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# DRUG UTILIZATION PATTERN OF PANTOPRAZOLE MONOTHERAPY COMPARISION WITH PANTOPRAZOLE AND ITOPRIDE HCL COMBINATION THERAPY IN GERD" RETROSPECTIVE STUDY IN TERTIARY CARE HOSPITAL

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## ABSTRACT

**Background**: An oesophageal condition known as gastroesophageal reflux disease is characterised by a back flow of acid from the stomach and other gastric fluid into the oesophagus, which can irritate and inflame the tissue. The pathophysiology of the GERD continues to remain slightly misunderstood, but it's now considered to be a multifactorial disease. H2 agonists as well proton pump inhibitors are two common medications used for the management of GERD disease. There are some well-known clinical agents including Pantoprazole and a prokeinetic agents like Itopride Hydrochloride that are prescribed to treat the GERD patients to prevent the disease progression and for prophylaxis as well. as Pantoprazole inhibits gastric acid and basal acid secretion by linking covalently to the H+/K+ ATP pump in the stomach's digestive parietal cell. Dopamine D2 receptor antagonist and acetylcholine esterase inhibitor itopride HCl is prescribed for the treatment of functional

dyspepsia symptoms as well as those associated with other gastroesophageal diseases. This study shows the drug utilization pattern for the GERD disease treatment with the use of Pantoprazole monotherapy in comparison with itopride Hydrochloride combination therapy to see which is the better approach in the treatment of the patients, keeping in mind the cost of the drugs given to the patients.

**Objective:** To estimate utilization and prescribing trends of pantoprazole agents alone and it's combination with itopride in gastroesophageal reflux disease. To determine the cost analysis of combination therapy (pantoprazole+itopride) in GERD patients. To determine if pantoprazole and its combination provides maximum clinical benefits and minimum risks to the patients.

**Materials and Methods**: It is a retrospective observational study conducted at a single centre done by obtaining the data of the patients receiving PPI agents and prokinetic agents for the treatment of the GERD. Drugs utilization evaluation and cost analysis of Pantoprazole and Itopride Hydrochloride is done. Total 100 patients' data was collected and observed from Parul sevashram Hospital. In the data collection analysis form, the data was reported and analysed using graphical, chart, figures and tabulations and summarised visually. Unpaired t-test, chi-square, and an analysis of variance (ANOVA) were used in MS-Excel's statistical analysis, and the p-value was calculated.

**Results**: Total out of 100 patient's data 50 were prescribed with pantoprazole and 50 were prescribed with pantoprazole and itopride combination in which 20% of participants showed recovery in less than a week, 37% in one to two weeks, 36% in two to four weeks, and 7% in four to six weeks. According to the recommended therapy, there were 64% male and 36% female participants.

**Conclusion**: pantoprazole 40 mg and pantoprazole-itopride hcl 150 mg both drugs are showing same healing rate into this study. However more research and large sample size required for comparision of efficacy in both drugs.

**Keywords**: **GERD (gastroesophageal reflux disease), pantoprazole, pantoprazole-itopride hydrochloride, TLESR (transient LES relaxation), Reflux mechanism**

## INTRODUCTON

### GERD: GASTROESOPHAGEAL REFLUX DISEASE

A group of experts worked together to define and categorise reflux disease in a way that has gained wide acceptance.

The gastroesophageal reflux disease frequently has an impact on the digestive system. Inflammation and irritation are brought on by the digestive juices and acid from the stomach flowing back into the oesophagus.

Following a meal, a reflux of acid from the gut into the oesophagus happens physiologically. As a result, the occurrence of other symptoms, such as reflux of the esophageal tract, is not regarded as a disease. Although the pathophysiology of GERD remains poorly comprehended, it is now acknowledged as an illness with multiple causes. The provocation or worsening of reflux has been linked to a number of factors, including obesity, a sliding hiatus hernia, low lower esophageal sphincter pressure, transient lower esophageal sphincter relaxation, the acid pocket, prolonged esophageal clearance, and delayed gastric emptying. The junction of muscle that connects the oesophagus and the gut is affected by this gastrointestinal condition **[1]**. Lower oesophageal sphincter is the name of this ring. Acid reflux can irritate the lining of the oesophagus. If this happens, you may experience heartburn or acid indigestion. A small percentage of GERD patients (20%) have LES ineffectiveness due to either significantly reduced LES exertion (LESP), an elevated intra-abdominal pressure (IAP) associated with the pregnancy or obesity, or along with LES that is significantly shorter than average (2 to 5 cm). Additionally, a lot of people with GERD have adequate LESP. The exact mechanism of pathophysiological reflux in this group of patients is frequently found toward being frequent transient LES relaxation (TLESR). Whereas understanding of TLESRs is still limited, stomach constriction aggravated by postmeal satiety or air in the stomach is suspected to be one of the major contributing factors. TLESRs may not be more prevalent in GERD, however a greater percentage of them also have acid reflux **[2, 3]**. When GERD symptoms are mild, they can be treated with diet and lifestyle changes; however, in severe cases, medications and surgery are required. Serious GERD can result in significant morbidity and impairment in standard of living, and illness at work absence, as well as If left untreated, complications such as peptic stricture, Barrett's oesophagus, along with esophageal adenocarcinoma may develop **[4]**. GERD is affected by a multitude of factors. Previous research has linked GERD with esophageal visceral hypersensitivity. NERD and RE are two

different diseases, but they are strikingly comparable as regards of clinical presentation, seriousness, occurrence, comorbidities, impact on quality of life, and associated comorbidities.

GERD has evolved from a primarily esophageal disorder into a group of syndromes that reflect the various manifestations of reflux disease.

**INTRODUCTION OF PANTOPRAZOLE**

Pantoprazole is an inhibitor of the stomach hydrogen-potassium adenosine triphosphatase (H+/K+-ATPase). It shares comparable qualities.[5]

Other proton-pump inhibitors (PPIs) with presently available active ingredients

PPIs are a class of medications that consistently and significantly lower the production of stomach acid. They achieve this by impairing the stomach's H+/K+ ATPase proton pump irreversibly. They are the most potent acid secretion antagonists available today. H2-receptor antagonists, a class of drugs with comparable effects but a different mode of action, have been largely replaced by PPI.

**PHARMACODYNAMIC:**

It is observable that the reduction in gastric corrosive emission directly correlates with the amount of PPI bound to the protein. In any case, measuring the amount of PPI restricting in vivo is very difficult, so we really need another boundary to substitute the amount of PPI restricting **[6]**. The inhibitory movement was not directly correlated with the medication's plasma level. However, it was observed that the total portion and AUC were related to the gastric anti-secretory effect. However, at higher doses of the medication, this association between the inhibitory movement and the AUC did not appear. The association between AUC and the restraint was indirect at larger doses of the drug due to the medicine's short lifespan and the compound's limited openness to the medication, but overall, AUC reliably demonstrated the medication's effectiveness.

While the plasma concentration chance for the greatest plasma concentration varied widely from 1 to 5 hours depending on the drug definition and food impact, all PPIs have a disposal half-life of about an hour.

**MECHANISM OF ACTION OF PANTOPRAZOLE:**

Proton pump inhibitors, of which pantoprazole is a member, work by permanently inhibiting the hydrogen/potassium adenosine exchanger.

The stomach parietal cells' triphosphatase chemical framework, often known as the H+/k+ ATPase or, more broadly, the gastric proton syphon. The proton syphon is the best target for inhibiting corrosive discharge since it is directly responsible for releasing H+ particles into the stomach lumen as the last stage of gastric corrosive discharge. A family of drugs that are

essentially more effective than H2 antagonists and lower stomach corrosive emission by up to almost 100% have been developed by focusing on the obstruction's irreversible character and the terminal progress in corrosive output **[7]**.

Reduced stomach acid can aid in the healing of duodenal ulcers and lessen the severity of indigestion and acid reflux. Notwithstanding, stomach acids are expected to process proteins, vitamin B12, calcium, and different supplements, and too little stomach corrosive causes the condition hypochlorhydria. The Pantoprazole are given in a dormant structure, which, under acidic circumstances, swiftly penetrates cell films into intracellular spaces (such as the parietal cell canaliculus) because it is inherently charged and lipophilic. during a hostile environment, the idle medication is protonated and adjusts into its dynamic structure. As depicted over, the dynamic structure will covalently and irreversibly tie to the gastric proton siphon, deactivating it. In H. pylori annihilation, Pantoprazole help by expanding the stomach pH, making the bacterium shift out of its coccoid structure which is impervious to the two acids and anti-toxins. PPIs likewise show a few more vulnerable unexpected impacts in destruction.

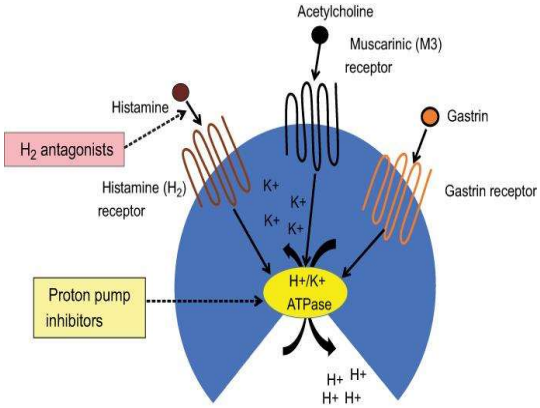


**Figure 1: mechanism of action of pantoprazole**

**HOW DO PANTOPRAZOLE WORKS:**

The stomach generally produces acid to help with the breakdown of foods and to kill microorganisms. Since this acid erodes stomach lining, your body produces a natural mucus barrier to stop this from happening.

In certain people, the membrane may have been breached, enabling stomach acid to damage the tissue and cause an ulcer. The sphincter, a muscular ring at the upper part of the stomach that maintains the stomach securely closed, may cause problems for certain people. Because of this, the gullet may itch and the acid may leak out (oesophagus). This is referred to as "acid reflux," which may cause heartburn and oesophageal (gullet) irritation.

Pantoprazole stops the production of too much acid by the cells that line the stomach. This could speed up the healing process or work to stop ulcers from forming. By reducing the quantity of acid, they can also help to lessen acid reflux-related symptoms like heartburn.

The hydrogen-potassium adenosine triphosphatase digestive enzyme mechanism, sometimes referred to by the term "proton pump," is blocked or inhibited by it. Pantoprazole is frequently referred to as a proton pump inhibitor. The cells in the stomach lining contain a chemical system that produces stomach acid.

**PHARMACOKINETIC OF PANTOPRAZOLE:**

**Chemical formula**- C16H14F2N3NaO4S

**IUPAC name-** (RS)-6-(Difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1H-benzo[d]imidazole

**Pantoprazole's chemical structure**:

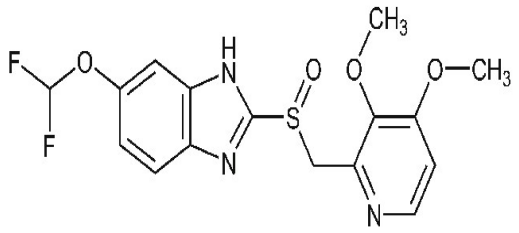

**Figure 2: Structure of pantoprazole**

**Absorption:**

Due to the drug's sensitivity to degradation in the stomach's acidic environment, enteric-coated formulations of pantoprazole are used.

Pantoprazole, an enteric-coated 40 mg tablet, is rapidly absorbed when taken orally, with peak plasma concentrations (Cmax) reaching 2 to 4 (mean 2.7) hours (tmax) after oral administration **[8]**.

**Distribution:**

The mean apparent volume of distribution of pantoprazole is 0.16 L kg at steady state. due to its high plasma protein binding (roughly 98%), which suggests limited tissue distribution.

**Metabolism:**

CYP450 (CYP) enzymes oxidatively metabolise a wide range of medicines. The primary enzyme found in this microsomal family that converts pantoprazole to inactive metabolites is the 2C 19 isoform. Some persons (2% to 3% of white and black people and 17% to 25% of Asians), referred to as slow metabolizers, exhibit poor morphological manifestations of the enzymes responsible for CYP2CI9 in relation to people with normal enzyme activity, or normal metabolizers. Although pantoprazole metabolism is slower in this subgroup (terminal a half-life [tl/2] >3.5 hours), no dose change is required. Pantoprazole has no effect on the pharmacokinetics of a variety of drugs that are metabolised by different CYP isoenzymes, and the reverse is also true. Additionally, the CYP isoenzyme (CYP2E1) brought on by ethanol intake, a prominent cause of liver illness, is not involved in the metabolism of pantoprazole **[7]**.

**Elimination:**

Approximately 80% of an oral dosage is eliminated in the form of urine metabolites., renal excretion accounts for the majority of

elimination. The remainder, which mostly comes from biliary secretion, is excreted in the faeces. Pantoprazole's elimination half-life was almost 6 hours for poor metabolizers compared to 1.3 hours for normal metabolizers **[8]**.

## INTRODUCTION OF ITOPRIDE HYDROCHLORIDE

Itopride is a recently developed benzamide analogue intended for therapeutic application as an oral gastroprokinetic medication. Itopride is predicted to increase gastric emptying by improving the ability to move the gastric in a patient with non-ulcer dyspepsia who specifically feels stomach pain owing to delayed gastric emptying.

Itopride, also known as N-[p-[2-(dimethylamino)ethoxy]benzyl]vera tramide hydrochloride, is a new gastroprokinetic used to treat the symptoms of epigastric discomfort.

Because of its high polarity, which prevents it from crossing the blood-brain barrier and from significantly affecting prolactin levels or the Q-T interval, it does not result in any CNS-related adverse drug reactions. In a multicenter, randomised, double-blind, placebo-controlled trial, itopride dramatically decreased symptoms in FD patients and showed a greater reaction time than placebo **[9]**.

## PHARMACOLOGY OF ITOPRIDE:

**Chemical formula**: $C_{20}H_{27}ClN_2O_4$

**IUPAC name**: N-[[4-(2-Dimethylaminoethoxy)phenyl]methyl]-3,4-dimethoxybenzamide

**Itopride HCl molecule structure**:

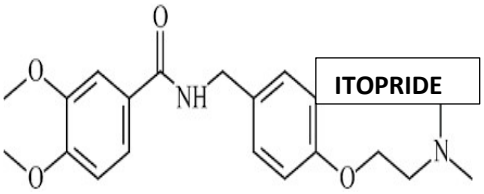


**Figure 3: Structure of itopride**

## MECHANISM OF ACTION OF ITOPRIDE:

Itopride has both:

(1)-dopamine D2 receptor antagonistic and

(2) anticholinesterase (AchE) activity

Acetylcholine (ACh), which is generated by enteric nerve terminals and induces smooth muscle spasms by binding to M3 receptors, is widely known to contain M3 receptors in the smooth muscle layer of the gut. The AChE enzyme hydrolyzes the produced ACh, rendering it inactive and reducing stomach motility, which results in a number of digestive diseases. The digestive system contains considerable levels of dopamine in along with ACh. Through a variety of mechanisms, such as as lowering intragastric pressure and relaxing the lower oesophageal sphincter, it decreases gastrointestinal motility. It appears that the suppression of the emission of ACh from the myenteric motor neurons is what causes these responses, which are mediated by the D2 subtype of dopamine

receptors. By attaching to the dopamine D2 receptor in an antagonistic manner, itopride removes the blockage of Ach release. ACh does not degrade because it also inhibits the activity of the enzyme AchE. ACh concentration increases as a whole, which improves gastro-duodenal coordination, promotes stomach motility, increases pressure on the lower oesophageal sphincter, and hastens gastric emptying. The dual mode of action of itopride sets it apart from other prokinetic medications now on the market.

This drug's absorption and distribution have not yet been thoroughly established. It will need additional investigation to ascertain how itopride functions.

**Metabolism**:

In humans, itopride is extensively metabolised in the liver. The N-oxide produced by oxidising the N-dimethyl group of the tertiary amine is the main metabolite in humans. It has been established that flavin containing monooxygenase 3 (FMO3) is the primary isozyme involved in the primary metabolic pathway **[10]**. The metabolic pathway's enzymes, however, have not yet received complete characterization. hence, the flavin-containing monooxygenase enzyme, not the cytochrome P450 enzyme system, is responsible for the metabolism of itopride, in contrast to cisapride and mosapride citrate. Inhibitors of the cytochrome P450 enzyme, such as macrolides and azole antifungal medications, it therefore poses no significant risk of pharmacokinetic drug interaction **[14]**.

**Elimination:**

Following a single therapeutic dosage of itopride given orally, healthy subjects had urinary excretions of 3.7 and 75.4% of its N-oxide, respectively **[11]**.

A 2005 pilot research on the efficacy and safety of itopride for the treatment of GERD symptoms found that all symptoms, particularly heartburn, a prominent symptom of the condition, significantly improved following treatment with 150 and 300 mg of itopride **[12]**.

## MATERIALS AND METHODS

### Study Design

Retrospective observational research conducted in a single centre.

### Ethical Consideration

The Institutional Ethical Committee of Parul Sevashram Hospital in Vadodara approved the study request with permission number PUIECHR/PIMSR/00/081734/4201. The study was given the ethical committee's permission after peer interviews and evaluation.

### Study Criteria

1) **Inclusion Criteria**
   - 18 years and above.
   - Patient with any existing medical condition such as DM, kidney

disease, hypertension, etc

- Patient diagnosed with GERD (gastroesophageal reflux disease)

**2) Exclusion Criteria**

- Patient with age <18 year
- Pregnant or lactating women.
- Patients files with missing any data

**Designing of Patient Data Form**

The creation and validation of a particularly tailored patient data gathering form. The patient data collecting form is included in ANNEXURE I and was utilised to get accurate data from the medical record department. It contains information about the patients' racial and ethnic backgrounds, as well as their age, sex, date of birth, reason for admission, medical history, social history, and treatment history, including dosage, route, frequency, and other data.

**Data Analysis**

Data were collected from medical record department and then statistically analysed. Data were gathered, collated, and statistically examined. To graphically summarise the data, a variety of graphs, figures, and tables are employed.

**Statistical Analysis**

To summarise categorical data, counts and percentages were utilised. Data were summarised using graphical data presentations. Nominal data were represented by percentage frequency, and categorical data by mean and standard deviation. The data from more than two independent samples were compared using the Chi-Square test. To compare the means of three or more independent groups, the ANOVA test was utilised. Statistical significance was determined by a P-value of 0.05.

**RESULTS AND DISCUSSION**

**1) Age Wise Distribution**

For this study, total 100 numbers of patients were observed/reported. According to inclusion and exclusion criteria, age of 100 patients 18-25yr (16%), 26-35yr (35%), 36-45yr (30%), 46-55yr (11%), 56-65-yr (5%), 65-yr and above (3%). Most of the patients were found to be between the ages of 26-35yr (35%) and the Mean ± SD was (17.6 ± 15.40). The p-value was found to be <0.0001 which was significant. The outcomes are shown in **Table 1** and **Figure 4**.

**Table 1: Age wise distribution**

| Age | No of patient (n=100) | Percentage (%) |
|---|---|---|
| 18-25 | 16 | 16% |
| 26-35 | 35 | 35% |
| 36-45 | 30 | 30% |
| 46-55 | 11 | 11% |
| 56-65 | 5 | 5% |
| 65 < | 3 | 3% |
| Total | 100 | 100% |

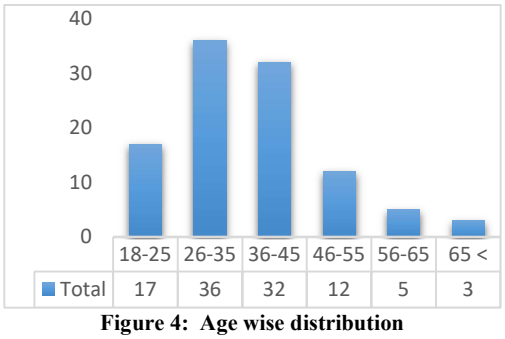


**Figure 4: Age wise distribution**

## 2) GENDER WISE DISTRIBUTION

100 patients in all were enrolled in the research; 66 (or 66%) of these patients were determined to be men, while 34 (or 34%) were found to be women. after analysing this data it was found that majority of the patients belonged to male gender. The p-value was found to be 0.0985 which is significant. These results are expressed in **Table 2** and **Figure 5**.

**Table 2: Gender wise distribution**

| Gender | No of patient (n=100) | Percentage (%) |
|---|---|---|
| Male | 66 | 66% |
| Female | 34 | 34% |
| total | 100 | 100% |

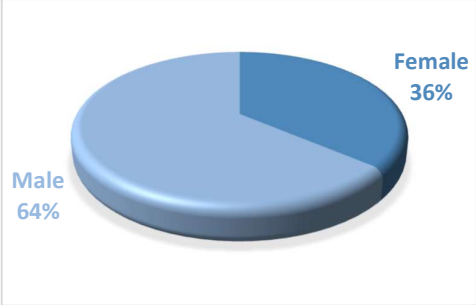


**Figure 5: Gender wise distribution**

## 3) Distribution According to Clinical Manifestation

The results of distribution according to clinical manifestation most of the patients were suffering from vomiting with 97 number of patient, 77 number of patient suffering from heart-burn,44 patient presented with abdominal pain ,whereas 40 patient were presented with Regurgitate food and liquid, 35 were having chest pain while 11 patient with sore throat, 3 patient were suffering from hoarseness and 28 patient were presented with others clinical manifestation, Their Mean ± SD was (32.45 ± 9.41). it was determined that the p value was 0.003< 0.05, which is statistically significant. These results are expressed in **Table 3** and **Figure 6**.

**Table 3: Distribution according to clinical manifestation**

| Clinical manifestation | No of patient (n=100) | Percentage % |
|---|---|---|
| heart burn | 77 | 77% |
| chest pain | 35 | 35% |
| Regurgitate food and liquid | 40 | 40% |
| dyspepsia | 18 | 18% |
| vomiting | 97 | 97% |
| sore throat | 11 | 11% |
| Hoarseness | 3 | 3% |
| Cough that does not improve | 3 | 3% |
| Eating while having food clogged in the oesophagus | 1 | 1% |
| abdominal pain | 44 | 44% |
| others | 28 | 28% |

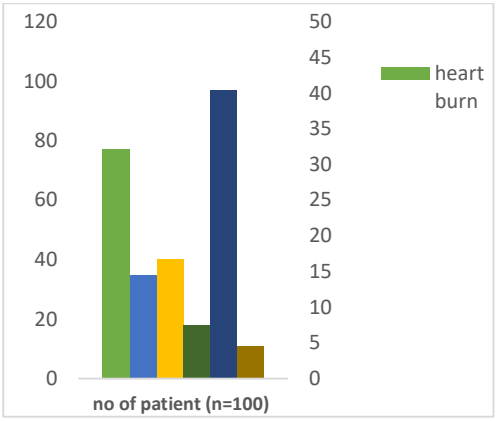


**Figure 6: Distribution according to clinical manifestation**

## 4) Stage Wise Distribution

As per the stage wise distribution, about 50 (50%) patients were found to be in the second stage of the GERD and about 38 patients (38%) were in the first stage of the GERD, being in the mildest stage among all the others. However, 12 of the patients were found to be in the third severe stage of the GERD and none of the patients were in the

fourth stage. The p value here was found to be 0.05 which is insignificant because it should be <0.001 and the Mean ± SD was (25.00 ± 23.007). The results are mentioned in the **Table 4** and **Figure 7**.

**Table 4: Stage wise distribution**

| Type of gerd | No. of patient(n=100) | Percentage% |
|---|---|---|
| stage 1 mild acid reflux | 38 | 38% |
| stage 2 moderate acid reflux | 50 | 50% |
| stage 3 severe acid reflux | 12 | 12% |
| stage 4 oesophageal cancer | 0 | 0% |

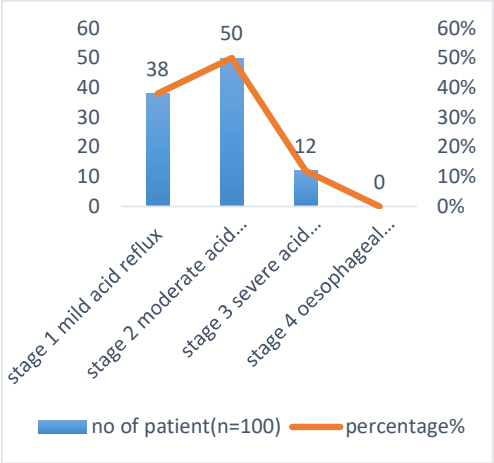


**Figure 7: Stage wise distribution**

## 5) Comparison of Drugs with Stages

The people receiving Pantoprazole monotherapy as their primary treatment included 17 patients in stage 1, 25 patients in stage 2, 8 patients in stage 3, and none in stage 4 of the GERD, according to the study comparing the medications used to treat GERD patients. As of, there were 19 patients in stage 1, 26 patients in stage 2, 5 patients in stage 3, and none in stage 4 of the Pantoprazole+itopride HCl combo therapy regimen.

P value was found to be 0.1162 >0.05 which was not significant. **Table 5** and **Figure 8** in the section below show the results.

**Table 5: Comparison of drugs with stages**

| STAGES | PANTOPRAZOLE | PANTOPRAZOLE+ITOPRIDE |
|---|---|---|
| 1 | 17 | 19 |
| 2 | 25 | 26 |
| 3 | 08 | 05 |
| 4 | 00 | 00 |
| TOTAL | 50 | 50 |

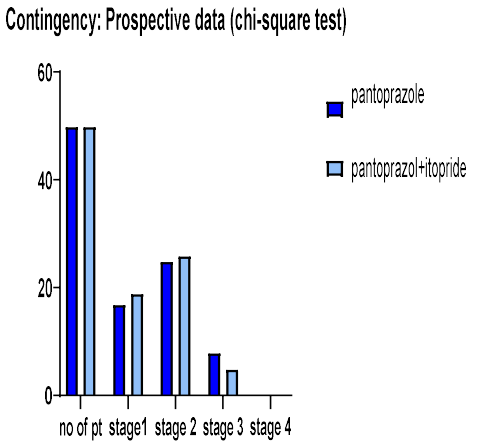


**Figure 8: Comparison of drugs with stages**

## 6) Distribution of Factors Aggravated Acid Production

In the results of the factors that may worsen the symptoms or the condition of the patients in the GERD, Out of 100 %, there were about 16% of the patients found to be drinking certain beverages like coffee/alcohol that may increase the acid production in the patients, 11% of the patients were found to be having large meals later at night, 26% of the patients were found to be smoking cigarettes, 2% of the patients were taking medicine like

aspirin that may increase the acid production in the GERD, 12% of the patients were addicted to chewing tobacco and about 53% of the patients did not have any aggravating factors in their case. The Mean ± SD was found to be (20.00 ± 17.94) and the p value was >0.0001 which is not significant. The data findings are shown in **Table 6 and Figure 9.**

**Table 6: Distribution of factors aggravating acid production**

| Aggravated factors | No of pt.(n=100) | Percentage% |
|---|---|---|
| Drinking certain beverages, such as alcohol or coffee | 16 | 16% |
| Eating large meals or eating late at night | 11 | 11% |
| Smoking | 26 | 26% |
| Taking certain medications, such as aspirin | 2 | 2% |
| Tobacco addiction | 12 | 12% |
| NONE | 33 | 33% |

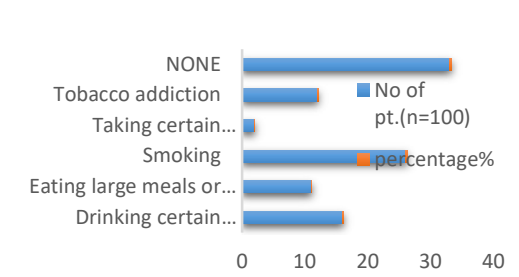


**Figure 9: Distribution of the factors aggravating acid production**

## 7) Distribution According Type of Diet

The results of the diet parameter were found to be having 37% of the patients with vegetarian diet, 8% of the patients had non-vegetarian diet and about 55% of the patients had mixed diet out of 100 % as total. The Mean ± SD was found to be 0.3 ± 0.23) and the P VALUE was found to be <0.0001 which was significant. The results are displayed in **Table 7** and **Figure 10**.

**Table 7: Type of diet of the patients with GERD condition**

| Type of diet | No of pt.(n=100) | Percentage% |
|---|---|---|
| Veg | 37 | 37% |
| Non-veg | 8 | 8% |
| mixed | 55 | 55% |

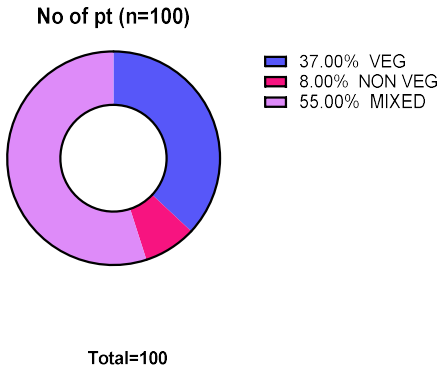


**Figure 10: Pie- chart of the diet type of the patients with GERD condition**

## 8) Gender Wise Distribution According Etiological Conditions

The etiological condition distribution results were found to be having 5 male and 0 female patients that had asthma, 3 male and 2 female patients had hiatal hernia, 6 male and 2 female patients had hypertension and 3 male and 1 female patient had DM-type 2 as their etiological factor for the GERD disease development. The p value for the data here was found to be 0.0462 which being < 0.05 is considered to be significant. The data and results are depicted in the **Table 8-9** and **Figure 11**.

**Table 8: Etiological condition distribution in male and female patients**

| Etiological condition | Male(n=64) | Female(n=36) |
|---|---|---|
| asthma | 5 | 0 |
| hiatal hernia | 3 | 2 |
| hypertension | 6 | 2 |
| diabetes type-2 | 3 | 1 |

**Table 9: Data test results of the etiological condition distribution in male and female patients**

| Unpaired t test | |
|---|---|
| P value | 0.0150 |
| P value summary | * |
| Significantly different (P < 0.05)? | Yes |
| One- or two-tailed P value? | Two-tailed |
| Number of pairs | 4 |

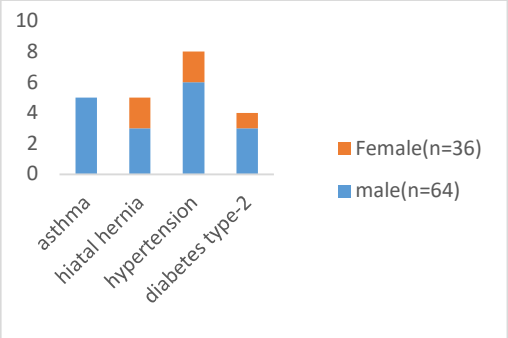


**Figure 11: Distribution according etiological condition in male and female patients**

## 9) Gender Wise Distribution of Diagnostic Test

The results of the gender wise distribution of diagnostic tests used to detect the GERD condition in the patients were found to be having 63 male and 36 female patients who had endoscopy done and 63 male and 36 female patients who had USG abdomen test done to detect the GERD. Whereas three more test was done to detect disease condition in which 11 male and 12 female were done esophageal pH test,13 male and 9 female were done acid reflux test and 1 male and 2 female were done esophageal monometry. The p- value of the given data set was found to be 0.0116 which was < 0.05 and so considered as significant. The data is displayed in **Table 10** and **Figure 12**.

**Table 10: Gender wise distribution of diagnostic tests used to detect gerd**

| Special diagnostic test | Male (n=64) | Female (n=36) | Total no of pt. (n=100) |
|---|---|---|---|
| Endoscopy | 64 | 36 | 100 |
| USG abdomen | 63 | 36 | 99 |
| Esophageal pH test | 11 | 12 | 23 |
| Acid reflux (barrium swallow | 13 | 9 | 22 |
| Esophageal manometry | 1 | 2 | 3 |

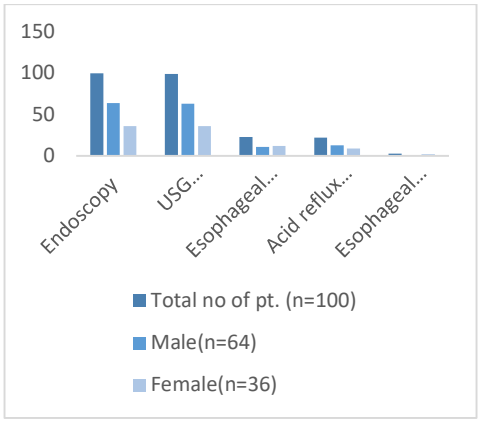


**Figure 12: Gender wise distribution of diagnostic tests used**

## 10) Cost Analysis

Patients with GERD were treated with ptz+ito. We calculated the overall cost of treatment and the average cost divided with different brands in which pantop IT was taken by 2 patient, their average cost of 167 rs per patient per strip, pantocid IT was taken by 2 patients whereas 9 patients were taking protera I and 37 no. of patients were taking ganaton total and their average prices were 190,213 and 318 rs per patient

per strip. Cost analysis is shown in **Table 11**. The p value found to be <0.0001 which was significant.

Total =50 people group who were taking pantoprazole 40mg+itopride 150 mg

**Table 11: Average cost analysis per patient of treatment**

| ECONOMIC EVALUATION PTZ+ITO | TOTAL COST | NO OF PT. | AVERAGE COST/Pt. (Rs)/Strip |
|---|---|---|---|
| pantop IT | 335 | 2 | 167 |
| pantocid IT | 380 | 2 | 190 |
| protera I | 1917 | 9 | 213 |
| Ganaton total | 11766 | 37 | 318 |

**Table 12: P value and level of significance**

| P value and statistical significance | |
|---|---|
| Test | Chi-square |
| Chi-square, df | 1772, 6 |
| P value | <0.0001 |
| P value summary | **** |
| One- or two-sided | NA |
| Statistically significant (P < 0.05)? | Yes |

## 11) Distribution According Length of Stay

The distribution of the patients according to their duration of stay in the hospital included 20% of individuals who stayed less than a week, 37% of patients who stayed for 1-2 weeks, 36% of the patients stayed for 2-4 weeks and about 7% of the patients stayed in a hospital for 4-6 weeks. The p-value of the given data was found to be <0.0001 and is considered significant.

**Table 13: Distribution of patients according to the length of their stay**

| No of days | No of pt.(n=100) | Percentage% |
|---|---|---|
| <1 week | 20 | 20% |
| 1-2 week | 37 | 37% |
| 2-4 week | 36 | 36% |
| 4-6 week | 7 | 7% |

.

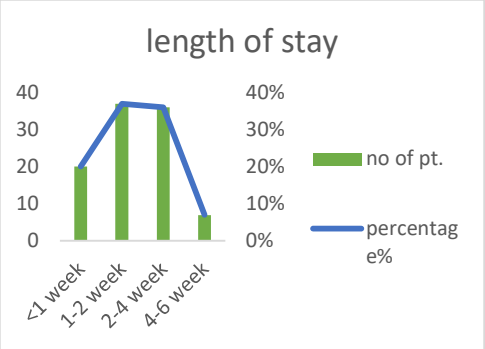


**Figure13: Distribution of patients according to the length of their stay**

## 12) Gender Wise Distribution According Length of Stay to Compare the Effectiveness Of Both Drugs

The given information illustrates the no of patients stay according to medication which was divided in two groups of patients. There were randomly selected two different groups among them one were taking pantoprazole and other were taking ptz+ito. according to length of stay there were 20 patients among the 100 recovered in less than 1 week, 37 patients were recovered in between 1-2 week,36 of patients were 2-4 week and 7 patients were recovered in between 4-6 week. Gender wise ration and medication prescribed shown in the **Table 14 and Figure 14** below. TWO way ANOVA test was performed to find the level of significance and p value which is also mention the below **Table 15**.

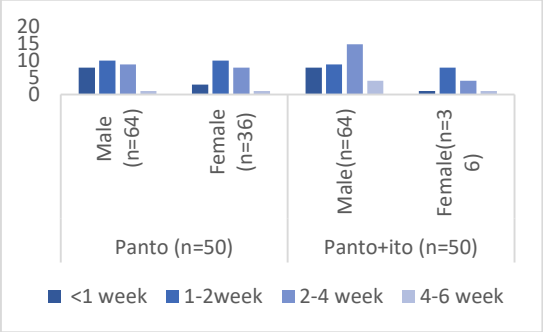


**Figure 14: Gender wise ration and medication prescribed**

### 13) Gender Wise Distribution of Stomach pH According Different Medication Group

According to the study's findings, two groups of patients were receiving ptz and their combination therapy. After receiving ptz therapy, the stomach pH of 14 male patients showed an increase and 20 patients indicated a decrease, compared to 9 female patients who showed an increase and 14 patients who showed a decrease After receiving the ptz+ito combination therapy, 9 male patients showed an increase, 21 male patients showed a decrease in stomach pH, While the stomach pH of 6 female patients increased and 7 female patients decreased. according to Two way ANOVA p value was found to be >0.05 which was not significant. The findings are displayed in **Table 16** and **Figure 15**.

**Table 16: Stomach pH in different group of people according to medication prescribed**

| | Male (n=64) | | Female (n=36) | |
|---|---|---|---|---|
| Stomach pH | increased | decreased | increased | decreased |
| pantop | 10 | 18 | 9 | 13 |
| ptz+ito | 12 | 24 | 6 | 8 |

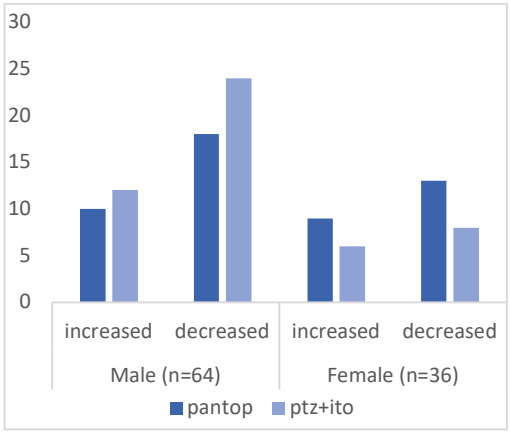


**Figure 15: Stomach pH in different group of people**

## DISCUSSION

Worldwide, there is an increasing incidence of gastroesophageal reflux disease (GERD), a prevalent condition marked by severe symptoms brought on by the reflux of stomach contents into the oesophagus. It frequently manifests as regurgitation, heartburn, or dysphagia and raises the possibility of esophagitis, stricture, Barrett's metaplasia, as well as a significant loss in quality of life. The reality that GERD raises the probability of esophageal adenocarcinoma underscores the need of early detection and appropriate treatment for the condition. GERD has been treated with a wide range of medicines, however acid suppression therapy remains the predominant form of treatment. Approximately one-third of GERD patients still endure chronic symptoms that don't react well to typical PPI dose, despite the fact that proton pump inhibitors are the most efficient acid suppressants and have

high efficacy in treating esophagitis and reducing complaints.

In clinical practise, PPI is frequently supplemented with antacids, alginate, histamine type-2 receptor antagonists, and prokinetic drugs. The primary objective of study and development for novel treatment drugs has been on the underlying processes of GERD, including transitory lower esophageal sphincter relaxation, motility problem, mucosal protection, and esophageal hypersensitivity. This is due to the fact that quality lifestyle is increased and dyspeptic symptoms are totally eliminated when a prokinetic medicine like itopride is used with a PPI like pantoprazole. Gastroesophageal reflux disease (GERD), a widespread public health problem, results in higher expenses and a decreased standard of living. The most frequently prescribed drugs are prokinetics and proton pump inhibitors (PPI). It is still debatable whether prokinetic and PPI therapy combined is safe and effective for treating GERD.PPIs and other strong acid-suppressing medications are used to treat GERD. There is still a need to address the positive effects of prokinetics like itopride being added to acid-suppressive therapy. In our study, we compared the clinical and diagnostic outcomes of a pantoprazole and itopride combination with symptomatic GERD patients to pantoprazole alone. By contrasting the mean symptom scores after 8 weeks, we were able to assess the effectiveness of the two regimens. A novel aspect of our study was the application of two drugs pantoprazole 40 mg and pantoprazole itopride 150 mg in different groups of people among them 50% were taking pantoprazole 40 mg and 50% were taking a combination of pantoprazole+itopride 150 mg. clinical manifestation shown the symptoms relief rate in total no of the patient. in which majority 97% were suffering from vomiting and 77% were suffering from heart burn. Their Mean ± SD was (32.45 ± 9.41). The p value was found to be 0.003< 0.05 was statistically significant. The endoscopic examination before and after therapy serves as proof as, Pantoprazole and the combination of Pantoprazole plus Itopride, according to Pradeep Kumar BT *et al*, both provide more effective healing of esophagitis **[40]** comparatively Our study tried to compare effectiveness of two medication therapy pantoprazole 40mg and patoprazol-itopride 150 mg in different gender group there are no any significant result were occurred. In the current study, 20% of participants showed recovery in less than a week, 37% in one to two weeks, 36% in two to four weeks, and 7% in four to six weeks. According to the recommended therapy, there were 64% male and 36% female participants. ($p<0.05$).

Between the two gender groups, endoscopic healing of esophagitis was observed in 64% of the men and 36% of the women.63% of men and 36% of women had other diagnostic esophageal pH results, 13% of men and 9% of women had acid reflux healing results, and 1% and 2% of men and women had esophageal manometry results. ($p<0.05$).

During the entire study there were no any evidence of any serious adverse effects. According to a study by Bochenek *et al*, pantoprazole has an 11% headache and 7% diarrhoea incidence rate for side effects **[41]**. With Pantoprazole and Mosapride, Mild adverse effects such diarrhoea, pains in the abdomen, and flatulence were mentioned by Vigneri *et al* . Almost all of these symptoms disappeared on their own[(42)].There has only ever been one study that compared the efficacy of a prokinetic (cisapride) and a PPI (omeprazole) given in combination with a PPI to a PPI administered alone. According to Vigneri *et al*.'s study **[42]**. According to research by Kim YS *et al*., consuming itopride 100 mg three trice a day decreased esophageal exposure to acids and enhanced GERD symptoms **[12]**. Recovery ratios with pantoprazole plus mosapride were shown to be 70.5% greater than those with pantoprazole alone in a separate research reported Madan *et al* **[43]**.

## CONCLUSION

In summary, our study evaluated the clinical and diagnostic results of a pantoprazole and itopride combination in symptomatic GERD patients compared to pantoprazole alone. In comparison to pantoprazole alone, the addition of itopride did not statistically significantly improve symptom relief.

The results of the present research demonstrated that Pantoprazole and Pantoprazole and Itopride together promote more effective esophagitis recovery. The basis for data and results. The results of therapy did not seem to be significantly impacted by gender differences. According to a study, the effectiveness of pantoprazole 40 mg and the combination of pantoprazole and itopride 150mg is not significantly different. The same ratio of recovery with taking different therapy groups was seen according to the length of stay between the two groups. The research we conducted contributes to the growing body of evidence demonstrating the effectiveness of prokinetics when combined with PPI medication in the treatment of GERD. The combination of pantoprazole and itopride may be an improved therapeutic choice for GERD patients who still suffer symptoms while getting regular PPI medication. The results we obtained need to be supported by additional research that uses bigger sample sizes and longer follow-up periods to

demonstrate the safety and efficacy of combination treatment.

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