



# A PROSPECTIVE OBSERVATIONAL COMPARATIVE STUDY TO ASSESS THE QUALITY OF LIFE IN PATIENTS TAKING RABEPRAZOLE MONOTHERAPY VERSUS RABEPRAZOLE AND ITOPRIDE COMBINATION THERAPY IN GASTRO- ESOPHAGEAL REFLUX DISEASE -A PILOT STUDY.

ALANA KALAM S<sup>1\*</sup>, HASBI HABEEB PH<sup>1\*</sup>

DR. SUBASH CHANDRAN M P<sup>2</sup>, DR. KARTHIKA LAL B<sup>3</sup>, DR. JACOB PHILIP<sup>4</sup>, DR. NITHIN MANOHAR R<sup>5</sup>  
DR. PRASOBH G R<sup>6</sup>

<sup>1</sup>Fifth Pharm D Students, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram, Kerala, India.

<sup>2</sup>Professor and Head of Department of Pharmaceutics, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram, Kerala, India.

<sup>3</sup>Assistant Professor, Department of Pharmacy Practice, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram, Kerala, India.

<sup>4</sup>Senior Consultant, Department of Gastroenterology, Cosmopolitan Hospitals Post Graduate Institute of Health Science and Research, Thiruvananthapuram, Kerala, India.

<sup>5</sup>Professor and Head of Department of Pharmacy practice, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India.

<sup>6</sup>Principal, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram, Kerala, India.

## ABSTRACT

**Background:** A disorder known as gastro-esophageal reflux disease develops when stomach acid reflux causes unpleasant symptoms and/or consequences. Proton pump inhibitors (PPIs) are used in gastric acid suppression therapy to treat GERD. Here, Rabeprazole used since it provides better efficacy than other PPIs and Itopride a novel gastro prokinetic agent stimulate the movement of the gastrointestinal tract, which speeds up the emptying of the stomach and modifies the sensorimotor function of the stomach.

When prokinetic drugs like itopride and proton pump inhibitors are used together to treat gastro-esophageal reflux disease, they work in combination to reduce acid production and improve therapeutic response.

### Aim:

To compare the quality of life and medication adherence in patients taking Rabeprazole monotherapy versus Rabeprazole and Itopride combination therapy in gastro-esophageal reflux disease.

### Objective:

The objectives of the study include

- To assess the quality of life.
- To assess the medication adherence.

### Materials and Methods:

The prospective observational comparative study was carried out in 30 patients with GERD. Patients were assigned into two groups, Group A and Group B. Group A received Rabeprazole 20mg twice daily as monotherapy and group B received Rabeprazole and Itopride 20/150mg once daily as combination therapy; 30 minutes before food respectively for 0, 4 and 8 weeks. Patient's Quality of Life will be measured at the beginning of the therapy and patient counselling will be done using Patient Information Leaflet (PIL), then follow-up was taken after 4<sup>th</sup> and 8<sup>th</sup> weeks of treatment using Gastroesophageal Reflux Disease-Health Related Quality of Life questionnaire (GERD-HRQL). Patient's medication adherence will be assessed by using Adherence to Refill and Medication Scale (ARMS).

### Result:

There is a significant improvement in Health-Related Quality of Life of patients who were treated with Rabeprazole and itopride combination therapy is more than that of Rabeprazole monotherapy in Gastroesophageal Reflux Disease. It was also found that patient counselling has an important role in improving the Medication Adherence and Quality of Life of patients.

### Conclusion:

Patients taking Rabeprazole and Itopride combination therapy provides more improvement in Quality of Life and medication adherence in Gastro Esophageal Reflux Disease than Rabeprazole monotherapy after 8 weeks of treatment.

## KEYWORDS

Gastro esophageal reflux disease, Health related Quality of Life, Adherence to refill and medication scale.

## INTRODUCTION

Gastro-esophageal reflux disease is the abdominal retrograde movement of gastric contents from the stomach to esophagus. This occurs when the lower esophageal sphincter is weak or relaxes inappropriately. The main cause of gastro-esophageal reflux is incompetence of the anti-reflux barriers at the esophago-gastric junction. The goal of Gastro-esophageal reflux disease therapy is completely resolution of symptoms like long standing history of heartburn and a shorter history of regurgitation. The most effective treatment for the healing of Gastro-esophageal reflux disease symptom is gastric acid suppressive therapy with Proton Pump Inhibitor because of its efficacy and fast healing rate. Among the proton pump inhibitors, Rabeprazole reduce acid production and have high healing rates of reflux symptoms. Itopride, a novel gastro prokinetic agent stimulate Gastro-intestinal motor activity which accelerate gastric emptying and modulates gastric sensorimotor function. [1]

### Etiology:

Currently, there is no known cause to explain the development of GERD.

- Motor abnormalities includes,
  - Esophageal dysmotility causing impaired esophageal acid clearance
  - Impairment in the tone of the lower esophageal sphincter (LES)
  - Transient LES relaxation
  - Delayed gastric emptying are included in the causation of GERD
  
- Anatomical factors include,
  - Presence of hiatal hernia
  - Increase in intra-abdominal pressure
  
- Other factors include,
  - Age  $\geq 50$  years [2]
  - Low socio-economic status
  - Tobacco use
  - Consumption of excess alcohol
  - Connective tissue disorders

- Different classes of drugs which include anticholinergic drugs, benzodiazepines, NSAID or aspirin use, nitroglycerin, albuterol, calcium channel blockers, antidepressants, and glucagon [3].

### Signs and Symptoms:

GERD syndromes can be described as symptom-based or esophageal tissue injury-based.

- Heartburn
- Regurgitation
- Hypersalivation
- Dysphagia
- Odynophagia [4]
- Chronic cough
- Epigastric pain
- Asthma
- Dental enamel erosion

Besides pain, you may also have,

- Abdominal bloating or fullness
- Gas or belching
- Heartburn or Indigestion
- Diarrhea or Constipation
- Reactions or intolerance to specific foods or food groups
- Difficulty swallowing [4]

Certain foods may trigger GERD symptoms in some people. These include:

- Greasy foods
- Spicy foods
- Chocolate
- Peppermint
- Coffee
- Foods containing tomato products
- Alcoholic drinks

**Risk Factors:**

- Overweight or obesity
- Smoking or smoke inhalation, alcohol consumption
- Some asthma medications
- Calcium channel blockers, which people take for high blood pressure
- Benzodiazepines
- Tricyclic antidepressants
- Non-steroidal anti-inflammatory drugs <sup>[5]</sup>
- Other risk factors and co-morbidities includes
  - Family history
  - Certain medications and foods
  - Respiratory diseases
  - Reflux chest pain syndrome

**Complication:**

- Esophagitis
- Strictures
- Barrett esophagus
- Esophageal adenocarcinoma

**Diagnosis:**

- Clinical history
- Endoscopy <sup>[6]</sup>
- Ambulatory pH monitoring
- Empiric trial of a proton pump inhibitor as a diagnostic test for GERD
- Manometry
- Barium radiography <sup>[7]</sup>

**Treatment:**

Acid suppressive therapy using PPI provides symptomatic relief and prevents complications in many individuals with GERD. Prokinetic drugs increase the gastrointestinal tract's smooth muscle activity. It could be taken along with medication that suppresses acid production. Treatment of GERD symptoms have been associated with significant improvement in quality of life, including decreased physical pain, increased vitality, physical and social function, and emotional wellbeing <sup>[8]</sup>.

**RABEPRAZOLE: -**

Rabeprazole is a proton pump inhibitor that decreases the amount of acid produced in the stomach. Rabeprazole is usually given for up to 8 weeks at a time while esophagus heals. The process of hydrochloric acid (HCl) secretion into the gastric lumen is primarily controlled by the proton pump's  $H^+ / K^+ -ATPase$ , which is highly expressed by the stomach's parietal cells. The parietal cell membrane contains an enzyme called ATPase, which helps the cell exchange hydrogen and potassium. Normally, this causes potassium to be extruded and HCl (gastric acid) to be formed. <sup>[9]</sup>.

**ITOPRIDE: -**

Itopride, a novel gastro prokinetic agent stimulate Gastro-intestinal motor activity which accelerate gastric emptying and modulates gastric sensorimotor function. It works by both antagonizing dopamine receptors and inhibiting the activity of acetylcholinesterase. Itopride helps to strengthen the lower esophageal sphincter (LES) and cause the contents of the stomach to empty faster. This allows less time for acid reflux to occur <sup>[10]</sup>.

**MATERIALS AND METHODS**

**Data source:** All the relevant information for the research was gathered through direct interviews with patients and caregivers as well as case files using appropriately created proforma. The study was approved by Research and Ethical Committee of Cosmopolitan hospital, Thiruvananthapuram.

**Study population:** Patients were taken from Gastroenterology department of Cosmopolitan Hospital. Informed consent was obtained. The study was conducted for the period of 2 months.

**Assessment of symptoms:** Details were collected from case records of the GERD patients and direct interview with the patient's caregivers.

**Assessment of QOL:** Details were collected from case records of the GERD patients and direct interview with the patients and caregivers which is been recorded in GERD-HRQL questionnaire <sup>[11]</sup>.

**Assessment of medication adherence:** Details were collected by direct interviewing the patients and

caregivers which is been recorded in ARMS Scale <sup>[12]</sup>.

**Statistical Analysis:** Comparison of quantitative variables between two groups was analyzed by Paired-T Test according to the nature of the data.

## OBSERVATION AND RESULTS

The proposed study entitled, “The Quality of Life in patients taking Rabeprazole Monotherapy versus Rabeprazole and Itopride Combination therapy in Gastro-esophageal reflux disease and Assessment of Medication Adherence” was a prospective observational comparative study carried out in a multi-specialty tertiary care hospital. In this study, the data was collected from 30 patients diagnosed with GERD and was analyzed. Among the 30 patients selected, 15 were taking Rabeprazole Monotherapy and 15 were taking Rabeprazole and Itopride Combination therapy. The study aimed to compare the Quality of Life of Patients taking Rabeprazole Monotherapy versus Rabeprazole and Itopride Combination therapy and to assess the Medication Adherence of patients with GERD.

### DEMOGRAPHIC DETAILS OF THE PATIENTS;

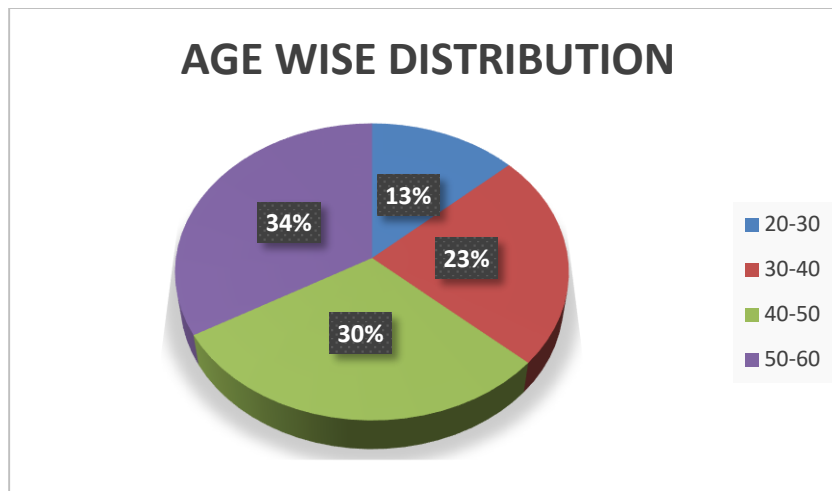
The data related to demographic details of patients were collected and recorded.

#### AGE WISE DISTRIBUTION

**Table: 1 Age distribution of study population**

Age (in years)	No: of patients (n=30)	Percentage (%)
20-30	4	13.3%
30-40	7	23.3%
40-50	9	30%
50-60	10	33.3%

As per the demographic data of the study population, GERD patients were found to be more in the age group of 50- 60 with a percentage of 33.3%. Followed by which the age group of 40-50 with 30%, the age group of 30-40 with 23.3% and 13.3% of patients were in the age group of 20-30.



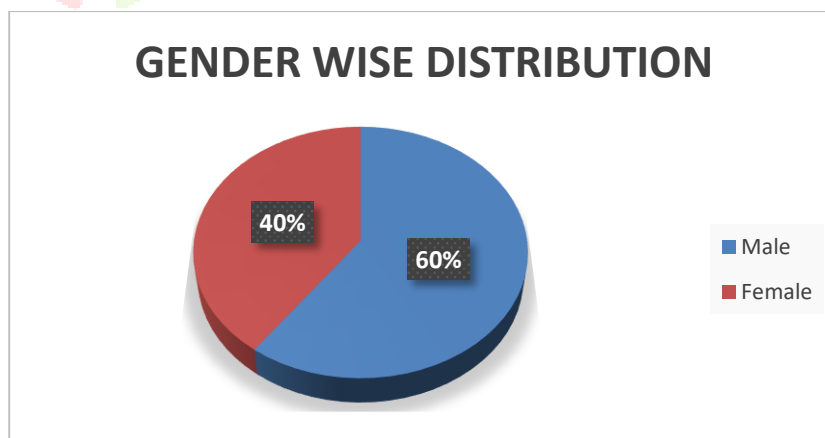
**Fig 1: -** Age wise distribution of study population

## GENDER WISE DISTRIBUTION

**Table: -2 Gender wise distribution**

Gender	No: of patients (n=30)	Percentage (%)
Male	18	60%
Female	12	40%

Gender wise distribution of the overall study population indicate that male population over-rides female population with 60% dominance over 40%. The entire study population include 18 male patients and 12 female patients, which indicates that the incidence of GERD in female is less than that of male population.



**Fig 2: -** Gender wise distribution of study population

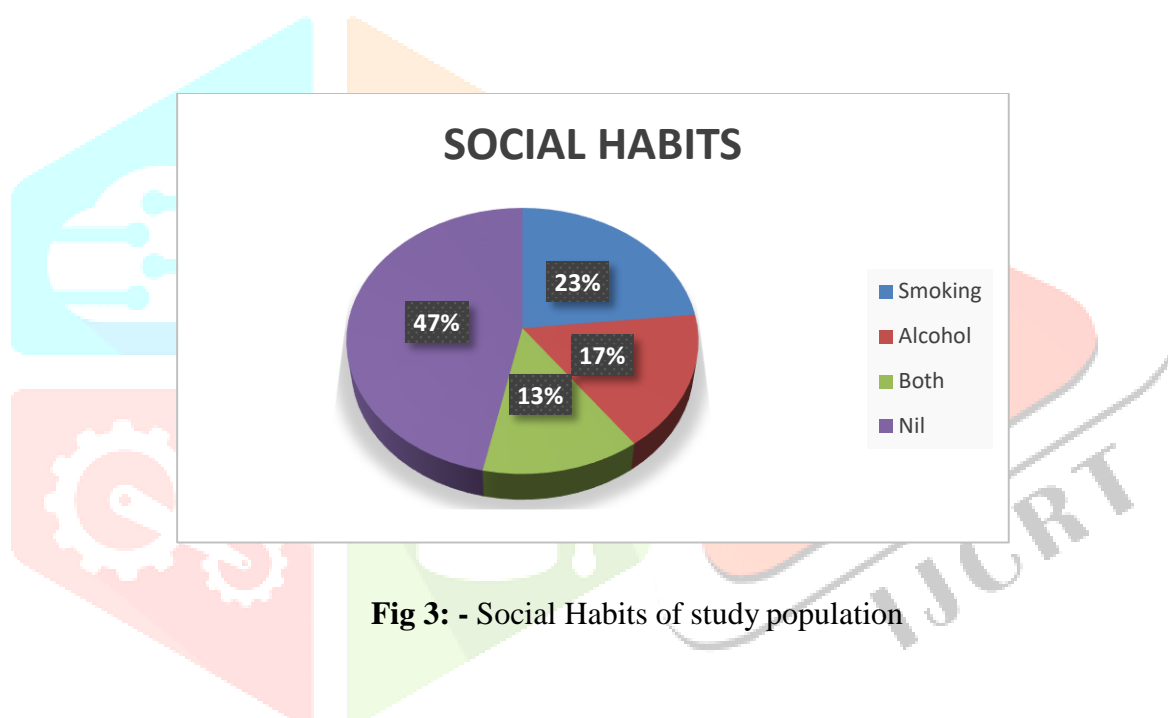


## SOCIAL HABITS

**Table 3: - Percentage of Social Habits**

Habits	No: of patients (n=30)	Percentage (%)
Smoking	7	23.3%
Alcohol	5	16.6%
Both	4	13.3%
Nil	14	46.6%

Social history of the overall study population indicates that patients who smokes are 23.3%, alcoholics are 16.6%, both are 13.3% and none are 46.6%.



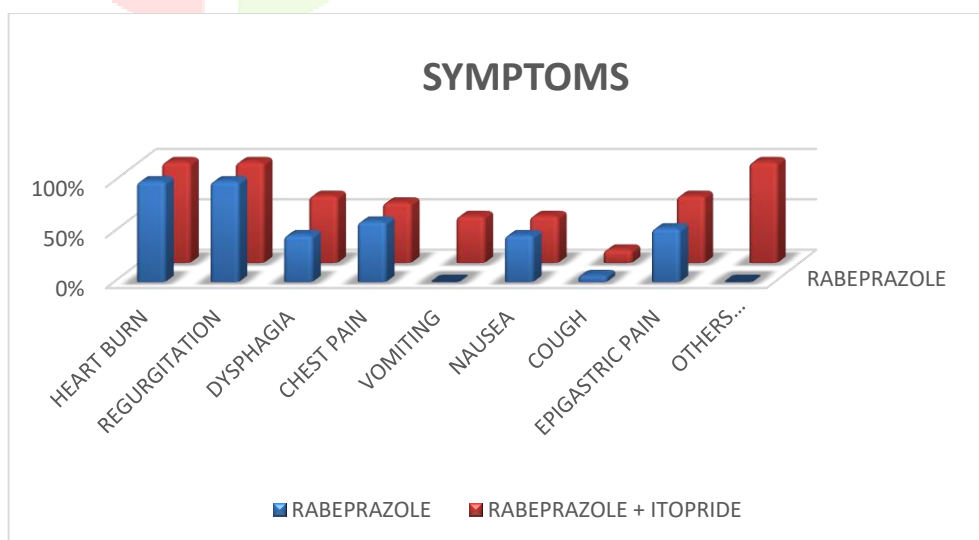
**Fig 3: - Social Habits of study population**

## PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON SYMPTOMS

**Table 4: Percentage of distribution of patients based on symptoms**

SYMPTOMS	RABEPRAZOLE		RABEPRAZOLE + ITOPRIDE	
	No:of patients (n=15)	%	No:of patients (n=15)	%
Heart Burn	15	100%	15	100%
Regurgitation	15	100%	15	100%
Dysphagia	7	46.6%	10	66.6%
Chest pain	9	60%	9	60%
Vomiting	0	0	7	46.6%
Nausea	7	46.6%	7	46.6%
Cough	1	6.6%	2	13.3%
Epigastric pain	8	53.3%	10	66.6%
Others (Dysmotility)	0	0	15	100%

From the table 4, it was observed that out of the total patients taking Rabeprazole monotherapy, 100% had heart burn, 100% had regurgitation, 46.6% had dysphagia, 60% had chest pain, 46.6% had nausea and 6.6% had cough and 53.3% had epigastric pain. Out of total patients taking Rabeprazole and Itopride combination therapy, 100% had heart burn, 100% had regurgitation, 66.6% had dysphagia, 60% had chest pain, 46.6% had vomiting, 46.6% had nausea, 13.3% had cough, 66.6% had epigastric pain and 100% had dysmotility.



**Fig 4:** Diagrammatic representation of patient based on symptoms.

## ASSESSMENT OF GERD-HRQL

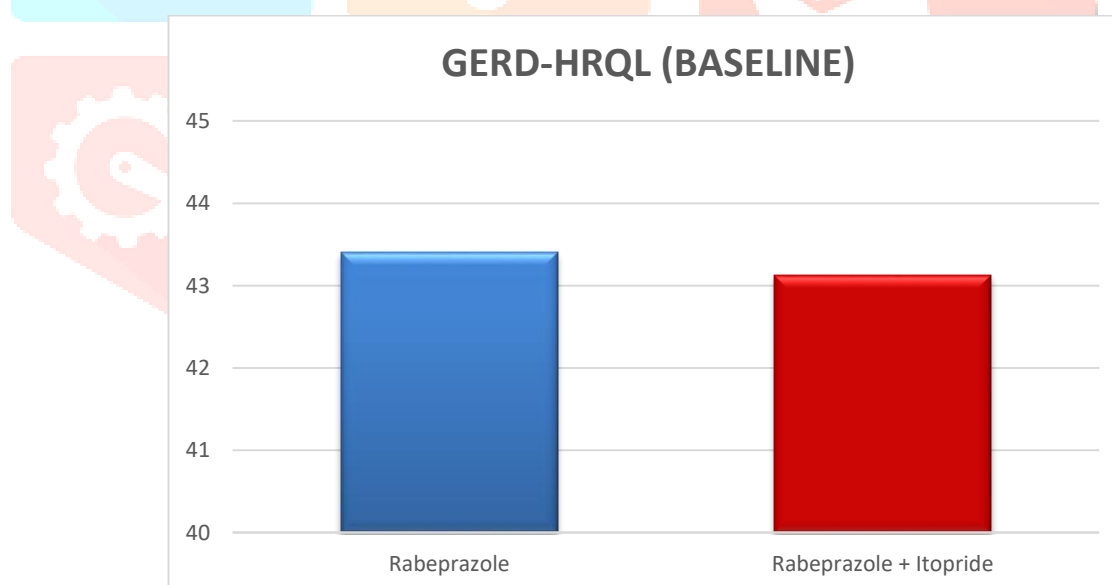
### ASSESSMENT OF GERD-HRQL AT THE TIME OF ADMISSION (BASELINE)

GERD-HRQL Questionnaire is used to measure the quality of life in patients with GERD. There are total of 10 questions, the score ranges up to 50. Higher the score, lower the QOL and vice versa.

**Table 5:** - Assessing the GERD-HRQL (Baseline)

Groups	No: of patients (n=30)	Mean $\pm$ SD
Rabeprazole	15	43.40 $\pm$ 2.22
Rabeprazole + Itopride	15	43.13 $\pm$ 2.61

The QOL is measured in the first week of treatment, mostly at the day of admission with the score range between 30-50. In 15 patients taking Rabeprazole alone, the mean score is 43.40  $\pm$  2.22 and in another 15 patients taking Rabeprazole and Itopride combination, the mean score is 43.13  $\pm$  2.61.

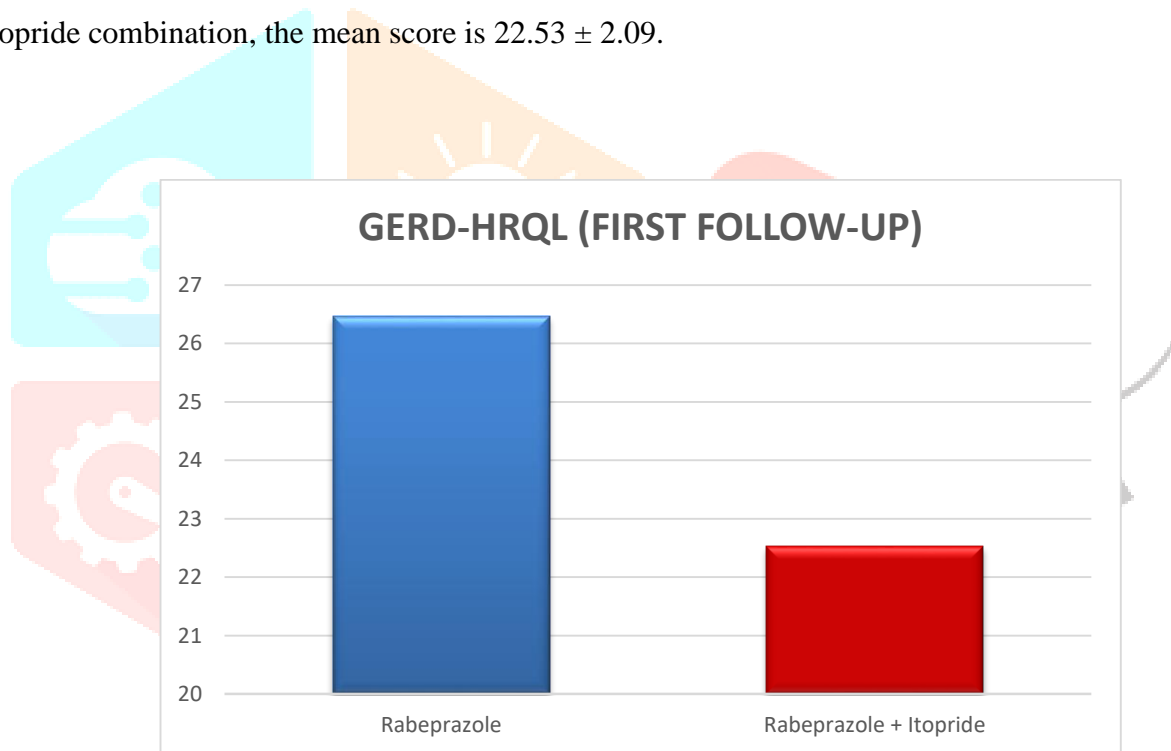


**Fig 5:** - Assessing of GERD-HRQL (Baseline)

**ASSESSMENT OF GERD-HRQL AT 4<sup>th</sup> WEEK (FIRST FOLLOWUP)****Table 6:** - Assessing the GERD-HRQL (First Follow-up)

Groups	No: of patients (n=30)	Mean $\pm$ SD
Rabeprazole	15	26.46 $\pm$ 1.45
Rabeprazole + Itopride	15	22.53 $\pm$ 2.09

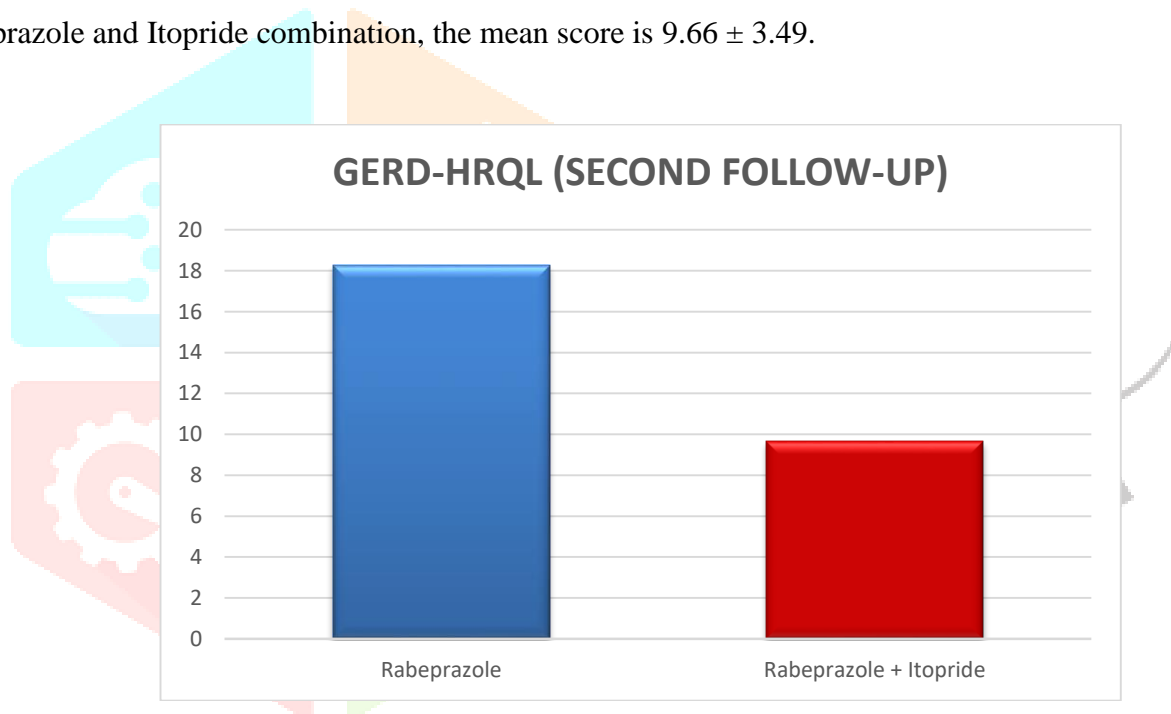
The follow up is taken in the end of 4<sup>th</sup> week of treatment, the score range was reduced from 30-50 to 20-30. A reduction in QOL score can be seen between the baseline and first follow-up measurement of QOL. In 15 patients taking Rabeprazole, the mean score is  $26.46 \pm 1.45$  and in another 15 patients taking Rabeprazole and Itopride combination, the mean score is  $22.53 \pm 2.09$ .

**Fig 6:** - Assessing the GERD-HRQL (First Follow-up)

**ASSESSMENT OF GERD-HRQL AT 8<sup>th</sup> WEEK (SECOND FOLLOWUP)****Table 7: - Assessing the GERD-HRQL (Second Follow-up)**

Groups	No: of patients (n=30)	Mean $\pm$ SD
Rabeprazole	15	18.26 $\pm$ 2.34
Rabeprazole + Itopride	15	9.66 $\pm$ 3.49

The follow up is taken in the end of 8<sup>th</sup> week of treatment, the score range was reduced from 20-30 to 5-20. A reduction in QOL score can be seen between the first follow-up and second follow-up measurement of QOL. In 15 patients taking Rabeprazole, the mean score is 18.26  $\pm$  2.34 and in another 15 patients taking Rabeprazole and Itopride combination, the mean score is 9.66  $\pm$  3.49.

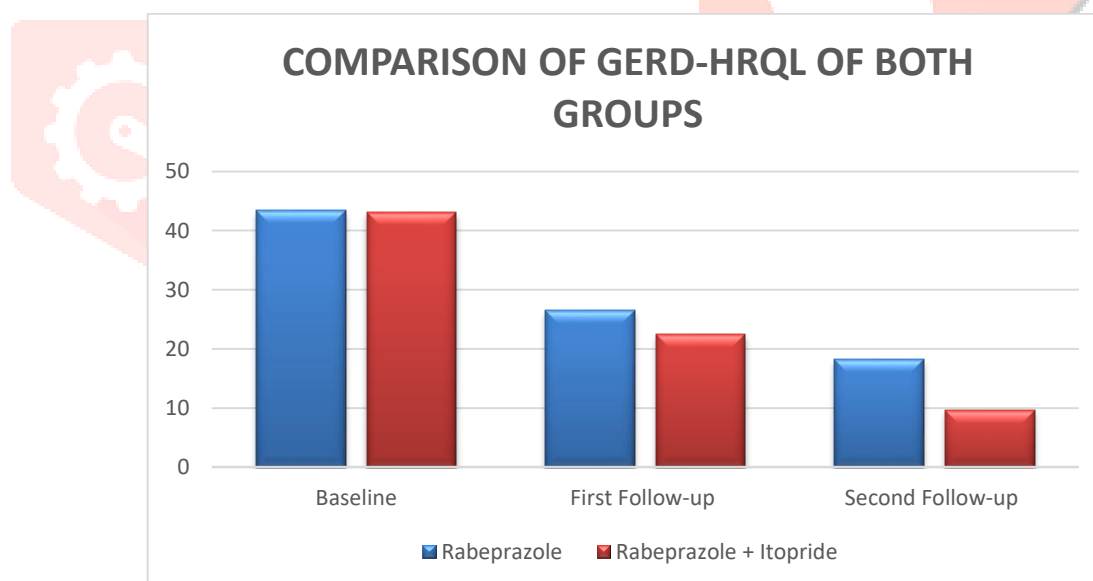
**Fig 7: - Assessing the GERD-HRQL (Second Follow-up)**

## COMPARISON OF GERD-HRQL OF BOTH GROUPS

**Table 8:** - Comparing the GERD-HRQL of both groups

Reviews	Rabeprazole	Rabeprazole+ Itopride	P value
Baseline	43.4 ± 2.22	43.13 ± 2.61	0.001*
First Follow-up	26.46 ± 1.45	22.53 ± 2.09	
Second Follow-up	18.26 ± 2.34	9.66 ± 3.49	

The group of patients taking Rabeprazole the baseline score was  $43.4 \pm 2.22$ , After the 4 weeks of treatment the score became  $26.46 \pm 1.45$  and after the 8 weeks of treatment the score became  $18.26 \pm 2.34$ . This demonstrates that on treating with Rabeprazole for a period of two months gives an improvement of patient's condition by 25.14%. The group of patients taking Rabeprazole and Itopride combination, the baseline score was  $43.13 \pm 2.61$ , after the 4 weeks of treatment the score became  $22.53 \pm 2.09$  and after the 8 weeks of treatment the score became  $9.66 \pm 3.49$ . This exhibit that on treatment with Rabeprazole and Itopride combination therapy for a period of two month improves the condition of the patient by 33.47%. The observed difference was  $p < 0.001$  which is statistically significant ( $p < 0.05$ ).

**Fig 8:** - Comparing GERD-HRQL of both groups

## ASSESSMENT OF MEDICATION ADHERENCE

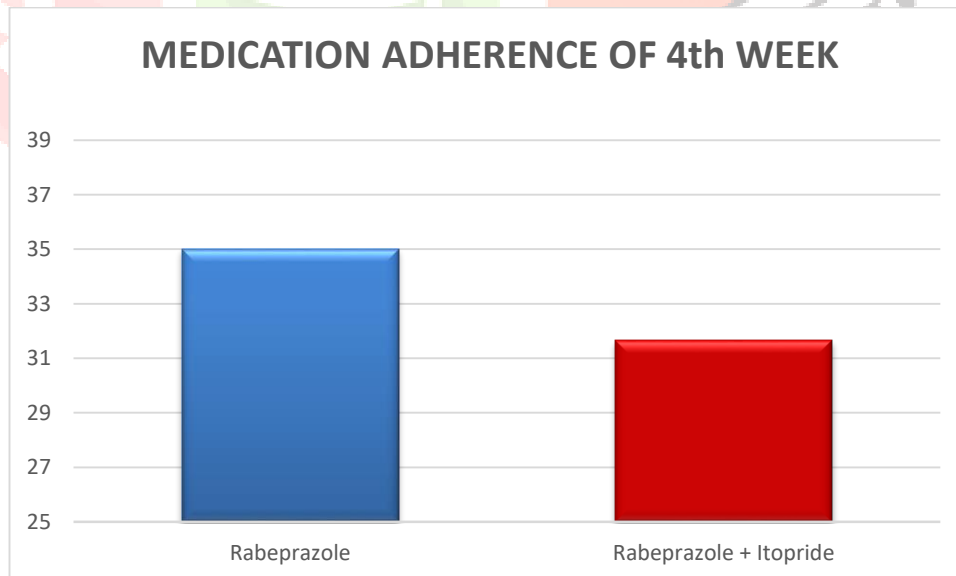
### ASSESSMENT OF MEDICATION ADHERENCE (4<sup>th</sup> WEEK)

Medication adherence is measured by using ARMS scale. There are 12 questions and the possible score ranges between 12 to 48. The lowest score indicates better adherence. The baseline of adherence is measured during the 4<sup>th</sup> week of the treatment.

**Table 9:** - Assessing the medication adherence (4<sup>th</sup> week)

Groups	No: of patients (n=30)	Mean $\pm$ SD
Rabeprazole	15	35 $\pm$ 6.87
Rabeprazole + Itopride	15	31.66 $\pm$ 5.13

During the data collection, the score was highest recorded between 25-48. In 15 patients taking Rabeprazole, the mean score was found to be 35  $\pm$  6.87. Another 15 patients taking Rabeprazole and Itopride combination, the mean score was found to be 31.66  $\pm$  5.13.

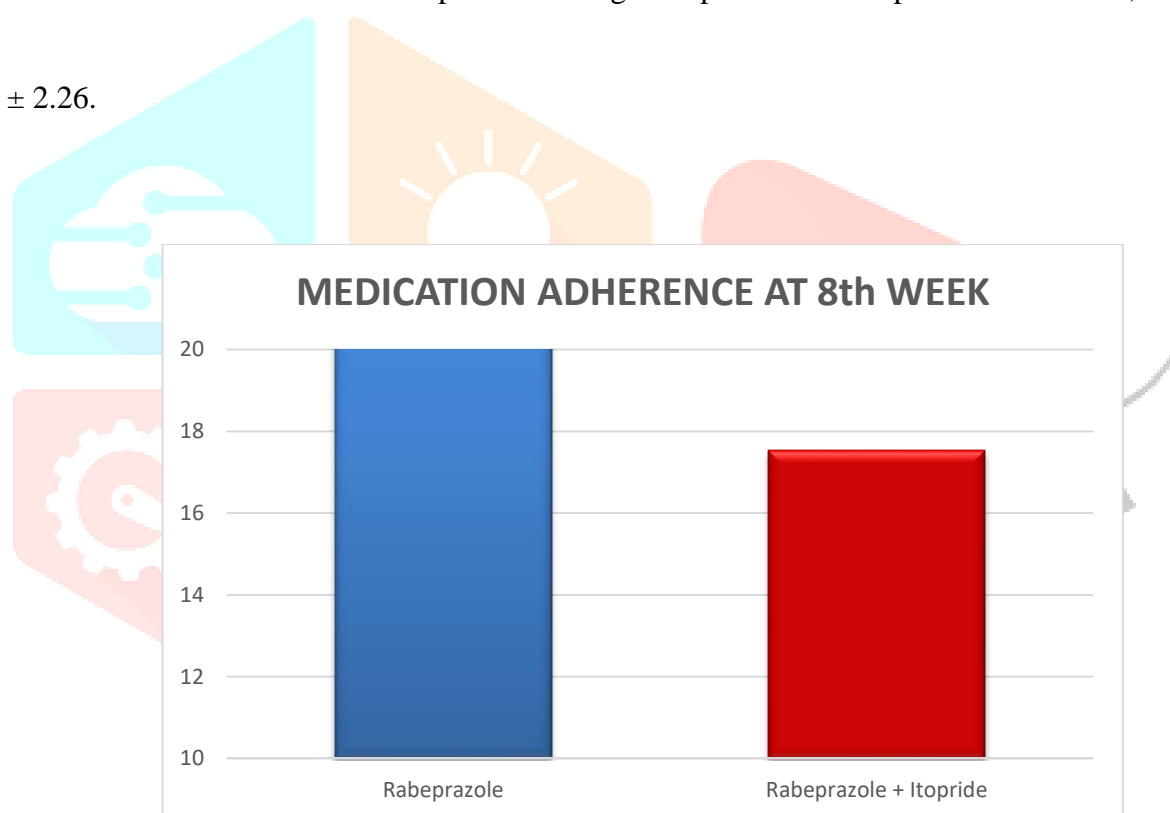


**Fig 9:** - Medication adherence of 4<sup>th</sup> week

**ASSESSMENT OF MEDICATION ADHERENCE (8<sup>th</sup> WEEK)****Table 10:** - Assessing the medication adherence (8<sup>th</sup> week)

Groups	No: of patients (n=30)	Mean $\pm$ SD
Rabeprazole	15	20.46 $\pm$ 3.24
Rabeprazole + Itopride	15	17.53 $\pm$ 2.26

After the end of 8<sup>th</sup> week, the follow up was conducted and the score reduced from 25-48 to 15-25. Reduction was seen from baseline to endline measurement of adherence. In 15 patients taking Rabeprazole, the mean score is  $20.46 \pm 3.24$  and in another 15 patients taking Rabeprazole and Itopride combination, the mean score is  $17.53 \pm 2.26$ .

**Fig 10:** - Medication adherence of 8<sup>th</sup> week

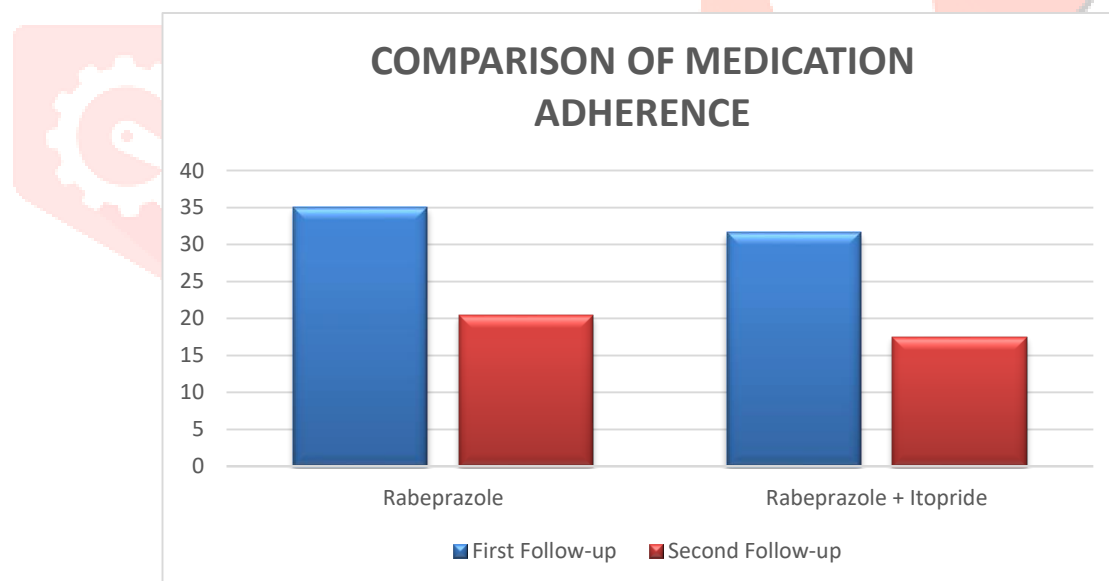


## COMPARISON OF MEDICATION ADHERENCE OF BOTH GROUPS

**Table 11:** - Comparing the medication adherence of both groups

Reviews	Rabeprazole	Rabeprazole+ Itopride	p value
First Follow-up	35 ± 6.87	31.66 ± 5.13	<.001
Second Follow-up	20.46 ± 3.24	17.53 ± 2.26	

The group of patients taking Rabeprazole the baseline score was  $35 \pm 6.87$  and after the end of treatment the score became  $20.46 \pm 3.24$ . This demonstrates that on treating with Rabeprazole for a period of two months gives an improvement of patient's condition by 14.54%. The group of patients taking Rabeprazole and Itopride combination the baseline score was  $31.66 \pm 5.13$  and after the treatment the score became  $17.53 \pm 2.26$ . This exhibit that on treatment with Rabeprazole and Itopride combination for a period of two month improves the condition of the patient by 14.13%. The observed difference was  $p < 0.001$  which is statistically significant ( $p < 0.05$ ).



**Fig 11:** - Comparing the medication adherence of both groups

## DISCUSSION

Gastro-esophageal reflux disease is the abdominal retrograde movement of gastric contents from the stomach to esophagus. Common symptoms include heartburn, regurgitation, dysphagia. The treatment of GERD includes gastric acid suppression therapy with a proton pump inhibitor because of its efficacy and fast healing rate. Among the proton pump inhibitors, Rabeprazole reduce acid production and have high healing rates of reflux symptoms. Itopride, a novel gastro prokinetic agent stimulate Gastro-intestinal motor activity which accelerate gastric emptying and modulates gastric sensorimotor function.

The two drugs concerned in the study are Rabeprazole and Itopride. Rabeprazole is used in the study than other PPI, since it provides superior healing rates and symptom relief in patients with GERD. Itopride helps to strengthen the lower esophageal sphincter (LES) and cause the contents of the stomach to empty faster. This allows less time for acid reflux to occur.

In this study 30 patients with GERD were taken. Among which, 15 patients taking Rabeprazole alone and 15 patients taking Rabeprazole and Itopride combination. Statistical analysis was performed using paired-t test and a detailed analysis was performed.

The main aim of our study is to compare the Quality of Life using GERD-HRQL and Medication Adherence using ARMS Scale in patients taking Rabeprazole monotherapy versus Rabeprazole and Itopride combination therapy in gastro-esophageal reflux disease. Better result was achieved in patients treated with Rabeprazole and Itopride combination therapy.

The observation of our study was similar to the result of the study conducted by **Johanson et.al**. In their study **“Rabeprazole Improves Health-Related Quality of life in Patients with Erosive Gastroesophageal Reflux Disease”**. This prospective study describes that Rabeprazole significantly improved health-related quality of life in erosive gastro-esophageal reflux disease patients and restored social functioning and emotional well-being.

The observation of our study was also similar to the result of the study conducted by **Kumar R et.al**. In their study **“Comparative evaluation of itopride and domperidone in gastroesophageal reflux disease”**. This study describes that Combination of itopride and rabeprazole showed insignificantly better results, both symptomatically and endoscopically in comparison to the combination of domperidone and rabeprazole.

The result of our study was similar to the study conducted by **Young Sun Kim et.al**. on the topic **“Sex and Gender Differences in Gastroesophageal Reflux Disease”** showed a predominance of Reflux Esophagitis in men, but a predominance of symptomatic GERD in women.

The result of our study was similar to the study conducted by **P J Kahrilas et.al** on the topic **“Mechanisms of Acid Reflux Associated with Cigarette Smoking”** suggested that smoking does seem

to impact significantly on gastroesophageal reflux disease and it is likely to exacerbate the disease.

The result of our study was similar to the study conducted by **Maxwell M Chait** on the topic **“Gastroesophageal Reflux Disease: Important Considerations for the Older Patients”** suggested that GERD and its associated complications are common in the older patient compared to the rest age group.

The GERD-HRQL questionnaire is used to assess patients' Quality of Life. Results indicate that patients receiving Rabeprazole had a score range of 25.14%, whereas patients taking Rabeprazole and itopride combination had a score range of 33.47%. This demonstrates that after eight weeks of treatment, individuals receiving a combination medication of Rabeprazole and itopride have a higher Quality of Life than those receiving Rabeprazole alone.

The ARMS Scale is used to evaluate medication adherence, and the results indicated that 14.54% of patients using Rabeprazole and 14.13% of patients taking Rabeprazole and Itopride. This demonstrates that toward the end of the eight weeks of treatment, the patient was more adherent with the regimen. To conclude, Rabeprazole and Itopride combination therapy is more effective than Rabeprazole alone for rapid relief of heartburn symptoms and acid reflux symptoms in patients with GERD.

## CONCLUSION

The conclusion of this study suggests that patients taking Rabeprazole and Itopride 20/150mg combination therapy provides more improvement in Quality of Life in patients with Gastro Esophageal Reflux Disease than Rabeprazole 20mg monotherapy after 8 weeks of treatment. It was also found that patient counselling has an important role in improving the Quality of Life and Medication Adherence of GERD patients who were taking Rabeprazole monotherapy and Rabeprazole and Itopride combination therapy. Impact of patient counselling yields better therapeutic outcome. Hence, the well- being of the patients is ensured.

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