the study was to compare the efficacy of Pantoprazole with or without Domperidone in the management of Reflux Disease by comparing the magnitude of change in Baylor Reflux Symptom Index score of patients based on symptoms.

**Ethical Considerations:** The study was conducted after obtaining ethical clearance from the institutional ethics committee of Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi.

**Inclusion Criteria:** Patients of both gender aged 18 to 60 years of age presenting with symptoms of

reflux disease according to Baylor Index >13. Those who gave consent to undergo the study.

**Exclusion Criteria:** Patients below 18 years of age and those with comorbidities such as cancer, hiatus hernia, etc. Those patients not willing to participate in the study were excluded.

**Study procedure:** The participants were informed about the nature of the study which was fully explained in the participant information sheet and only those who agreed to undergo the study signed in the informed consent form. Their participation was completely voluntary and right to deny to participate in the study was reserved. Privacy and confidentiality was maintained at all cost for each participant. The participants were divided into four groups using a random number table. The time of administration of drugs were compared to see the efficacy of the drugs. Baylor Reflux Index was used for the purpose of screening and statistical analysis for the patients clinically determined to have Reflux Disease and not for the diagnosis. The patients were treated for a total of 6 weeks. Follow up was done with Baylor Reflux Symptom Index every 2 weeks on treatment and then 4 weeks after completion of treatment i.e. total duration of 10 weeks.

In the study, the participants were divided into 4 groups based on the treatment received by each group.

|   |   |
|---|---|
| <b>GROUP 1</b><br>Pantoprazole 40 mg before breakfast                         | <b>GROUP 2</b><br>Pantoprazole 40 mg before sleep at night                        |
| <b>GROUP 3</b><br>Pantoprazole 40 mg with Domperidone 10 mg before breakfast. | <b>GROUP 4</b><br>Pantoprazole 40 mg with Domperidone 10 mg before sleep at night |

**Statistical Analysis:** The collected data was analysed using SPSS (Statistical Package for Social Sciences software) version 21.0. Microsoft word and Excel were used to generate graphs, tables etc. Descriptive statistics like frequency, percentage, mean, standard deviation and proportions were used. A probability value < 0.05 was considered as statistically significant.

## RESULTS

**Table 1: Baseline characteristics of the study population**

| Characteristics               | Pantoprazole 40 mg before breakfast (n=25) | Pantoprazole 40 mg before sleep at night (n=30) | Pantoprazole 40 mg with Domperidone 10 mg before breakfast (n=20) | Pantoprazole 40 mg with Domperidone 10 mg before sleep at night (n=22) |
|-------------------------------|--|---|---|--|
| <b>Age group</b>              |  |   |   |  |
| 18-25 years                   | 10 (40.0%)                                 | 8 (26.7%)                                       | 8 (40.0%)   | 2 (9.1%)   |
| 26-35 years                   | 7 (28.0%)                                  | 9 (30.0%)                                       | 3 (15.0%)   | 7 (31.8%)  |
| 36-45 years                   | 5 (20.0%)                                  | 8 (26.7%)                                       | 7 (35.0%)   | 7 (31.8%)  |
| >45 years                     | 3 (12.0%)                                  | 5 (16.7%)                                       | 2 (10.0%)   | 6 (27.3%)  |
| <b>Gender</b>                 |  |   |   |  |
| Male                          | 9 (36.0%)                                  | 8 (26.7%)                                       | 6 (30.0%)   | 9 (40.9%)  |
| Female                        | 16 (64.0%)                                 | 22 (73.3%)                                      | 14 (70.0%)  | 13 (59.1%)   |
| <b>Symptoms</b>               |  |   |   |  |
| Hoarseness of voice           | 18 (72.0%)                                 | 22 (73.3%)                                      | 16 (80.0%)  | 18 (91.8%)   |
| Clearing of throat            | 21 (84.0%)                                 | 28 (73.3%)                                      | 19 (95.0%)  | 21 (95.5%)   |
| Excess mucous/post nasal drip | 20 (80.0%)                                 | 27 (90.0%)                                      | 18 (90.0%)  | 22 (100.0%)  |

|                              |             |            |             |             |
|------------------------------|-------------|------------|-------------|-------------|
| Difficulty in swallowing     | 15 (16.0%)  | 17 (56.7%) | 11 (55.0%)  | 13 (59.1%)  |
| Coughing after eating        | 7 (28.0%)   | 12 (40.0%) | 10 (50.0%)  | 8 (36.4%)   |
| Breathing difficulty/choking | 16 (64.0%)  | 21 (70.0%) | 14 (70.0%)  | 13 (59.1%)  |
| Troublesome/annoying cough   | 9 (36.0%)   | 10 (33.3%) | 7 (35.0%)   | 8 (36.4%)   |
| Lump in throat sensation     | 25 (100.0%) | 29 (96.7%) | 17 (85.0%)  | 21 (95.5%)  |
| Heartburn, chest pain        | 24 (96.0%)  | 29 (96.7%) | 20 (100.0%) | 22 (100.0%) |

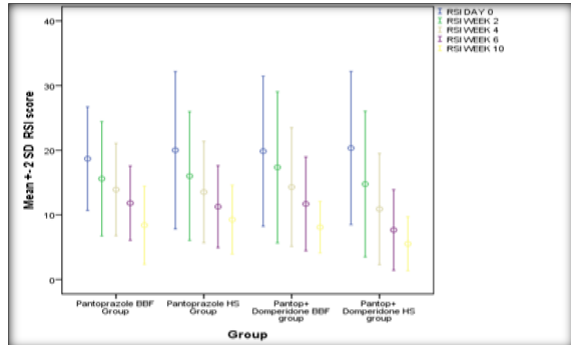
The baseline characteristic of the study population is listed in Table 1. The age distribution in our study had majority of the participants in the age group between 18-25 years. The mean age of the study population in Group 1 was 31.56±11.08 years, Group 2 was 34.73±10.49 years, Group 3 was 33.70±12.03 years and Group 4 was 38.14±9.20 years. The gender distribution in the study had females in majority with 67% (65), while male constituted 33% (32) among the total 97 participants. The most common presenting symptom was heartburn in 98% (95) patients and only 35% (34) patients had annoying cough as a symptom (Table 1).

#### Comparison of Reflux Symptom Index (RSI) scores at different interval

In our study, RSI scores in all the four groups improved from day 0 to week 2 and at week 4, the improvement was statistically significant with p value 0.03. The maximum improvement was seen in Group 4 (10.90 ± 4.30). At week 6, there was statistically highly significant improvement of RSI scores in all the four groups at p value <0.01 and maximum seen in Group 4 (7.67 ± 3.12), followed by Group 2 (11.27 ± 3.16). Also at week 10, statistically highly significant improvement of RSI scores was noted in all the four groups with p value <0.01 and maximum noted in Group 4 (5.52 ± 2.09), followed by Group 3 (8.10 ± 1.98), Group 1 (8.41 ± 3.01) and Group 2 (9.27 ± 2.66) (Table 2) (Figure 1).

**Table 2: RSI score in study subjects at different interval of treatment**

| RSI     | Pantoprazole BBF group | Pantoprazole HS group | Pantoprazole+ Domperidone BBF group | Pantoprazole+ Domperidone HS group | P value |
|---------|------------------------|-----------------------|-------------------------------------|------------------------------------|---------|
| Day 0   | 18.40±3.89             | 19.3±5.94             | 19.85±5.81                          | 20.23±5.80                         | 0.68    |
| Week 2  | 15.59±4.42             | 16.0±4.98             | 17.35±5.84                          | 14.76±5.64                         | 0.45    |
| Week 4  | 13.91±3.58             | 13.54±3.92            | 14.30±4.59                          | 10.90±4.30                         | 0.03    |
| Week 6  | 11.82±2.87             | 11.27±3.16            | 11.70±3.63                          | 7.67±3.12                          | <0.01   |
| Week 10 | 8.41±3.01              | 9.27±2.66             | 8.10±1.98                           | 5.52±2.09                          | <0.01   |



**Figure 1: Error plot showing RSI score in study subjects at different interval**

#### Comparison of efficacy of treatment between the four groups

At the end of our study at 10 week, the Reflux Symptom Index scores in all the four groups showed improvement, with statistically significant p value <0.01. The maximum in Group 4 (Pantoprazole 40 mg with Domperidone 10 mg before sleep at night) (14.81 ± 5.04) followed by Group 3 (11.75±4.45), Group 2 (10.73 ± 4.66) and then Group 1 (10.27 ± 3.60) (Table 3) (Figure 2).

**Table 3: Efficacy of treatment between the four groups**

| Treatment Group   | RSI change | P value |
|---|------------|---------|
| Group 1 : Pantoprazole 40 mg before breakfast                             | 10.27±3.60 | <0.01   |
| Group 2 : Pantoprazole 40 mg before sleep at night                        | 10.73±4.66 |         |
| Group 3 : Pantoprazole 40 mg with Domperidone 10 mg before breakfast      | 11.75±4.45 |         |
| Group 4 : Pantoprazole 40 mg with Domperidone 10 mg before sleep at night | 14.81±5.04 |         |

**Table 4: Change in different component of Reflux Symptom Index (RSI) at 10 weeks**

|                               | Pantoprazole BBF group | Pantoprazole HS group | Pantoprazole+ Domperidone BBF group | Pantoprazole+ Domperidone HS group | P value |
|-------------------------------|------------------------|-----------------------|-------------------------------------|------------------------------------|---------|
| Hoarseness of voice           | 0.41±0.66              | 1.31±1.28             | 0.70±0.86                           | 1.57±1.16                          | <0.01   |
| Clearing of throat            | 1.64±1.13              | 1.76±1.75             | 1.45±0.99                           | 1.81±0.74                          | 0.50    |
| Excess mucous/post nasal drip | 1.13±1.20              | 0.77±1.10             | 1.40±0.94                           | 1.61±1.07                          | 0.04    |
| Difficulty in swallowing      | 0.50±0.80              | 1.11±1.53             | 1.20±1.43                           | 1.52±1.43                          | 0.13    |
| Coughing after eating         | 0.50±0.85              | 0.96±1.28             | 0.90±1.20                           | 1.0±1.37                           | 0.65    |

|                              |           |           |           |           |       |
|------------------------------|-----------|-----------|-----------|-----------|-------|
| Breathing difficulty/choking | 0.86±0.83 | 1.65±1.32 | 1.35±1.38 | 1.90±1.78 | 0.16  |
| Troublesome/annoying cough   | 0.35±0.64 | 0.38±0.63 | 0.60±1.04 | 1.04±1.65 | 0.61  |
| Lump in throat sensation     | 1.50±0.91 | 1.42±0.90 | 1.40±0.94 | 2.38±1.24 | 0.01  |
| Heartburn, chest pain        | 2.0±1.23  | 1.73±0.96 | 1.85±1.13 | 3.0±1.41  | <0.01 |

### Comparison of change in Reflux Symptom Index (RSI) scores of different components at week 10

The improvements of RSI scores at week 10 was statistically significant for the symptoms of hoarseness or change in voice with p value <0.01, excessive throat mucus or postnasal drip with p value 0.04, lump in throat sensations with p value 0.01 and heartburn, dyspepsia with p value <0.01. (Table 4) (Figure 3).

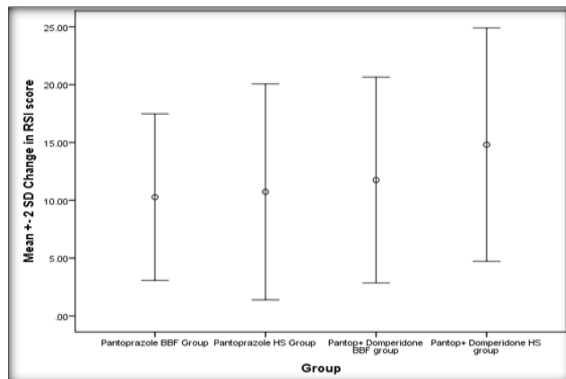


Figure 2: Error plot showing Change in RSI at 10 weeks in study subjects

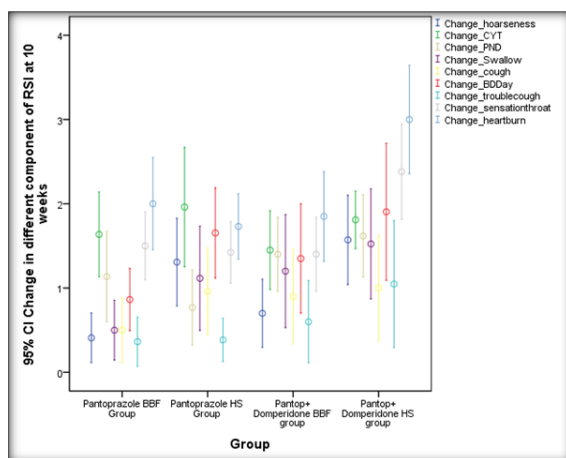


Figure 3: Error plot showing Change in different component of RSI at 10 weeks

## DISCUSSION

In our study of 97 patients to compare the efficacy of pantoprazole with or without domperidone in the management of Reflux Disease based on Baylor Reflux Index, the majority of the patients were in the age range of 18-25 years. The mean age for Group 1 was 31.56 + 11.08 (20-43) years, Group 2 was 34.73 + 10.49 (24-45) years, Group 3 was 33.70 + 12.03 (22-46) years and Group 4 was 38.14 + 9.20 (29-47) years. Taghvaei T et al<sup>[8]</sup> in their study reported a mean age of 37.31 + 9.29 years in the group that received proton pump inhibitors alone

and a mean age of 35.92 + 9.97 years in the group that received proton pump inhibitors with prokinetics.

The gender distribution in our study had females in majority. In a similar study, Hunchaisri N et al<sup>[9]</sup> reported female gender as in majority. However, the mean age was higher than in our study. This suggests that females are more prone to reflux disease compared to males.

According to Baylor Reflux Index, Reflux Symptom Index (RSI) >13 is suggestive of Reflux Disease. In our study, we used Baylor RSI as a scoring tool instead of a diagnostic tool. Thus treatment was initiated in all patients who presented with symptoms suggestive of Reflux Disease in their first visit.

In our study, there was improvement in use of proton pump inhibitors but more benefit was seen when domperidone was added resulting in improving the Reflux Symptom Index scores. Also, the improvement in the severity of reflux disease was maximum when pantoprazole and domperidone were taken half hour before sleep at night. A combination of prokinetic with proton pump inhibitors gave higher therapeutic benefits in the treatment of reflux disease. Handa KK et al<sup>[10]</sup> in a similar study reported that with the addition of prokinetics with proton pump inhibitors there was high symptom improvement rates with adequate safety.

At the end of our study at 10 week, the Reflux Symptom Index scores in all the four groups showed improvement, with statistically significant p value <0.01 and maximum in Group 4 (pantoprazole plus domperidone before sleep at night) which suggests that the Group 4 had a higher total rate of effective treatment. The combination of drugs are more efficacious in ameliorating the symptoms of reflux disease.<sup>[11,12,13]</sup>

Based on our study, the combination of pantoprazole plus domperidone is more beneficial for the treatment of reflux disease especially if it is taken half hour before sleep. This is due to the synergistic effect of proton pump inhibitors and prokinetic drugs in decreasing the production of acid and increasing the lower esophageal sphincter tone which enhances the upper gastrointestinal motility and accelerates the gastric emptying leading to rapid transit of proton pump inhibitors to the upper intestine, which is essential to prevent retention of proton pump inhibitors in the stomach and further preventing impaired acid suppression, thus producing a better therapeutic result.<sup>[14]</sup>

Also when prokinetic drugs are combined with proton pump inhibitors, it improves the effect of proton pump inhibitors. In our study, we chose domperidone as the prokinetic drug since it does not

cross the brain barrier and has lesser side effects as compared to other prokinetics and also has the benefit of lower cardiovascular side effects and better clinical efficacy. In contrary to the findings of our study, Hunchaisri N et al,<sup>[9]</sup> in their study reported that the high success rate of treatment is due to proton pump inhibitors alone rather than the addition of domperidone.

In our study of the different components of Reflux Symptom Index at week 10, the analysis of data shows that the components of Reflux Symptom Index, i.e. hoarseness, excessive throat mucus, lumpy sensation, and heartburn improved maximum when pantoprazole and domperidone are taken half hour before sleep. This may be explained by the efficacy of the combined drugs in reducing the acid reflux, decreasing the mucosal irritation of larynx and esophagus, thus reducing the symptoms.

Marakhouski KY et<sup>[15]</sup> in their study of 60 patients among two groups, where group 1 received omeprazole alone and group 2 received omeprazole with domperidone administered daily for 8 weeks and then followed up. The severity of heartburn assessed by visual analogue scale showed significant reduction in group 2 (start of study = 77.9 + 11.7, end of study = 1.7 + 3.30) as compared to group 1 (start of study = 77.5 + 12.7, end of study = 9.1 + 6.48). The study showed that the combined drugs were more effective in providing symptomatic relief to patients with reflux disease and the drugs were well tolerated.

## CONCLUSION

The conclusion drawn from the study is that pantoprazole with domperidone taken before sleep is most efficacious in improving the symptoms of reflux disease. The drug combination resulted in high symptom improvement rates based on the Reflux Symptom Index with adequate safety as evidenced by the Reflux Symptom Index score before and after treatment.

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