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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.

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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. The aim is 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. The objectives of the study is to assess the quality of life and to assess the medication adherence.

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 4th and 8th 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).

The result of the study involves 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.

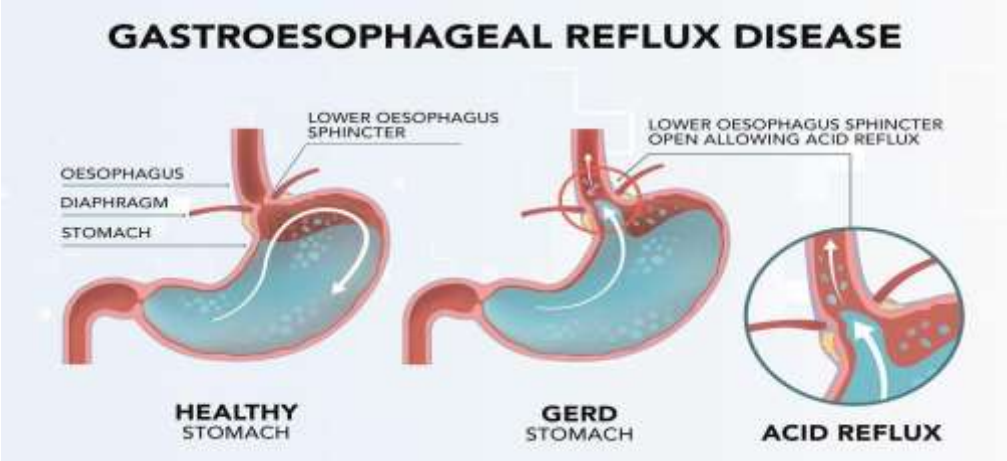
The Conclusion is the Patients taking Rabeprazole and Itopride combination therapy provides more improvement in Quality of Life and medication adherence in Gastro Esophageal Reflux Disease than Rabeprazole monotherapy after 8 weeks of treatment.

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 ≥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 [5]
- 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 [6]
- Ambulatory pH monitoring
- Empiric trial of a proton pump inhibitor as a diagnostic test for GERD
- Manometry
- Barium radiography [7]

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 [8].

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. [9].

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 [10].

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 6 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 thepatients and caregivers which is been recorded in GERD-HRQL questionnaire [11].

Gastroesophageal Reflux Disease-Health Related Quality of Life questionnaire

Question	Score					
1. How bad is your heartburn?	0	1	2	3	4	5
2. Heartburn when lying down?	0	1	2	3	4	5
3. Heartburn when standing up?	0	1	2	3	4	5
4. Heartburn after meals?	0	1	2	3	4	5
5. Does heartburn change your diet?	0	1	2	3	4	5
6. Does heartburn wake you from sleep?	0	1	2	3	4	5
7. Do you have difficulty swallowing?	0	1	2	3	4	5
8. Do you have pain with swallowing?	0	1	2	3	4	5
9. Do you have bloating or gassy feelings?	0	1	2	3	4	5
10. If you take medication, does this affect your daily life?	0	1	2	3	4	5

No symptoms= 0; Symptoms noticeable, but not bothersome= 1; Symptoms noticeable and bothersome, but not every day= 2; Symptoms bothersome every day= 3; Symptoms affect daily activities= 4; Symptoms are incapacitating, unable to do daily activities= 5

Assessment of medication adherence: Details were collected by direct interviewing the patients and caregiverswhich is been recorded in ARMS Scale [12].

ADHERENCE TO REFILLS AND MEDICATIONS SCALE (ARMS)

It is common for people to miss taking their medicine from time to time, or to take it differently than prescribed. I would like to ask you about how you actually take your medicines. There are no right or wrong answers. For each question, please answer "none of the time," "some of the time," "most of the time," or "all of the time."

	None	Some	Most	All
1. How often do you forget to take your medicine?	1	2	3	4
2. How often do you decide not to take your medicine?	1	2	3	4
3. How often do you forget to get prescriptions filled?	1	2	3	4
4. How often do you run out of medicine?	1	2	3	4
5. How often do you skip a dose of your medicine before you go to the doctor?	1	2	3	4
6. How often do you miss taking your medicine when you feel better?	1	2	3	4
7. How often do you miss taking your medicine when you feel sick?	1	2	3	4
8. How often do you miss taking your medicine when you are careless?	1	2	3	4
9. How often do you change the dose of your medicines to suit your needs (like when you take more or less pills than you're supposed to)?	1	2	3	4
10. How often do you forget to take your medicine when you are supposed to take it more than once a day?	1	2	3	4
11. How often do you put off refilling your medicines because they cost too much money?	1	2	3	4
12. How often do you plan ahead and refill your medicines before they run out?	1	2	3	4

Scoring: Item 12 should be reverse coded. Then add 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.

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, "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" carried out in a multispecialty tertiary care hospital. In this study the data was collected from 60 patients diagnosed with GERD and was analyzed. Among the 60 patients selected, 30 were taking Rabeprazole monotherapy and 30 were taking Rabeprazole and Itopride combination therapy. During the study period 60 patients had completed the follow-up.

DEMOGRAPHIC DETAILS OF THE PATIENTS

In this section, the data related to demographic details of patients were collected and recorded

PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON AGE

Table:1 Percentage distribution of patients based on Age

Age (in years)	No: of patients (n=60)	Percentage (%)
20-30	10	16.6%
30-40	14	23.3%
40-50	16	26.6%
50-60	20	33.3%

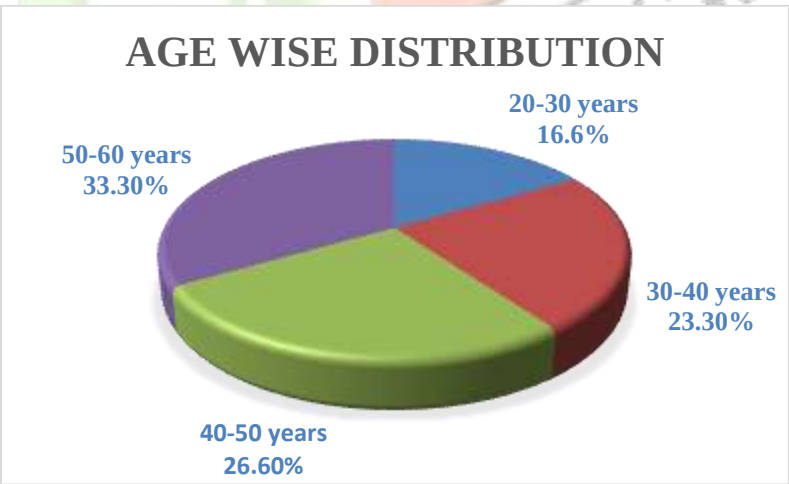


Fig 1: - Diagrammatic representation of patients based on Age

In this study, patients from the group of 20-60 were included. It was observed that majority of the patient presenting with GERD were from the group of 50-60 followed by the patient in the age group of 40-50.

PERCENTAGE DISTRIBUTION OF PATIENT BASED ON GENDER

Table: -2 Percentage distribution of patient based on Gender

Gender	No: of patients (n=60)	Percentage (%)
Male	41	68.3%
Female	19	31.6%

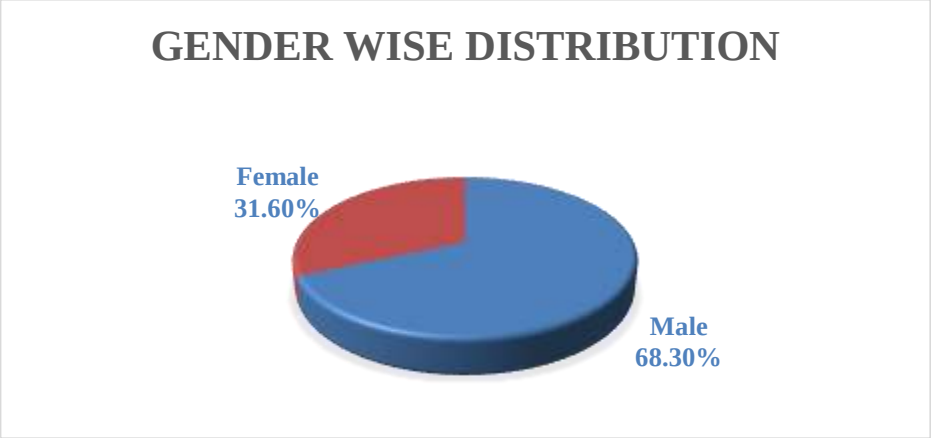


Fig 2: - Diagrammatic representation of patients based on Gender

Amongst a total of 60 patients included in this study, a preponderance of male patients was observed. In this study 41 patients were female (68.30%) while 19 patients were male (31.60%).

PERCENTAGE WISE DISTRIBUTION OF PATIENTS BASED ON SOCIAL HABITS

Table 3: - Percentage wise distribution of patients based on Social Habits

Habits	No: of patients (n=30)	Percentage (%)
Smoking	21	35%
Alcohol	10	16.6%
Both	9	15%
Nil	20	33.3%

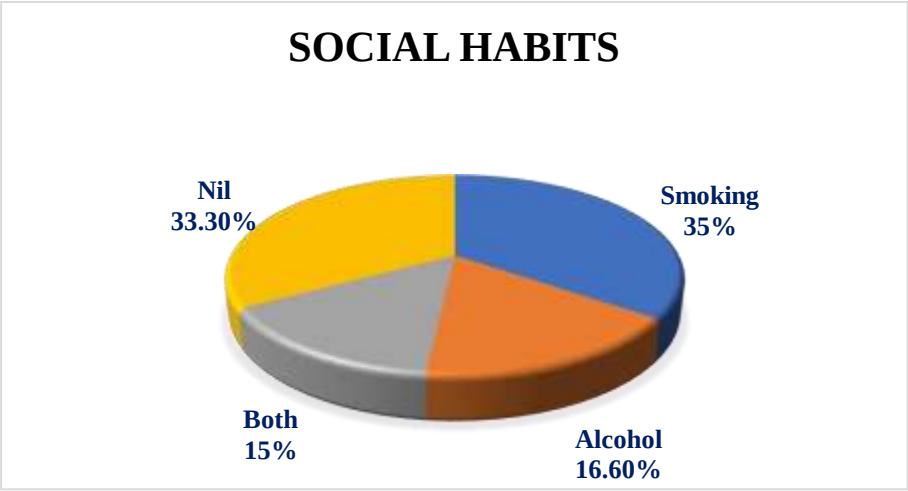


Fig 3: - Diagrammatic representation of patients based on Social Habits

Social history of the study population concludes that 35% of patients were smokers, 16.6% were alcoholics, and 15% were both smokers and alcoholics, and 33.3% of patients were non-alcoholics and non-smokers.

PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON SYMPTOMS

Table 4: Percentage wise distribution of patients based on symptoms

Symptoms	No. of patients (n=60)	Percentage (%)
Heartburn	60	100%
Regurgitation	60	100%
Dysphagia	32	53.3%
Chest pain	25	41.6%
Vomiting	30	50%
Nausea	29	48.3%
Cough	14	23.3%
Epigastric pain	29	48.3%
Others (Dysmotility)	30	50%

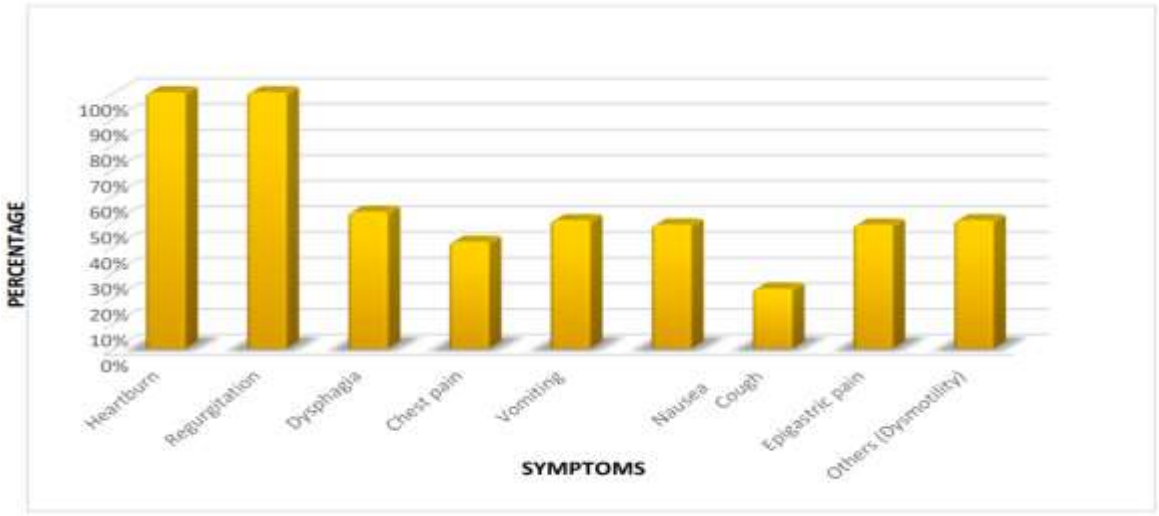


Fig 4: Diagrammatic representation of patient based on symptoms.

Out of the total patients 100% present with both heart burn and regurgitation, 50% had both vomiting and dysmotility, 53.5% dysphagia, 48.3% epigastric pain, 41.6% chest pain, 48.3% nausea and 23.3% cough.

ASSESSMENT OF QUALITY OF LIFE USING GERD-HRQL QUESTIONNAIRE

BASELINE ASSESSMENT OF GERD-HRQL

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: - Baseline assessment of GERD-HRQL

Groups	**No: of patients (n=60)**	**GERD-HRQL Score Mean ± SD**
Rabeprazole	30	43.93 ± 2.66
Rabeprazole + Itopride	30	44.4 ± 2.58

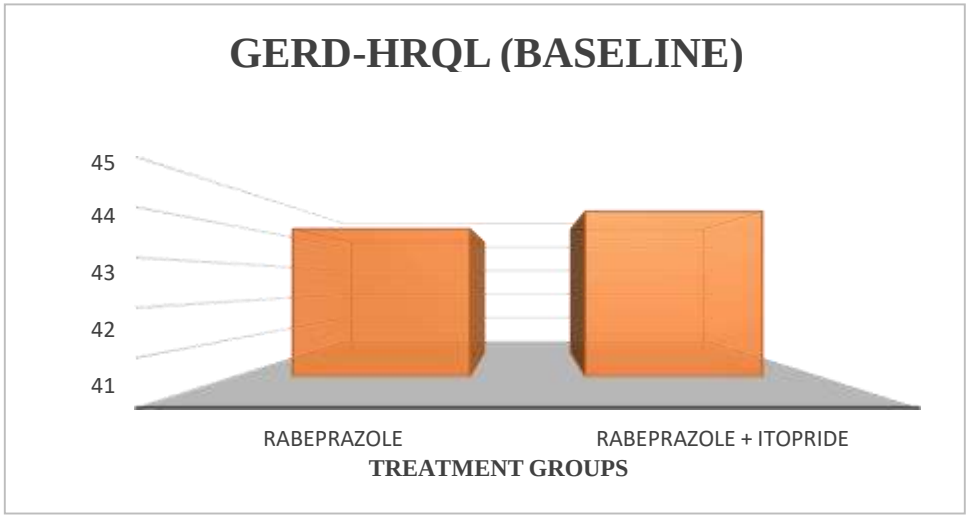


Fig 5: - Baseline GERD-HRQL

From table 5, GERD-HRQL score of 30 patients from each Group A and Group B were found to be respectively 43.93% and 44.4%.

ASSESSMENT OF GERD-HRQL AT 4th WEEK (FIRST FOLLOWUP)

Table 6: - Assessment of GERD-HRQL at 4th week

Groups	No: of patients (n=60)	GERD-HRQL Score Mean ± SD
Rabeprazole	30	26.63 ± 1.40
Rabeprazole + Itopride	30	22.93 ± 2.30

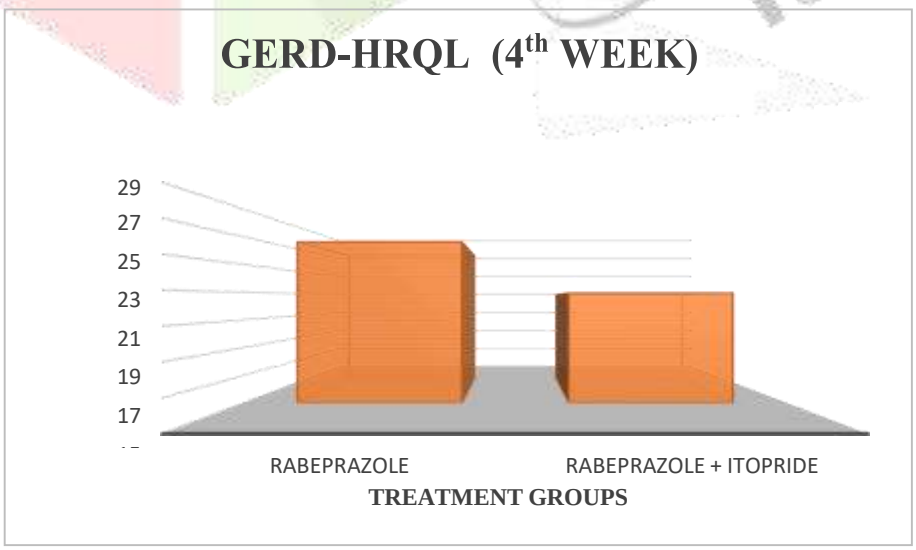


Fig 6: - Assessment of GERD-HRQL at 4th week

From table 6, GERD-HRQL score of 30 patients from each Group A and Group B were found to be respectively 26.63% and 22.93%. Thus, from table 6 the Quality of life in patients taking Rabeprazole and Itopride combination is comparatively high.

ASSESSMENT OF GERD-HRQL AT 8th WEEK (SECOND FOLLOW-UP)

Table 7: - Assessment of GERD-HRQL at 8th week

Groups	No: of patients (n=60)	GERD-HRQL Score Mean ± SD
Rabeprazole	30	18.23 ± 2.43
Rabeprazole + Itopride	30	10.36 ± 3.32

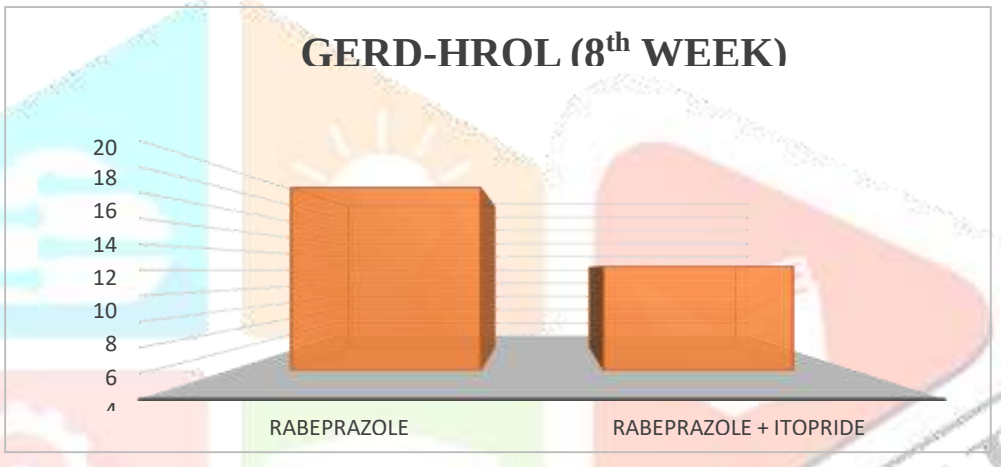


Fig 7: - Assessment of GERD-HRQL at 8th week

From table 7, GERD-HRQL score of 30 patients from each Group A and Group B were found to be respectively 18.23% and 10.36%. Thus, from table 7 the Quality of life in patients taking Rabeprazole and Itopride combination is comparatively high.

COMPARISON OF GERD-HRQL OF BOTH GROUPS

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

GROUPS	BASE LINE	AT 4th WEEK	AT 8th WEEK	P-VALUE
Group-A (Rabeprazole)	43.93 ± 2.66	26.63 ± 1.40	18.23 ± 2.43	0.001*
Group-B (Rabeprazole +Itopride)	44.4 ± 2.58	22.93 ± 2.30	10.36 ± 3.32	

*p value < 0.05 was considered to be significant. P value < 0.001

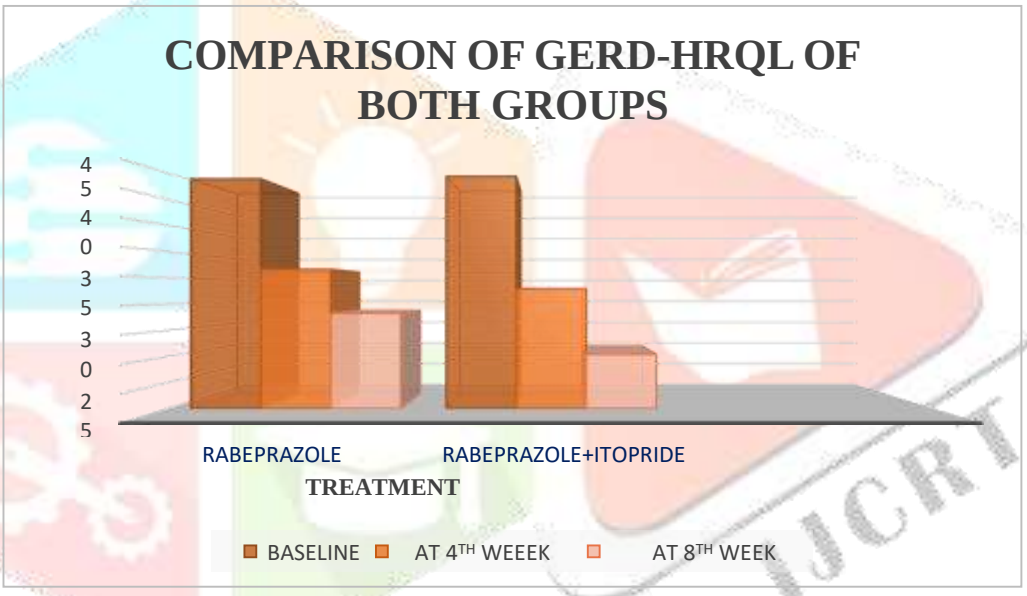


Fig 8: - Comparing GERD-HRQL of both groups

The GERD-HRQL of both groups are compared with a paired t-test and found that the paired mean difference is drastically decreased and this is found to be statistically significant. This exhibits that on treatment with Rabeprazole and Itopride combination for a period of two month improves the condition of the patient by 34.04%. The p-value= 0.001

ASSESSMENT OF MEDICATION ADHERENCE USING ARMS SCALE

ASSESSMENT OF MEDICATION ADHERENCE AT 4th WEEK

Medication adherence is measured by using ARMS (Adherence to Refill and Medication scale) scale.There are 12 questions and the possible score ranges from 12 to 48. The lowest score indicates better adherence. The medication adherence is measured during the 4th and 8th week of the treatment respectively.

Table 9: - Medication Adherence at 4th week

Groups	No: of patients (n=60)	Mean ± SD
Group-A (Rabeprazole)	30	35.26 ± 7.16
Group-B (Rabeprazole + Itopride)	30	33.26 ± 4.67

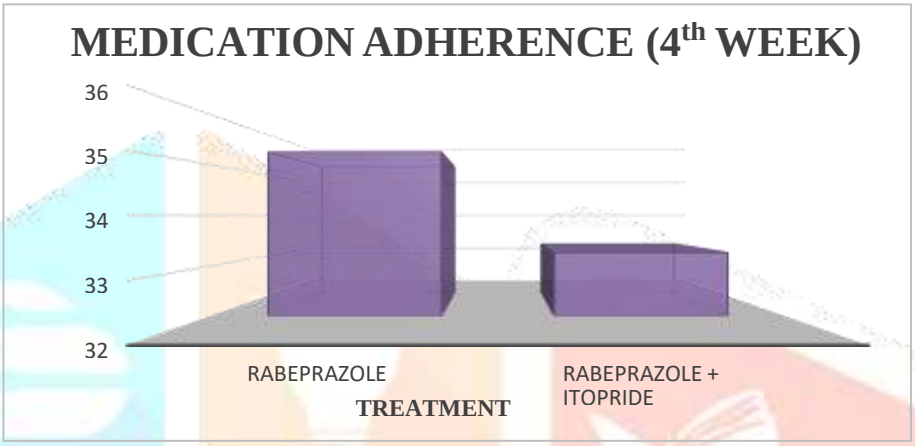


Fig 9: - Medication adherence at 4th week

From table 9, ARMS score of 30 patients from each Group A and Group B were found to be respectively 35.26% and 33.26%.

ASSESSMENT OF MEDICATION ADHERENCE AT 8th WEEK

Table 10: - Medication adherence at 8th week

Groups	**No: of patients (n=60)**	**ARMS Score Mean ± SD**
Group-A (Rabeprazole)	30	20.06 ± 3.37
Group-B (Rabeprazole + Itopride)	30	17.7 ± 2.29

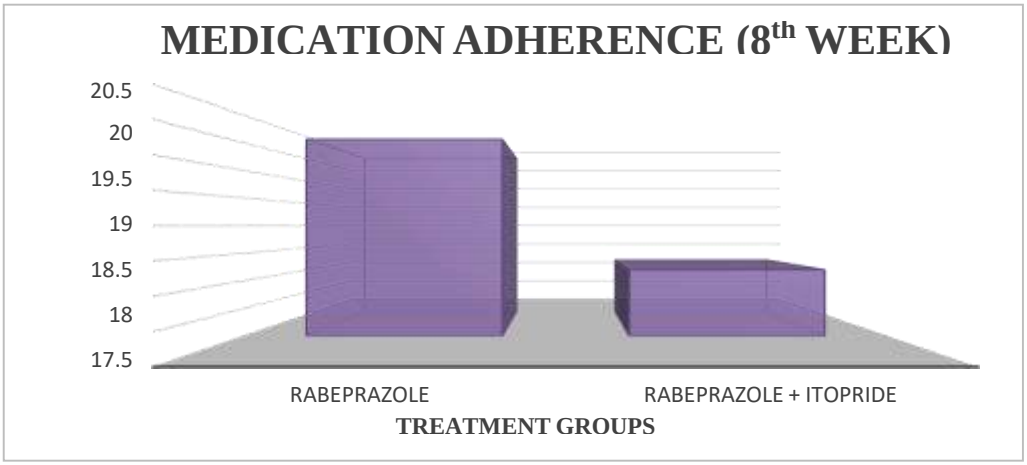


Fig 10: - Medication adherence at 8th week

From table 10, ARMS score of 30 patients from each Group A and Group B were found to be respectively 20.06% and 17.7%. Thus, from the above table the Medication adherence in patients taking Rabeprazole and Itopride combination is comparatively high.

COMPARISON OF MEDICATION ADHERENCE OF BOTH GROUPS

Table 11: - Comparing the medication adherence of both groups

GROUPS	AT 4TH WEEK	AT 8TH WEEK	P-VALUE
Group-A (Rabeprazole)	35.26 ± 7.16	20.06 ± 3.37	0.001*
Group-B (Rabeprazole + Itopride)	33.26 ± 4.67	17.7 ± 2.29	

*p value < 0.05 was considered to be significant. P value < 0.001

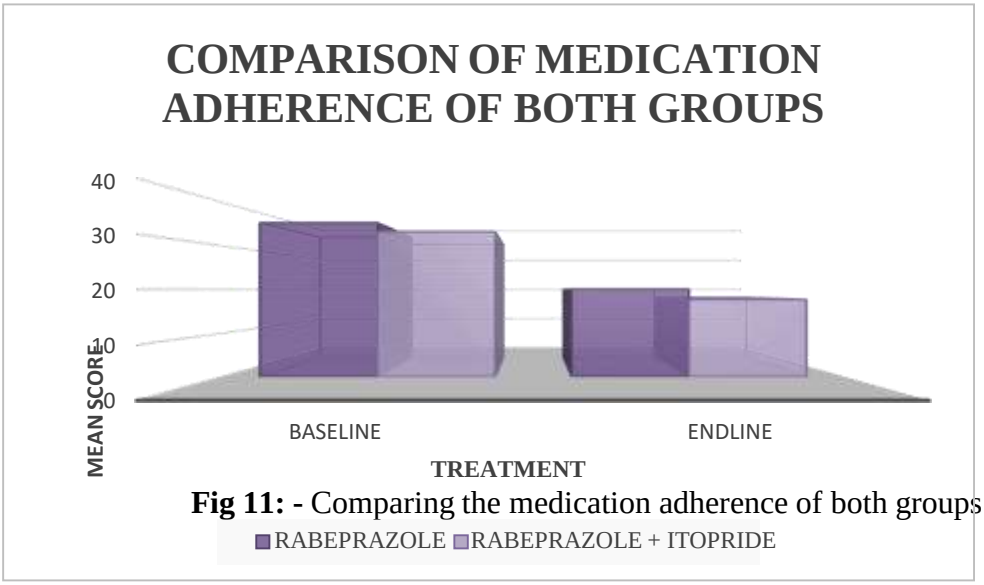


Fig 11: - Comparing the medication adherence of both groups

The Medication adherence of both groups are compared with a paired t-test and found that the paired mean difference is drastically decreased and this is found to be statistically significant. This exhibits that on treatment with Rabeprazole and Itopride combination for a period of two month improves the condition of the patient by 15.56%. The p-value=0.001

SUMMARY

A Prospective observational comparative study was conducted in the Department of Gastroenterology at Cosmopolitan Hospital on " **Assessment of the quality of life in patients taking Rabeprazole monotherapy versus Rabeprazole and Itopride combination therapy in Gastro-Esophageal Reflux Disease** " after getting clearance from Ethical committee. The objectives of the study were to assess the Quality of Life using GERD-HRQL Questionnaire and Medication Adherence using ARMS Scale. The selection of patients was based on the inclusion and exclusion criteria. The estimated sample size was 60. Patient's demographic details, social habits, symptoms were collected.

- Analysis of the demographic data revealed that the majority of the patient presenting with GERD were from the group of 50-60 followed by the patient in the age group of 40-50, comprising 33.3% of the study population.
- Amongst a total of 60 patients included in this study, a preponderance of male patients was observed. In this study 41 patients were female (68.30%) while 19 patients were male (31.60%).
- Social history of the study population concludes that 35% of patients were smokers, 16.6% were alcoholics, and 15% were both smokers and alcoholics, and 33.3% of patients were non-alcoholics and non-smokers.

Symptom prevalence among participants showed 100% experiencing heartburn and regurgitation, 50% present with vomiting and Dysmotility, Dysphagia noted in 53.5%, Chest pain in 41.6%, Nausea in 48.3%, Cough in 23.3%, Epigastric pain in 48.3% of cases.

- 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 at the end of the eight weeks of treatment, the patient was more adherent with the regimen. In summary, the combination therapy of Rabeprazole and Itopride proves to be more efficacious than Rabeprazole alone for rapid relief of heartburn and acid reflux symptoms in GERD patients.
- The findings indicate that treatment with the rabeprazole and itopride combination yielded superior outcomes in both enhancing Quality of life and improving Medication adherence among GERD patients.

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 therapeuticoutcome. Hence, the well- being of the patients is ensured.

For the study a total of 60 patients were selected. The study was conducted on two groups, one group taking Rabeprazole Monotherapy and the other group taking Rabeprazole and Itopride combination therapy. Group A and group B involve 30 patients each. 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 higherQuality 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.

The results assessed from the study clearly indicates that the treatment with Rabeprazole and Itopride combination showed better outcome in both aspects of improvement in Qualityof Life and Rate of adherence in GERD patients. Even though the Rabeprazole produces more outcome, the treatment with Rabeprazole and Itopride combination is far beneath in case of outcome.

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