

# To See the Synergistic Effect of PPI and Itopride in Functional Dyspepsia

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## ABSTRACT

**Objective:** To see the synergistic effect of PPI and Itopride in functional dyspepsia

**Study Design:** Prospective descriptive study.

**Place and Duration of Study:** The study was conducted in a tertiary care hospital, Al-Tibri Medical College & Hospital, a three hundred bedded hospital from Feb 2011 to Dec 2011.

**Materials and Methods:** The patients reported in the OPD were included in this study and they were screened according to inclusion criteria with complained of upper abdominal pain, fullness, chest burning and bloating. All the data were recorded in a preset performa and result were analyzed by SPSS version 15.

**Results:** A total of 54 cases were included. Male were 25 and females were 29. All the patients were presented to OPD with upper abdominal pain 51 cases, chest burn 49 cases, abdominal fullness 43 cases and bloating in 37 cases. The symptoms were persistent for more than two weeks. The entire patients were inquired about the comorbidities, like hypertension, diabetes mellitus, ischemic heart disease, rheumatism, or on steroids and that all excluded from the study. All the patients had negative H Pylori status and had undergone upper gastrointestinal endoscopies. All the patients were started on PPI and itopride in low and high dose regime according to the symptoms. Improvement of the symptoms was accessed at the end of fifth day. Nearly 82 % of the patients had improved on the fifth day of the therapy while the other the rest of the patients were started with a higher dose and additional 10 % were benefited at the end of 2<sup>nd</sup> week. All the patients were treated for four week and then they were followed for next four week for the recurrence of the symptoms. In the first follow-up of four weeks 44% of the patients had sustained complete response in their symptoms.

**Conclusion:** The combination of PPI and Itopride has synergistic effect in functional dyspepsia. Further studies are required to prove their efficacy

**Key Words:** dyspepsia, abdominal pain, bloating, chest burn

## INTRODUCTION

Dyspepsia is an acute, chronic or recurrent upper abdominal discomfort. The patient should be present with either abdominal pain or fullness or both. The chest burning<sup>1</sup> is either due to increased secretions of the acid or decreased lower esophageal sphincter pressure that will lead to the reflux of the gastric content to the esophagus that will finally cause chest burning. Rome III committee has defined functional dyspepsia<sup>2</sup> as epigastric pain or burning, early satiety or post prandial fullness. Dyspepsia<sup>3</sup> occur in 15 % of the adult population and account 3 % of general medical office visit

The causes of dyspepsia<sup>4</sup> are many: it is either eating too much, too quickly, high fat foods, stress, lot of coffee, alcohol, drugs like NSAIDs, aspirin, antibiotics like metronidazole and macrolides, metformin and many others. H Pylori is also a contributor in peptic ulcer disease; it has less impact on dyspepsia<sup>5</sup>. The nature of the symptoms is nonspecific. It relates with food, stress and other field of life. The upper abdominal pain, burning, early satiety, fullness, bloating, nausea and vomiting are the few symptoms of dyspepsia. The patient background like eating<sup>6</sup> habits, alcohol intake, mental health, employment, physical and sexual abuse,

anxiety<sup>7</sup> and depression are the contributors in the pathogenesis of dyspepsia.

The symptoms above do not differentiate between functional dyspepsia<sup>8</sup> and organic gastrointestinal disorders. The physical examination is not enough to label the case, so upper gastrointestinal endoscopy is the gold standard in each and every case. Sign like weight loss, melana, organomegaly, abdominal mass should be further evaluated. H Pylori<sup>9</sup> is causing gastritis so should be confirmed either by serology or direct vision on histopathological slides. Ultrasound of abdomen will give idea about pancreatic and biliary disease.

The dyspepsia<sup>10</sup> is a very common disorder in OPDs. Sometimes<sup>11 12</sup> it is the main disorder otherwise it was also a consequence of many diseases and drugs. It is better to exclude all the possible comorbidities like hypertension, diabetes, heart diseases, rheumatic diseases, bronchial asthma and drugs that are causing upper abdominal pain. Initial treatment should be advised to patient who are younger and have no alarming sign. Upper gastro-intestinal endoscopy is mandatory in cases where any of the alarming symptoms is present or those who do not response to the conventional treatment. The treatment<sup>13 14</sup> approach is started from life style modification to the adding of

PPI and some time a prokinetic drug like itopride may add to the treatment and beneficial result are acquired. The itopride enhances the release of gastric acetylcholine through direct inhibition of D 2 receptor and acetyl cholinesterase. Low dose antidepressant may be used in functional dyspepsia in some patients. Psychotherapy<sup>15 16</sup> and hypnotherapy may be beneficial in some of the patients.

## MATERIALS AND METHODS

This is an prospective descriptive study conducted in the medical department of Al Tibri Medical College & hospital , a 300 bedded hospital in district Malir. It is situated near AL Ibrahim Eye Hospital old thana. The college has an OPD of 175/day patients in different areas of the field of undergraduate teaching MBBS. The average OPD is 40 /day in the medical department. The OPD was conducted daily. All the patients were adults. The duration of the study was from Feb 2011 to Dec 2011. The patients, taken in this study were complaining of abdominal pain chest burning, abdominal fullness and bloating for more than six weeks and these symptoms appeared on and off and persistent for more than two weeks. The PPI used in this particular study was esomeperazole and Itopride as a prokinetic drug.

Detailed history and clinical examination was done in every case and the basic biodata was recorded in a preset Performa. The symptoms, sign and detailed laboratory investigations were recorded. The data was analyzed on SPSS version 15.

### Inclusion criteria

- 1) Patients were adults
- 2) Patient fulfilled the ROME III criteria
- 3) H Pylori status was negative
- 4) Upper Gastrintestinal endoscopy was normal
- 5) No comorbid.

### Exclusion criteria

- 1) H Pylori was positive
- 2) With comorbid like DM and HTN
- 3) Patient on ulcerogenic drugs like steroids

All the patients were seen by one of the authors of this article and upper gastrointestinal endoscopy was done by one of the authors in each and every case. All the patients were H. Pylori negative serologically. The upper G.I. endoscopies were normal. A total 193 patients were screened out of which 54 were included in this study. The PPI and itopride were started together in a dose of 20mg once daily and 25mg thrice a day respectively in majority of cases . the first follow-up was on the fifth day of commencement of treatment and those who had not improved started on a higher dose of PPI 40mg and itopride 50 mg twice a day. The response was assessed subjectively by one of the author as improvement of the symptoms. The subjects were divided into two groups according to the response and dose of the drug.

## RESULTS

A total of 54 cases were taken. Out f which 25 were male and 29 were females. All were H pylori negative and had normal upper G.I. endoscopies. The patient presented with abdominal pain in 51 cases, chest burning in 49 cases, abdominal fullness in 43 cases and bloating in 37 cases. Besides these additional data were shown in Table No. 1 All the patients were started on PPI 20mg once daily and Itopride 25mg thrice a day at the end of 5<sup>th</sup> day 82 % (44 cases) were improved while remaining 10 cases were switched to PPI 40 mg once daily and Itopride 50mg twice daily for a week more 10 % ( 5 cases) were improved more. The treatment was followed for total four weeks. Table No. 2 showed the dose of the drugs. Table No. 3 showed the response of the treatment. These subjects were followed for next four weeks to see the stability of the symptoms. 44 % of the cases were achieved complete control of their symptoms after the end of eight week of follow-up.

**Table No 1: Biodata**

Total cases	54
Male	25
Female	29
Age in mean	33 ± 13
Marital status (Married)	42
Unmarried	12
Working	39
Jobless	15
Smokers	20
Non smokers	34
Obese	29
Under weight	07
Abdominal Pain	51
Chest burning	49
Abdominal fullness	43
Bloating	37

**Table No. 2: Dose of PPI and Itopride**

Drugs	Group I	Total No of cases	Group II	Total No. of cases
PPI	20 mg OD	44 cases	40mg OD	10 cases
Itoptide	25mg TDS		50mg BD	

**Table No 3: Response of the treatment**

Drugs	Early response	Delayed response
PPI and Itopride	44 cases	05 cases

## DISCUSSION

Dyspepsia<sup>17</sup> is a disease of every age and every race. It occurs in 15 % of the adult population. It may be

present with abdominal pain, chest burning, and abdominal fullness and bloating. All the features may not be present in each and every case of functional dyspepsia. The increased acid secretion or delayed exit of the gastric content is the contributing pathogenesis of functional dyspepsia. The combination of PPI<sup>18 19</sup> and prokinetic<sup>20</sup> drug had a benefit of decreasing the acid secretion and increased the exit of the gastric content and improve the upper G.I. symptoms. In this particular study the patient had negative H Pylori status and all had normal upper G.I. endoscopies. None of the patients were on drugs that cause gastritis and there was no co-morbid. The feeling of abdominal pain, abdominal fullness, abdominal burning and bloating were the major symptoms of the patient in this study<sup>21 22</sup>. The use of a combination of PPI as esomeperazole and Itopride had a clear advantage on both the drugs if using alone, as the result were 92% benefit after the continuous use of two weeks. In the follow-up for next four week 44 % percent were achieved a good control of the symptoms. The idea behind this study was functional dyspepsia which was a major problem and there was a slow exit and over production of acid<sup>23</sup> therefore the use of PPI and a prokinetic drug in combination has a synergistic effect. The central idea was that PPI would lower the acid production and the prokinetic drug would increase the gastric exit<sup>24</sup>. In studies of different authors, Wang<sup>18</sup> et al, Tally<sup>19</sup> NJ and Castillo<sup>21</sup> et al used PPI or Itopride<sup>25</sup> alone for functional dyspepsia that means both drugs had some advantage for the symptoms, so their combination would be a better choice. The result were quite satisfactory and over a period of eight weeks 44 % of patient had control over the disease.

The thing which is not the focus of the study i.e. the biodata that of marital status, financial states, job holding, obesity, smoker and living alone. They were the main contributors of the stress in general and functional dyspepsia in particular.

## CONCLUSION

The combination of PPI and Itopride has synergistic effect in functional dyspepsia. Further studies are required to prove their efficacy.

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