A Prospective Observational Study on the Efficacy and Side Effects of Pantoprazole - Domperidone Compared with Pantoprazole – Itopride Combination in Type 2 Diabetic Gastroparesis and Assessment of Quality of Life of Patients Before and After Therapy in A Tertiary Care Hospital

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ABSTRACT

Aim: - A hospital based prospective observational study was done at a tertiary care hospital over a period of six months. The aim of our study was to assess which of the combination was efficacious when comparing Pantoprazole-Itopride with Pantoprazole-Domperidone.

Diabetic Gastroparesis is outlined as a clinical condition that is characterised by upper Gastro Intestinal dyspeptic symptoms (nausea, bloating, vomiting, weight loss, postprandial fullness) in association with delayed gastric emptying leading to poor glycemic management, poor nutrition and dehydration. Usual management for Diabetic Gastroparesis includes Nutritional Assessment, Dietary modification, Glycaemic control, Prokinetic agents and Proton Pump Inhibitors.

Materials and Methods: - In this study, two groups each comprised of 23 subjects (i.e., total of 46 subjects) where group I administered with Pantoprazole 40mg – Itopride 150mg (Pantop-IT capsules) and group II with Pantoprazole 40mg – Domperidone 30mg (Pantop-DO capsules). The quality of life of patient were assessed using Patient Assessment of Upper Gastro Intestinal disorders (PAGI-QoL). Gastroparesis Cardinal Symptom Index (GCSI) were used to analyse symptomatic betterment. Nutritional statuses of patients were analysed using Mini Nutritional Assessment Scale (MNA). The questionnaire was given to the patients before and after the counselling. Side effect profile were monitored using General Assessment of Side Effects scale (GASE).

Results: - Pantoprazole – Itopride therapy efficiently improve the symptoms such as abdominal pain, regurgitation, loss of appetite, flatulence, belching, dyspepsia and bloating than Pantoprazole-Domperidone (18.36 ± 16.77; 18.69 ± 17.52). It is seen that, there was a statistically significant difference ($p < 0.05$) between Group I Pantoprazole – Itopride than Group II Pantoprazole-Domperidone.

Conclusion: - It can be concluded that the symptomatic betterment was achieved greater in patients receiving Pantoprazole - Itopride therapy with minimum side effect profile and better tolerance when compared to Pantoprazole – Domperidone combination. Quality of life was improved in patients receiving Pantoprazole – Itopride. Nutritional deficiency assessed in our study population was also improved in patients receiving Pantoprazole – Itopride.

Keywords: - Diabetic Gastroparesis, Itopride, Domperidone, Hyperglycaemia, Medication Adherence

1. INTRODUCTION

Diabetic gastropathy was delineated as a neuropathy occurring within the Gastro Intestinal system of diabetic patients presented with upper Gastro Intestinal tract symptoms suggestive of an upper motility disturbance in patients, whether or not delayed gastric emptying was present, as some patients with this syndrome may have rapid gastric emptying. [1]

1.2 EPIDEMIOLOGY

According to the International Diabetes Disease Federation (IDF) report estimates, global diabetes prevalence in 2020 is estimated to be 463 million people.[2] Diabetes is a growing challenge in India with estimated 8.7% diabetic population in the age group of 20 and 70 years.[3] In a study by Vijayakumar *et al*. (2019)**,** estimates that the cumulative incidence of Type 2 Diabetes in Kerala is 21.9% and the incidence of prediabetes is 36.7%.[4]

The age and sex-stratified diabetes prevalence was calculated for each country, accounting for diabetes prevalence differences in urban and rural areas.[2]

1.3 ETIOLOGY OF DIABETIC GASTROPARESIS

Gastric emptying depends on many factors such as reservoir relaxation, the depth of the constriction of the antral waves, the degree of pyloric opening, the receptive relaxation of the small intestine bulb and therefore the contracted pattern of the small intestine play a very important role. The motility of the abdomen can even, be altered with neurotransmitters, hormones, or medication.[5]

1.4 CLINICAL MANIFESTATIONS OF DIABETIC GASTROPARESIS

- Nausea
- Vomiting
- Early satiety
- Bloating
- Postprandial fullness
- Abdominal pain
- Weight loss/weight gain
- Constipation and/or diarrhea
- Wide glycaemic fluctuations [6]

1.5 MECHANISM OF DIABETIC GASTROPARESIS

Patients with gastroparesis typically indicates autonomic neuropathy. Studies show that each of the sympathetic and parasympathetic parts of the autonomic nervous system are affected in Diabetic gastroparesis since abnormalities are delineated within the axons and dendrites in prevertebral sympathetic ganglia. The pancreatic polypeptide response is dull and gastric secretion is reduced in patients with Diabetic gastroparesis, vagus nervus performance is stirred by sham feeding. Hyperglycaemia could cause vagus nervus dysfunction because of degenerative disorder. Once restoration of glycaemic control and kidney function with pancreas–kidney transplantation, diabetic autonomic and peripheral neuropathy will be partly reversible with improved gastric function.[7]

1.6 PANTOPRAZOLE – DOMPERIDONE

Anti-secretory agents such as Pantoprazole cause decrease in acid production and have high healing rates and rates of resolution of reflux symptoms, but they do not help to improve underlying disturbance in gut motility or improve tone of cardiac sphincter and relapse is common. Thus, addition of prokinetic such as Domperidone with antisecretory agent decreases relapse. Domperidone has much favourable adverse effect profile.[8]

Emphasizing that, addition of Domperidone with Pantoprazole is helpful by acting on multiple pathophysiological mechanisms of the disease. The data generated from other similar study leads to the point that combination of Pantoprazole and Domperidone has comparable healing rates and high symptom improvement rates with adequate safety. [9,10] Dose: - Pantoprazole 40mg + Domperidone 30mg BD

1.7 PANTOPRAZOLE – ITOPRIDE

The combination is synergistic by decreasing acid production as well as increasing lower oesophageal sphincter tone and oesophageal clearance, thus providing a better therapeutic response. Although proton pump inhibitor is the most potent acid suppressant and provides good efficacy in esophagitis healing and symptom relief.

In this regard addition of a prokinetic agent like Itopride along with Proton Pump Inhibitors like Pantoprazole, results in complete resolution of dyspeptic symptoms and improvement in the quality of life. Itopride is well tolerated and has no affinity for 5HT4 receptors which make this drug a better and safer Prokinetic agent. [11][12] Dose: - Pantoprazole 40mg + Itopride 150mg twice daily.

2. MATERIALS & METHODS

A hospital based prospective observational study was done at a tertiary care hospital over a period of six months. In our study we assessed the symptomatic betterment before and after therapy and medication adherence of Diabetic gastroparesis patients with group I receiving Pantoprazole - Itopride and with group II receiving Pantoprazole - Domperidone.

Prior to the therapy, most of the subjects showed significant gastrointestinal symptoms, but after the therapy most of these symptoms were reduced which implies that the subjects experienced symptomatic betterment from both the therapy.

2.1 INCLUSION CRITERIA

• 40-80 yrs. of age group
• Patients diagnosed as Diabetic Gastroparesis.
• Patients who gave written consent.

2.2 EXCLUSION CRITERIA

• Patients with**:**
  - Other endocrine disorders such as Hypothyroidism
  - With motor neuron disorders
  - Who are taking other Proton Pump Inhibitors and Prokinetic drugs
  - Eating disorders
• Drug induced gastroparesis such as Tricyclic antidepressants, Calcium channel blockers etc.
• Pregnant and Lactating women.

In this study, two groups each comprised of 23 subjects (i.e., total of 46 subjects) where group I administered with Pantoprazole 40mg – Itopride 150mg (Pantop-IT capsules) and group II with Pantoprazole 40mg – Domperidone 30mg (Pantop-DO capsules).
After completing the treatment, symptomatic betterment was analysed using Gastroparesis Cardinal Symptom Index (GCSI) scale, Adherence to Refills Medication Scale (ARMS) which was used to assess the medication adherence, Patient Assessment of Upper Gastrointestinal Disorders–Quality of Life (PAGI-QoL) has been used to assess quality of life in gastroparesis and other upper gastric disorders, using Mini Nutritional Assessment (MNA) scale, the nutritional status were assessed.

2.3 STATISTICAL METHODS

By considering dropouts of 10%, minimum sample size for the study was determined as 46. For data entry we had used the Microsoft excel and all the analysis were carried out with the help of statistical software SPSSv.22 version for WINDOWS. The improvement of symptoms was statistically assessed using paired t-test.

RESULTS

1. AGE WISE DISTRIBUTION OF POPULATION

Age in years	No of patients (N)	Percentage (%)
50 – 60	18	39.10
60 – 70	16	34.88
70 – 80	12	26.02

Table.1 Percentage distribution of age in patients participating in the study.

Among 46 patients screened, the age distribution data shows 39.1% of patients were in the age group of 50-60 years, 34.88% of patients were in the age group of 60-70 years and 26.02% of patients were in the group of 70-80 years.

2. GENDER WISE DISTRIBUTION OF POPULATION

Gender	P-IT		P-DO		Total	
	No. of Patients	Percentage (%)	No. of Patients	Percentage (%)	No. of Patients	Percentage (%)
Female	10	43.47	11	47.82	21	45.65
Male	13	56.53	12	52.18	25	54.35
Total	23	100	23	100	46	100

Table.2 Percentage of gender distribution in patients participating in the study.

Gender wise distribution data of overall study population is given in (Table 2) and it shows 54.35% of male patients and 45.65% of female patients participated in the study.

3. ASSESSMENT OF SYMPTOMATIC BETTERMENT

Gastroparesis Cardinal Symptom Index (GCSI) is a reliable and valid instrument for measuring the symptom severity in patients with gastroparesis. It is a 9-item questionnaire where the patient was asked to encircle the symptoms experienced by them. If the patient had not experienced a particular symptom 0 was encircled. If the symptom has been very mild, 1 was encircled. If the symptom has been mild, 2 was encircled. If it has been moderate, 3 was encircled. If it has been severe, 4 and for very severe, 5 was encircled respectively and the sum of their values were taken as total score.[13]

SYMPTOMS	P-IT		P-DO		Total	
	N	%	N	%	N	%
Abdominal pain	19	82.6	15	65.21	34	73.91
Regurgitation	18	78.2	22	95.65	40	86.95
Loss of appetite	14	60.86	16	69.56	30	65.22
Belching	11	47.8	13	56.52	24	52.17
Flatulence	13	56.52	14	60.86	27	58.69
Dyspepsia	21	91.30	23	100	44	95.65
Bloating	23	100	23	100	46	100

Table.3 Percentage of symptoms present in both groups before therapy

Table.3 depicts the percentage of symptoms in both the group therapies. The major symptoms presented were dyspepsia, bloating and regurgitation with a percentage of 100%, 95.65%, 86.95% from both the groups respectively.

3.1. ASSESSMENT OF SYMPTOMATIC BETTERMENT BEFORE AND AFTER THERAPY IN GROUP I PATIENTS

Group	N (No of subjects)	GASTROPARESIS CARDINAL SYMPTOM INDEX (GCSI) Mean Score	
P-IT	23	Before Therapy	18.36
	23	After Therapy	16.77

Table.4 Mean symptom score of patients before & after therapy in Group I patients

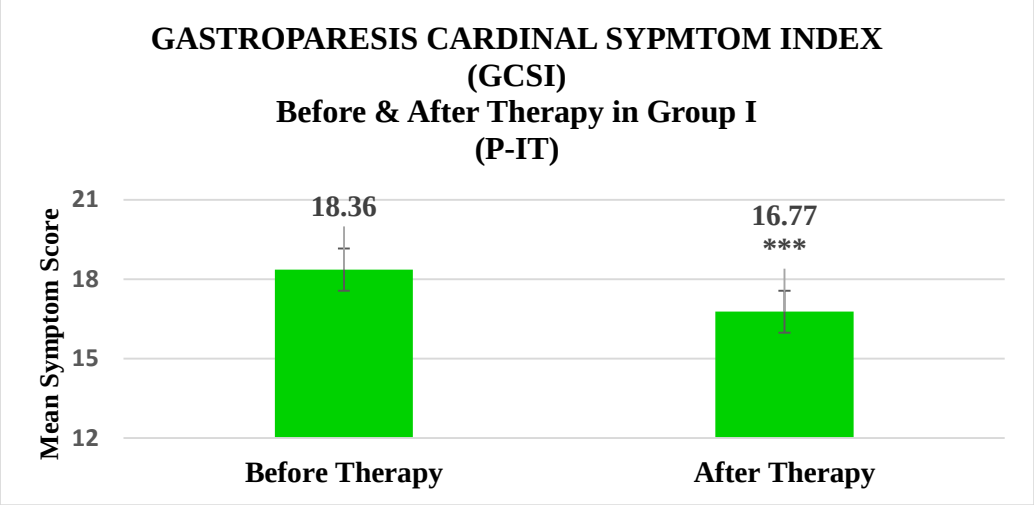

Figure.1 Comparison of symptomatic assessment before and after therapy in Group I

**** - p≤0.001*

The result shows that there was a significant symptomatic improvement in group I patients after receiving Pantoprazole-Itopride combination.

3.2. ASSESSMENT OF SYMPTOMATIC BETTERMENT BEFORE AND AFTER THERAPY IN GROUP II PATIENTS

Group	N (No of subjects)	GASTROPARESIS CARDINAL SYMPTOM INDEX (GCSI) Mean Score	
P-DO	23	Before Therapy	18.69
	23	After Therapy	17.52

Table.5 Mean symptom score of patients before & after therapy in Group II patients

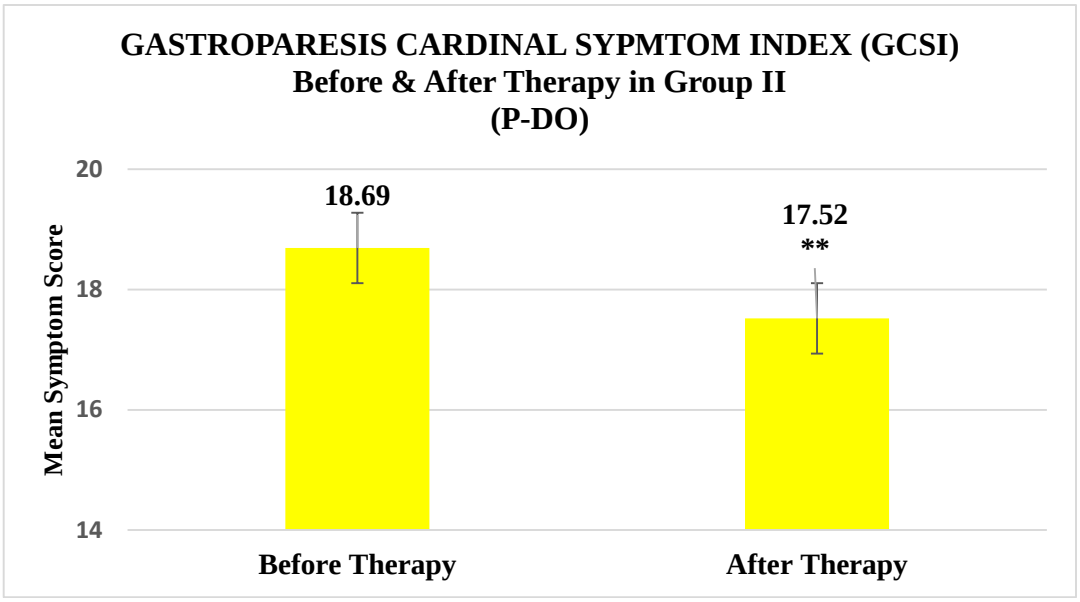

Figure.2 Comparison of symptomatic assessment before and after therapy in Group II

*** - p≤0.01*

From the above depicted graph, the patients in group II showed symptomatic improvement after receiving Pantoprazole-Domperidone.

3.3. PERCENTAGE OF SYMPTOMATIC ASSESSMENT BEFORE AND AFTER THERAPY IN GROUP I

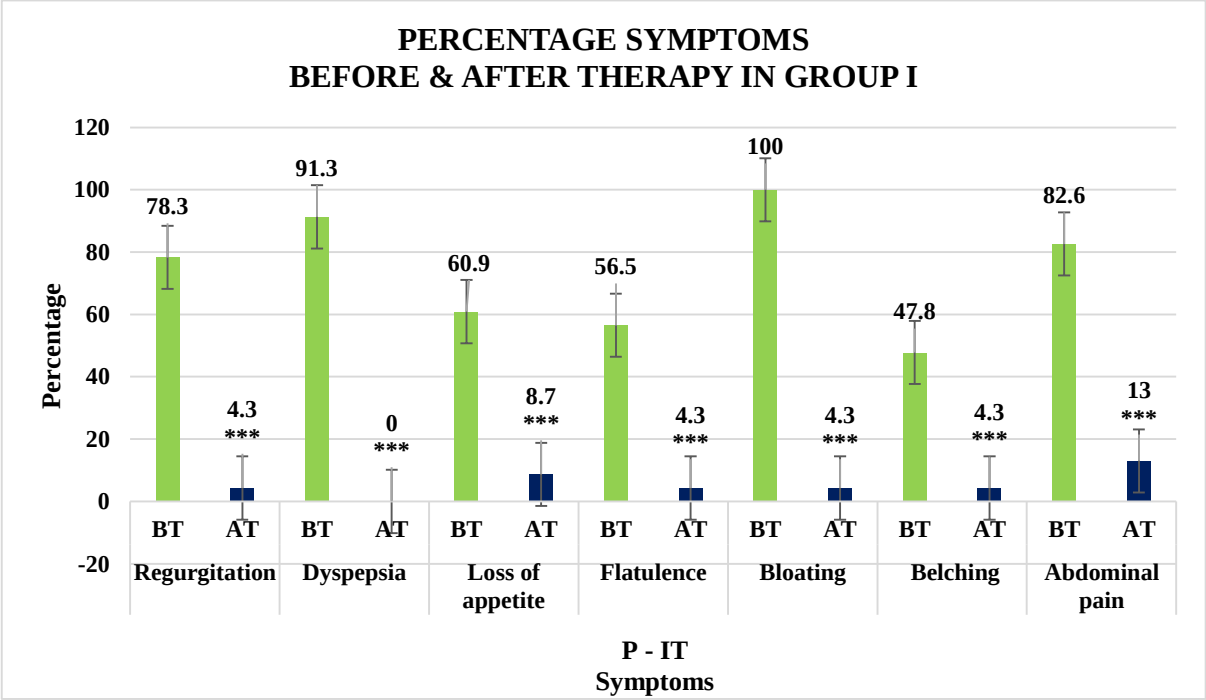

Figure.3 Comparison of symptomatic assessment before and after therapy in Group I

*** - p≤0.001(BT – Before Therapy, AT – After Therapy)*

3.4. PERCENTAGE OF SYMPTOMATIC ASSESSMENT BEFORE AND AFTER THERAPY IN GROUP II

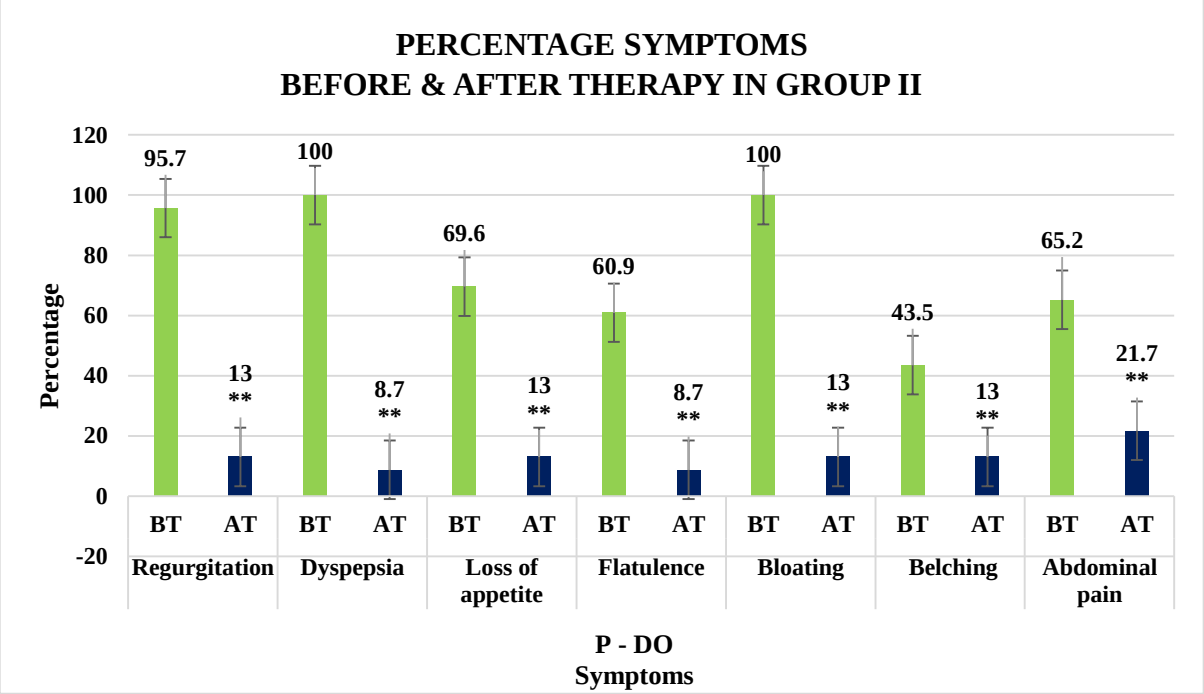

Figure.4 Comparison of symptomatic assessment before and after therapy in Group II

*** - p-0.01(BT – Before Therapy, AT – After Therapy)*

From figure 3 & 4, depicting the comparison in percentage of symptoms before and after therapy in both groups, shows drastic decrease in the percentage of symptoms after the therapy which was analysed using Wilcoxon signed rank test. While it was clearly seen that the patients receiving Pantoprazole – Itopride has significantly reduced the symptoms compared to Pantoprazole – Domperidone. Bloating being the major symptom experienced by the patient in Group I (100%) and Group II (100%) was reduced to 4.3% and 13% in Group I and Group II respectively. Belching being the minor symptom was reduced from 47.8% to 4.3% in Group I and 43.5% to 13% in Group II, respectively.

3.5. COMPARISON OF SYMPTOMATIC ASSESSMENT BEFORE AND AFTER THERAPY IN GROUP I & GROUP II

Group	N (No of subjects)	GASTROPARESIS CARDINAL SYMPTOM INDEX (GCSI) Mean Score	
		Before Therapy	After Therapy
P - IT	23	18.36	16.77
P-DO	23	18.69	17.52

Table.6 Mean symptom score of patients before & after therapy in Group I & Group II

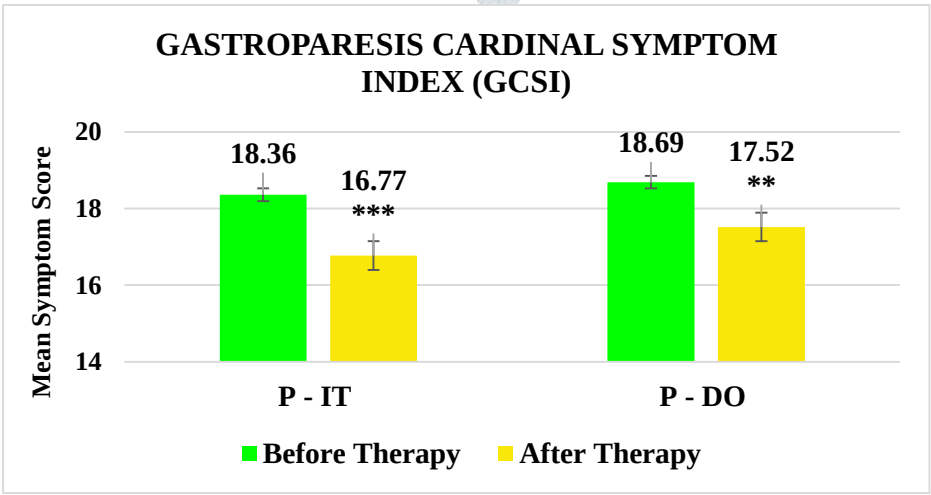

Figure.5 Comparison of symptomatic assessment before & after therapy in Group I & Group II

*** - p≤ 0.001, ** - p≤ 0.01*

By comparing the before and after therapy in both the groups, symptomatic betterment was achieved in both the groups. But with a p value of <0.001, the symptomatic betterment was greater in patients receiving Pantoprazole – Itopride when compared to patients receiving

Pantoprazole - Domperidone. Pantoprazole – Itopride therapy efficiently improve the symptoms such as abdominal pain, regurgitation, loss of appetite, flatulence, belching, dyspepsia and bloating than Pantoprazole-Domperidone.

4. ASSESSMENT OF MEDICATION ADHERENCE

Medication Adherence was measured by Adherence to Refills Medication Scale (ARMS), a 12-item questionnaire which should be reverse coded, then added up the points. The range of possible scores is 12 to 48. Lower scores indicate better adherence. Scores can be treated as a continuous measure or dichotomized as 12 or >12.

Group	N (No of subjects)	ADHERENCE TO REFILLS MEDICATION SCALE (ARMS)
		Mean Score
P-IT	23	13.86
P-DO	23	16.86

Table.7 Medication Adherence assessment in Group I and Group II

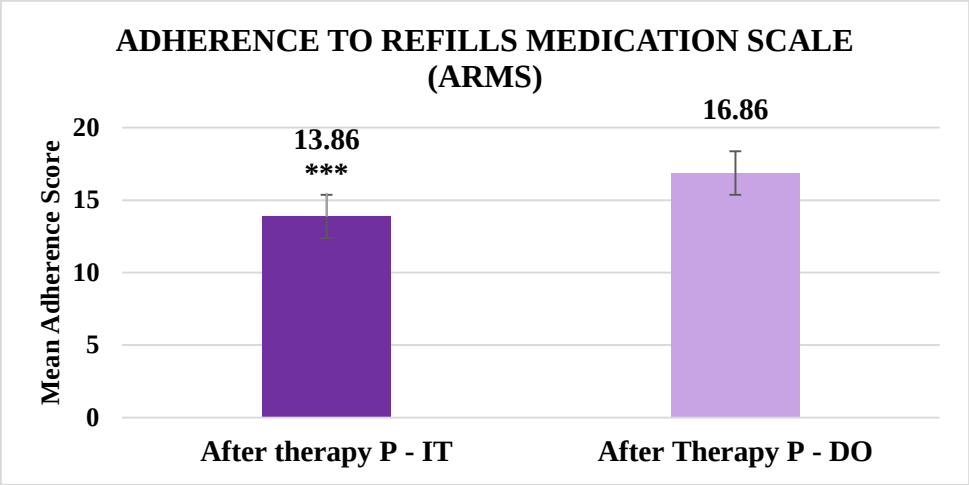

Figure.6 Medication Adherence assessment in Group I and Group II after therapy

**** - p≤ 0.001*

From the above graph it was seen that there was a statistically significant difference ($p < 0.05$) between the groups. Therefore, it can be concluded that the medication adherence was greater for Group I than Group II.

5. ASSESSMENT OF NUTRITIONAL STATUS

Nutritional Assessment was done by Mini Nutritional Assessment (MNA) scale which is a 6-item scale where the maximum points are 14.

Scoring as follows: -

- 12-14 points: Normal nutritional status
- 8-11 points: At risk of malnutrition
- 0-7 points: Malnourished

5.1 COMPARISON OF NUTRITIONAL STATUS BEFORE & AFTER THERAPY IN GROUP I

Group	N (No of subjects)	MINI NUTRITIONAL ASSESSMENT SCALE (MNA) Mean Score	
P-IT	23	Before Therapy	12.48
	23	After Therapy	14.5

Table.8 Nutritional Assessment in Before and After Therapy in Group I

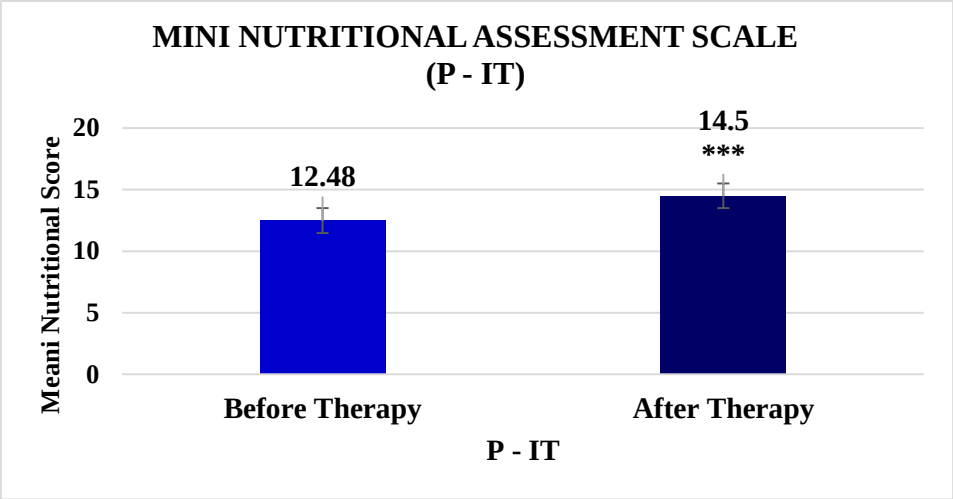

Figure.7 Comparison of Nutritional Status Before and After Therapy in Group I

**** - p ≤0.001*

By analysing the graph, there was statistically significant difference before and after the therapy. Hence it was concluded that there was significant improvement in the nutritional status of patients receiving Pantoprazole – Itopride.

5.2 COMPARISON OF NUTRITIONAL STATUS BEFORE AND AFTER THERAPY IN GROUP II

Group	N (No of subjects)	MINI NUTRITIONAL ASSESSMENT SCALE (MNA) Mean Score	
P-DO	23	Before Therapy	12.45
	23	After Therapy	13.01

Table.9 Nutritional Assessment Before and After Therapy in Group II

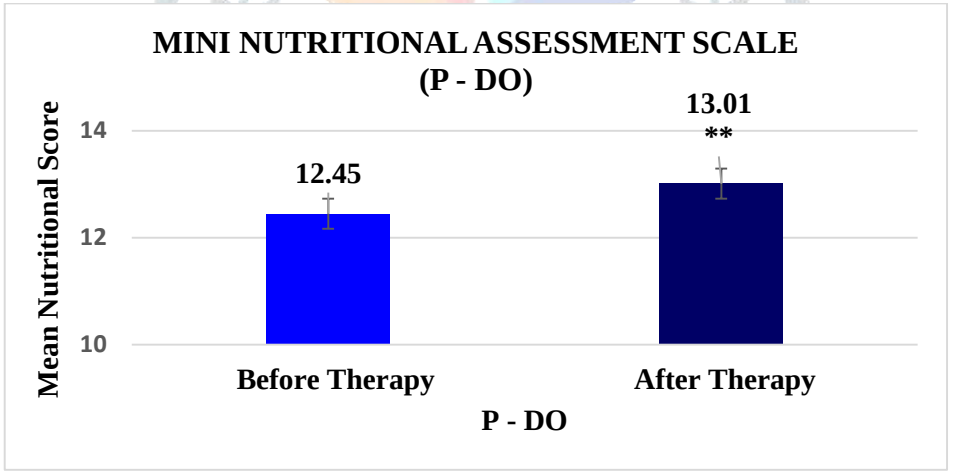

Figure.8 Comparison of Nutritional Status Before and after Therapy in Group II

***- p ≤0.01*

From the above graph it was assessed that the Group II receiving Pantoprazole-Domperidone showed significant improvement in the nutritional status.

5.3 COMPARISON OF NUTRITIONAL STATUS BEFORE AND AFTER THERAPY IN GROUP I AND GROUP II

Group	N (No of subjects)	MINI NUTRITIONAL ASSESSMENT SCALE (MNA) Mean Score	
		Before Therapy	After Therapy
P - IT	23	12.48	14.5
P - DO	23	12.45	13.01

Table.10 Comparison of nutritional status before and after therapy in Group I & Group II

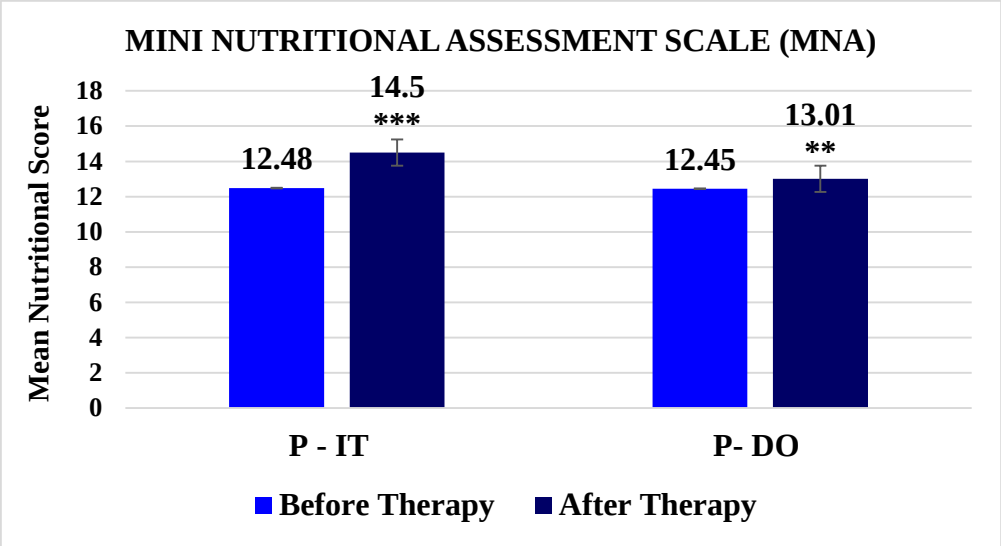

Figure.9 Comparison of nutritional status before and after therapy in Group I & Group II

******- p ≤ 0.001, **- p ≤ 0.01***

By comparing the nutritional status before and after therapy in both groups, it can be concluded that the nutritional status was better in patients receiving Pantoprazole–Itopride when compared to patients receiving Pantoprazole-Domperidone, even though there was no statistically significant difference. Also, both the groups received specific patient counselling on their diet plan. Although there was no accurate evidence to support the nutritional status improvement with any of the drug therapy in our study, Pantoprazole – Itopride group sufficiently improves the symptoms which hinders the nutritional adequacy as depicted in the above graph.

6. ASSESSMENT OF QUALITY OF LIFE IN PATIENTS

The Patient Assessment of Upper Gastro Intestinal Disorders-Quality of Life **(**PAGI-QOL) has been indicated for assessing the quality of life of patients in Gastroparesis, Gastro Esophageal Reflux Disease and Dyspepsia. Comprises of 30 items each having a 6-point Likert-type scale ranging from 0 = "None of the time" to 5 = "All of the time", and with a recall period: "the previous two weeks".

6.1 COMPARISON OF QUALITY OF LIFE BEFORE AND AFTER THERAPY IN GROUP I

Group	N (No of subjects)	PATIENT ASSESSMENT OF UPPER GASTROINTESTINAL DISORDERSQUALITY OF LIFE (PAGI-QoL) Mean Score	
P-IT	23	Before Therapy	37.4
	23	After Therapy	48.59

Table.11Quality of Life Assessment Before and After Therapy in Group I

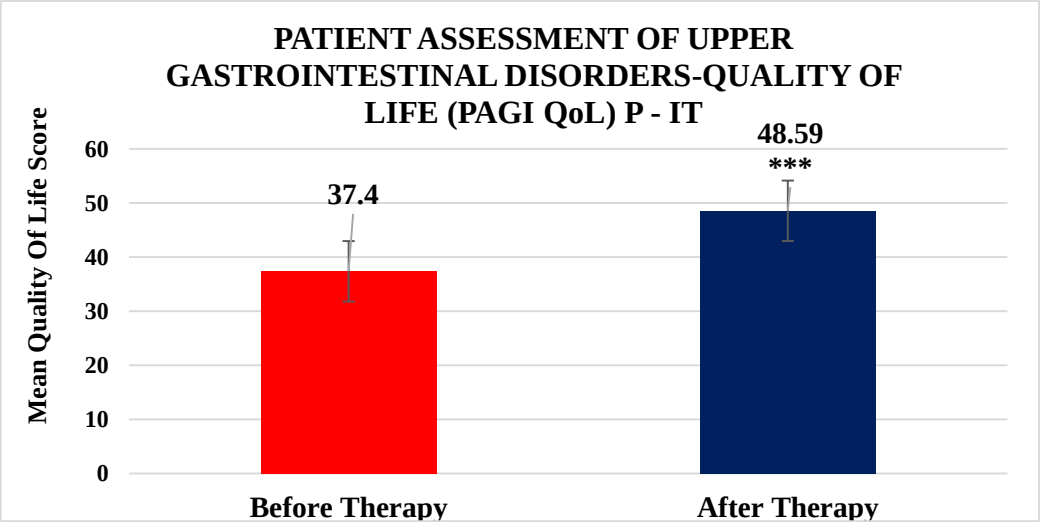

Figure.10 Comparison of quality of life Before and after Therapy in Group I

**** - p ≤0.001*

From the above graph, it can be assessed that the quality of life before receiving the treatment has improved to higher levels after treatment with Pantoprazole – Itopride. Higher scores indicated the improvement in the quality of life in patients.

6.2 COMPARISON OF QUALITY OF LIFE BEFORE AND AFTER IN THERAPY GROUP II

Group	N (No of subjects)	PATIENT ASSESSMENT OF UPPER GASTROINTESTINAL DISORDERS QUALITY OF LIFE (PAGI-QoL) Mean	
P - DO	23	Before Therapy	37.27
	23	After Therapy	47.04

Table.12 Quality of Life Assessment Before and After Therapy in Group II

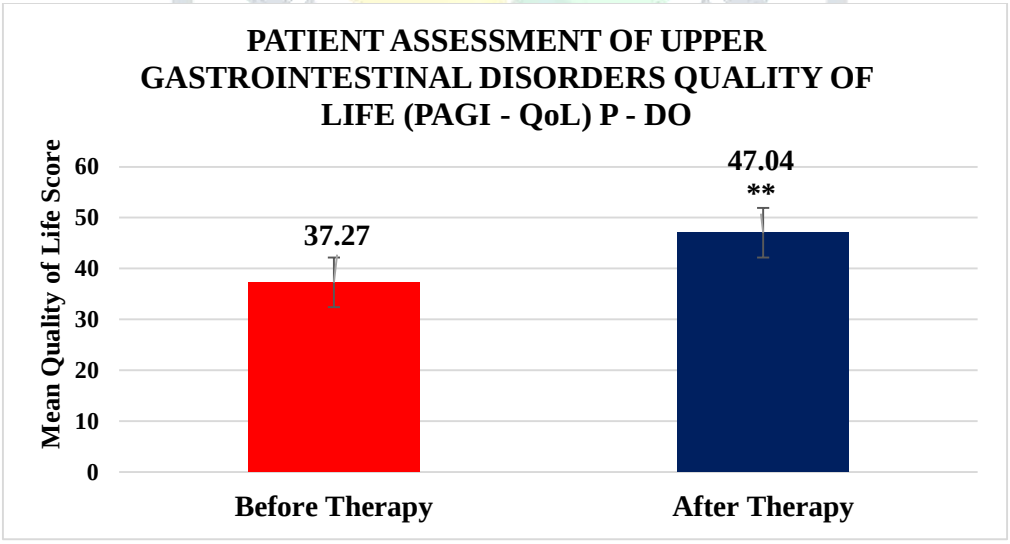

Figure.11 Comparison of quality of life Before and after Therapy in Group II

*** p ≤0.01*

The above graph shows that the quality of life of patients receiving the Pantoprazole – Domperidone has improved to higher levels which was understood by the high scores after receiving the treatment. The mean quality of life score before treatment was 37.27 which elevated to a score of 47.07, where a mean difference of 0.4 between the two groups can be considered as relevant in-Patient Assessment of Upper Gastro Intestinal Quality of Life (PAGI QoL) scale.

6.3 COMPARISON OF QUALITY OF LIFE BEFORE AND AFTER THERAPY IN GROUP I AND GROUP II

Group	N (No of subjects)	PATIENT ASSESSMENT OF UPPER GASTROINTESTINAL DISORDERS-QUALITY OF LIFE (PAGI - QoL) Mean Score	
		Before Therapy	After Therapy
P - IT	23	37.40	48.59
P - DO	23	37.27	47.04

Table.13 Comparison of quality of life before and after therapy in Group I & Group II

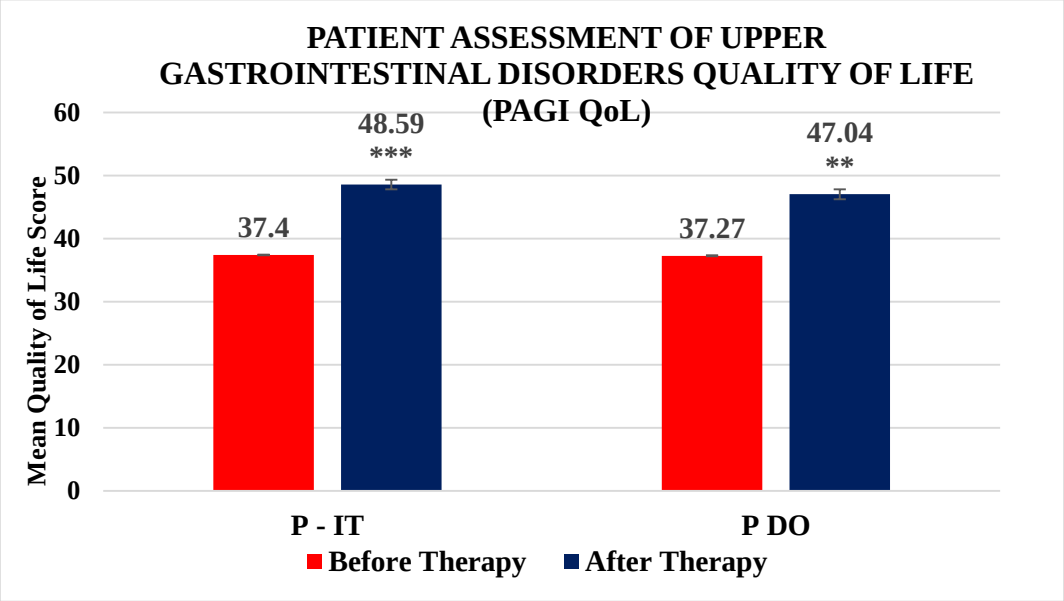

Figure.12 Comparison of quality of life before and after therapy in Group I & Group II

**** p ≤0.001, **p ≤0.01*

The above graph depicts the comparison of quality of life of patients with Diabetic gastroparesis, where it was clearly seen that, both the patient group experiences better quality of life after receiving the therapy. But with a mean value of 48.59 indicated in Pantoprazole – Itopride against a mean value of 47.04 for Pantoprazole – Domperidone which shows that the patient group receiving the former treatment has improved quality of life compared to the latter treatment. Therefore, it was understood that the patient population receiving Pantoprazole – Itopride improves quality of life in patients than Pantoprazole – Domperidone.

7. ASSESSMENT OF SIDE EFFECTS

Generic Assessment of Side Effects Scale (GASE) was used for assessing the generalised side effects due to a drug therapy where the patient was asked to encircle the scores indicating the experience, he or she had in the scale for the last 7 days. Each score was added up to get the final score.

- **0** = Complaint not present
- **1** = Mild: complaint causes mild distress or discomfort, but no impairment in daily functioning
- **2** = Moderate: complaint causes moderate distress or discomfort or at least some impairment in daily functioning
- **3** = Severe: complaint causes severe distress and discomfort, severe impairment in daily functioning, or acute danger to health

7.1 ASSESSMENT OF SIDE EFFECTS IN GROUP I AND GROUP II PATIENTS

Group	N (No of subjects)	GENERIC ASSESSMENT OF SIDE EFFECTS SCALE (GASE)
		Mean Score
P – IT	23	4.36
P – DO	23	5.45

Table.14 Comparison of side effects in Group I & Group II

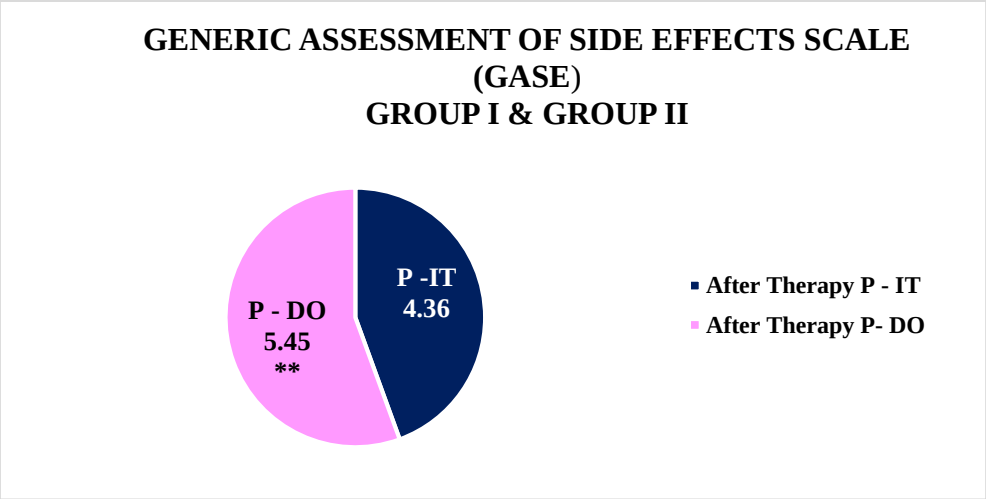

Figure.13 Comparison of side effects in Group I & Group II
***** p <0.05***

From the graph it was analysed that the patient experiences mild side effects from both the drug therapy. With significant statistical difference in the p value, Pantoprazole – Domperidone showed more side effects compared to Pantoprazole – Itopride. Even though Pantoprazole – Domperidone showed more side effects compared to Pantoprazole – Itopride.

DISCUSSION

Our results showed that both the drug combinations can resolve symptoms such as dyspepsia, regurgitation, abdominal pain, bloating, loss of appetite with Pantoprazole –Itopride having superior efficacy in symptomatic betterment compared to Pantoprazole - Domperidone.

The results of present investigation are consistent with the study carried out by Pradeep Kumar *et al.* (2019) [11]. which showed over all symptomatic betterment in Gastro Esophageal Reflux Disease patients receiving the combination of Pantoprazole and Itopride (74.5%) than pantoprazole alone (62.5%). Similarly, in another study by Pradeep Kumar *et al.* (2016) [12] also showed that, addition of Prokinetic agent like Itopride along with PPI like Pantoprazole, results in complete resolution of dyspeptic symptoms (regurgitation, vomiting, nausea etc) in Gastro Esophageal Reflux disease and improvement in quality of life. Singhal *et al.* (2005) [8] studied the drug combination of Pantoprazole and Domperidone, which achieved high endoscopic esophageal healing rates and our study also shows similar result when compared to this study. Another study by Malhotra *et al.* [14] showed that PPIs like pantoprazole have shown to effectively manage dyspeptic symptoms in DG and Pantoprazole is effective and well tolerated both in children as well as elderly. Improved quality of life (QoL) and high satisfaction levels has been shown with pantoprazole in dyspeptic patients. Pantoprazole has advantageous safety-tolerability, as it appears to be safest of all PPIs.

Domperidone is a dopamine-2 receptor antagonist which is effective in reducing symptoms like nausea and vomiting in patients with Diabetic Gastroparesis and does not cross the blood brain barrier and was associated with fewer central nervous system (CNS) effects. [15,16]

In a study by Gopesh *et al*. (2017) [17] found that Domperidone produced significant reduction in symptoms at 4 weeks compared to Itopride ($p<0.05$). On comparing the reduction in Subjective Global Assessment of relief score at 2 weeks and 4 weeks by the two drugs, there was no significant difference between them.

A study showing effects of Domperidone in combination with Omeprazole in the treatment of chronic superficial gastritis by Wang *et al.* (2017) [18] found that Omeprazole in combination with Domperidone was highly effective in treating chronic superficial gastritis, and it can accelerate cure and relieve the clinical symptoms of patients.

Aravind *et al*. (2008) [19] showed that the evidence for Domperidone as a prokinetic (i.e. its ability to accelerate gastric emptying) was also mixed with only 9 of 15 studies showing an improvement and with all 3 of the placebo-controlled studies that looked at this parameter did show a difference, suggesting that this effect was real. The study implies that Domperidone was effective in patients with gastroparesis symptoms.

A similar study by Abid Shah *et al*. (2014) [20] demonstrated that addition of Itopride before meals facilitates food delivery to the intestine, increases incretin secretion, and thus improves the glycaemic parameters implying the beneficial effects of Itopride in glycaemic management.

A study of Rahul Kumar *et al*. (2014) [21] where minority of the patients had symptoms of Gastro Esophageal Reflux Disease (GERD) were present without any endoscopically visible mucosal injury. At the end of the follow up, relief of symptoms was more with a combination of Itopride and Rabeprazole in comparison to the combination of Domperidone and Rabeprazole implying that the Itopride – Rabeprazole combination was symptomatically better than Domperidone - Rabeprazole. Similar results were found in our study implying that Pantoprazole - Itopride shows symptomatic betterment than Pantoprazole – Domperidone.

With a statistically significant difference (<0.05) comparing both the groups, it was concluded that the group I receiving Pantoprazole – Itopride showed better medication adherence than group II receiving Pantoprazole – Domperidone which was assessed using Adherence to Refills Medication Scales (ARMS). Both the groups tolerated the treatment very well without any discontinuation of therapy. In a study by Kripalani *et al*. (2009) [22] which shows that ARMS is a valid and reliable medication adherence scale when used even in chronic disease population, with good performance characteristics even among low-literacy patients. Thus, in our study, patients show better adherence by using Adherence to Refills Medication Scale (ARMS) which is a reliable scale to assess the medication adherence. Patients with Gastroparesis have symptoms associated with eating, resulting in food aversion and inadequate oral intake and may experience protracted nausea and vomiting, making it difficult to maintain hydration and nutrition. Thus, patients with Gastroparesis were at risk for weight loss, malnutrition, vitamin and mineral deficiencies [23] As symptoms such as bloating, dyspepsia, regurgitation, loss of appetite influences the daily activities, physical health and psychological state of a person, it was mandatory to provide symptomatic betterment in patients in order to improve the quality of life in them. Using Mini Nutritional Assessment (MNA) scale, the nutritional status were assessed and came to a conclusion that the nutritional status of Group I (P-IT) shows greater score than Group II (P-DO) patients as it reduces the symptoms (abdominal pain, regurgitation, bloating, dyspepsia)related to gastroparesis which causes delay in food absorption. Patient counselling was given on diet plan for those who were at risk of nutritional deficiency.

Patients were asked to have small frequent meals of semi liquid or liquid food which would be easier for their digestion. Parkman *et al*. (2011) [23] suggests that a nutritional consultation maybe helpful and should be considered in patients with gastroparesis. Dietary modifications improve the food intake in patients with gastroparesis thus reducing nutritional deficiencies and symptoms. Our study also shown similar results of nutritional improvement in patients after patient counselling on their diet.

Patient Assessment of Upper Gastrointestinal Disorders–Quality of Life (PAGI-QoL) has been used to assess quality of life in gastroparesis and other upper gastric disorders. In the study by Choi *et al*. (2005) [24] indicates that even if the functional gastro intestinal disorders were not life threatening but could significantly impair the quality of life (QoL) by hindering daily activities and may induce a major social and economic burden. Abdominal pain and dyspepsia along with bloating were the major symptoms contributing to the disease severity in our study which in turn affects the quality of life in patients. Therefore, it was mandatory to provide symptom specific treatment which can improve the quality of life in patients. A study by Tielemans *et al*. (2013) [25], indicated similar findings that subjects with gastro intestinal symptoms had an impaired health-related quality of life and that more severe symptoms correlated with a lower health-related quality of life. Our study results showed that Patient Assessment of Upper Gastro Intestinal Quality of Life (PAGI QoL) scale scores increased after receiving both the drug therapy with greater scores for patients receiving Pantoprazole – Itopride. Thus, from our study it was clearly proven that, both the drug therapy can improve the quality of life by improving the symptoms in the patients.

During the 14 days short term therapy, both the groups reported mild side effects which were monitored using Generic Assessment of Side Effects Scale (GASE) after one week of therapy in both the groups. Most of the patients in Group II (Pantoprazole – Domperidone) complained of headache, dry mouth and mild chest pain. On analysis we found that mild chest pain was reported in patients with history of cardiac disorders. As in Group I (Pantoprazole - Itopride) only complained about having headache and dizziness which was self-limited. Despite having complaints of mild side effects, both the groups continued the medication with proper counselling on the medication. Study by Kim *et al*. (2005) [26] showed that there were no significant adverse effects with Itopride given 150mg per day. Similarly, in our study, Pantoprazole – Itopride receiving patients showed lesser side effects. As our study was conducted for a short period, no major side effects of Pantoprazole – Domperidone therapy were reported. Both groups showed mild side effects among them, in which Pantoprazole – Itopride reported lesser side effects which indicates better tolerance.

CONCLUSION

From our study it can be concluded that the symptomatic betterment was higher in group I receiving Pantoprazole – Itopride compared to group II receiving Pantoprazole – Domperidone with an improved efficacy and tolerability profile. Due to the lesser number of sample and shorter study duration we could not completely assess the effects of drug therapy in patients with prior cardiac history. Therefore, larger sample size and longer duration of study are required to produce valuable and reliable results.

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