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ORIGINAL RESEARCH

To study the comparative effects of Itopride and Levosulpiride orally used in patients suffering from non-ulcer dyspepsia

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ABSTRACT

Background: Dyspepsia, commonly known as indigestion, refers to discomfort or pain in the upper abdomen. It can be a symptom of various underlying conditions or can occur on its own. Additionally, when eating, people may feel fuller earlier than they had anticipated. The present study was conducted to compare Itopride and levosulpiride in patients suffering from non-ulcer dyspepsia.
Materials and Methods: 60 patients with non-ulcer dyspepsia of both genders were divided into two groups of 30 each. Group I patients received one tablet of itopride hydrochloride, 50 mg, three times daily before meals, and group II patients received one tablet of levosulpiride, 75 mg, three times daily before meals. The grading of responses was marked or complete relief, moderate relief, slight relief, no relief, and worsening of symptoms.
Results: Group I had 17 males and 13 females, and Group II had 16 males and 14 females. In groups I and II, the responses were marked or complete relief in 18 and 12, moderate relief in 9 and 10, slight relief in 2 and 5, no relief in 1 and 2, and worsening of symptoms in 0 and 1 patient, respectively. The difference was significant ($P < 0.05$). In group I and group II, pre and post mean Hb (mg/dl) was 12.4 and 12.1 and 11.6 and 11.4, FBS (mg/dl) was 82.3 and 85.3 and 82.6 and 83.9, WBC-TC (/cumm) was 8567 and 8622 and 8122 and 8245, BUN (mg/ml) was 8.5 and 8.7 and 8.3 and 9.1, creatinine was 0.81 and 0.83 and 0.72 and 0.75, AST (units/L) was 27.4 and 27.3 and 25.6 and 23.1, ALT (units/L) was 30.2 and 29.5 and 30.7 and 29.4, ϒ-GT (units) was 30.5 and 33.4 and 24.7 and 26.3, Alk. Phos (units/ml) was 135.2 and 143.2 and 134.6 and 129.3, bilirubin (mg/dl) was 0.93 and 0.92 and 0.95 and 0.82, total cholesterol (mg/dl) was 167.3 and 163.2 and 168.4 and 162.4 and QT-Interval was 0.32 and 0.31 and 0.45 and 0.47 respectively. The difference was significant ($P < 0.05$).
Conclusion: Levosulpiride and itopride were equally effective in treating the symptoms of non-ulcer dyspepsia. Clinically and biochemically, both medications were well tolerated.
Keywords: Dyspepsia, Itopride, Levosulpiride

Introduction

Dyspepsia, commonly known as indigestion, refers to discomfort or pain in the upper abdomen. It can be a symptom of various underlying conditions or can occur on its own. Additionally, when eating, people may feel fuller earlier than they had anticipated.[1,2] A prevalent issue, dyspepsia is often brought on by either gastritis or gastroesophageal reflux disease (GERD). Aspirin, Metronidazole, Macrolides, Metformin, alphaglucosidase inhibitors, amylin analogues, GLP-1 receptor antagonists,

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angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists, niacin, fibrates, neuropsychiatric drugs like donepezil, rivastigmine, SSRIs like fluoxetine, sertraline, serotonin-norepinephrine-reuptake inhibitors like venlafaxine, duloxetine, Parkinson's medications like dopamine agonists, MAO-B inhibitors, corticosteroids, oestrogens, digoxin, iron, and opioids are just a few of the medications that can cause dyspepsia.[3]

Itopride is a derivative of prokineticbenzamide. It has a gastrokinetic action and inhibits the acetylcholine esterase enzyme and dopamine. Itopride is recommended for the management of many gastrointestinal disorders, including functional dyspepsia.[4]Itopride's most frequent adverse effects include diarrhoea and mildto-mmoderate abdominal pain. Additional side effects that could manifest are rash, giddiness, fatigue, headaches, constipation, increased salivation, back or chest pain, dizziness, galactorrhea, and gynecomastia. [5]Levosulpiride is an antipsychotic that is a substituted benzamide that is said to selectively block dopamine D2 receptor function in both the central and peripheral nervous systems. It functions as both a prokinetic and an atypical neuroleptic.[6]

Aims and objectives: The present study was conducted to compare itopride and levosulpiride in patients suffering from non-ulcer dyspepsia.

Materials & Methods

The present prospective cross-sectional study was conducted on 60 patients with complaints of non-ulcer dyspepsia of both genders. The study was conducted at the Department of Pharmacology. In collaboration with the General Medicine Department, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar, India. All were informed regarding the study, and their written consent was obtained. The Institutional Ethics Committee gave the study its approval. The duration of the study was February 2019 to July 2019.

Treatment chart and patient data collection form having demographic details such as name, age, gender, etc., complete medical, surgical, and drug history, laboratory data, endoscopy, and imaging results.

Inclusion criteria

- Patients are to give written informed consent.
- Patients presenting with complaints of non-ulcer dyspepsia like epigastricdistention or pain, nausea, or heartburn for at least 12 weeks
- Patients of either sex aged between 18 and 60 years
- Non-pregnant females.
- Available for follow-up.

Exclusion criteria

- Patients do not give written, informed consent.
- Patients of either sex aged < 18 years or > 60 years
- Patients with endoscopic evidence of ulcer disease and severe esophagitis
- History of the chronic intake of NSAIDS, anti-coagulants, and acid suppressants
- Patients with systemic diseases (renal dysfunction, cardiac problems)
- Patients on other diabetic medications, requiring hospitalisation
- Consuming alcohol, pregnant, and lactating women
- Not available for follow-up.

Procedure

Patients were randomly allocated into two groups. Patients were divided into 2 groups of 30 patients each.

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Group I (n = 30): Patients received one tablet of Itopride hydrochloride, 50 mg, three times daily before meals and

Group II (n = 30): patients received one tablet of Levosulpiride 75 mg three times daily before meals for two weeks and continued it up to three months.

Concomitant medication with any other prokinetic drugs—antacids, enzyme preparations, H2-blockers, or proton pump inhibitors—was not permitted during the study period.

The grading of responses was marked or complete relief, moderate relief, slight relief, no relief, and worsening of symptoms.

Statistical analysis: The data thus obtained were subjected to statistical analysis. The data was analysed using descriptive statistics such as mean, standard deviation, percentages, and proportions. The Chi-square test was used to assess categorical data, whereas the Analysis of Variance (ANOVA) was used to examine means. The findings were obtained by using suitable statistical tests utilising Microsoft Excel and the Statistical Package for Social Sciences (SPSS). A P value < 0.05 was considered significant.

Results: The present study included 60 patients. The male-to-female ratio was 1.30:1, and the mean age in group I (itopride hydrochloride) was 35.36±9.79 in group II (levosulpiride). A total 30 patients were included, with 16 males and 14 females. The male-to-female ratio was 1.14:1, and the mean age in group II was 35.1±9.65.

Table 1: Demographic distribution of patients

Gender	**Group I /I to pride Group (n=30)**	**Group II/ Levosulpiride group (n=30)**
M:F	17:13	16:14

Table 1 shows that group I had 17 males and 13 females, and group II had 16 males and 14 females.

Table 2: Response of treatment in patients with non-ulcer dyspepsia

Response	**Group I /Itopride Group (n=30)**			**Group II/Levosulpiride group (n=30)**			**P value**
	Male	Female	Total	Male	Female	Total	
Marked or complete relief	10	8	18	7	5	12	<0.05
Moderate relief	5	4	9	8	2	10	
Slight relief	1	1	2	3	2	5	
No relief	0	1	1	1	1	2	
Worsening of symptoms	0	0	0	0	1	1	
Total	16	14	30	19	11	30	

Table 2 and Figure 1 show that in groups I and II, the responses were marked or complete relief in 18 and 12, moderate relief in 9 and 10, slight relief in 2 and 5, no relief in 1 and 2, and worsening of symptoms in 0 and 1 patient, respectively. The difference was significant (P < 0.05).

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Figure 1: Response of treatment in patients

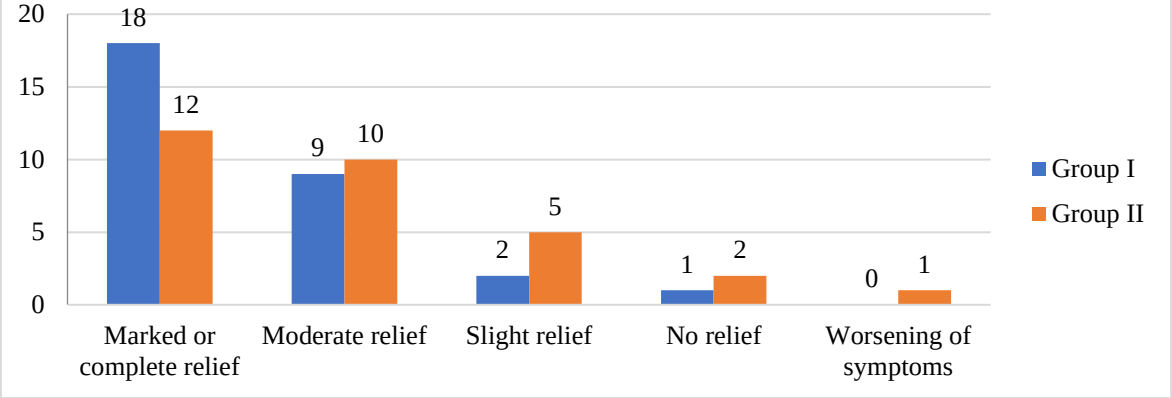

Table III: Effect of therapy on serum biochemistry and QT interval

Parameters	Group I(n=30)		Group II(n=30)		P value
	Pre	Post	Pre	Post	
Hb (mg/dl)	12.4±1.62	12.1±2.03	11.6±2.01	11.4±1.89	0.05
FBS (mg/dl)	82.3±16.53	85.3±9.20	82.6±10.50	83.9±8.75	0.12
WBC-TC (/cumm)	8767±2503	8622±2285	8122±2750	8245±2497	0.26
BUN (mg/ml)	8.5±1.40	8.7±1.20	8.3±1.52	9.1±2.05	0.04
Creatinine	0.81±0.15	0.83±0.12	0.72±0.16	0.75±0.14	0.35
AST (units/L)	27.4±12.50	27.3±11.61	25.6±8.91	23.1±7.81	0.92
ALT (units/L)	30.2±9.20	29.5±5.30	30.7±8.91	29.4±7.39	0.19
ϒ-GT (units)	30.5±11.80	33.4±10.75	24.7±16.43	26.3±18.90	0.03
Alk. Phos (units/ml)	135.2±20.72	143.2±24.50	134.6±27.90	129.3±33.05	0.42
Bilirubin (mg/dl)	0.93±0.2	0.92±0.4	0.95±0.1	0.82±0.2	0.68
Total cholesterol (mg/dl)	167.3±45.71	163.2±32.89	168.4±31.75	162.4±26.50	0.81
QT-Interval	0.32±0.050	0.31±0.041	0.45±0.01	0.47±0.08	0.05

Table III shows that in group I and group II, pre and post mean Hb (mg/dl) was 12.4 and 12.1 and 11.6 and 11.4, FBS (mg/dl) was 82.3 and 85.3 and 82.6 and 83.9, WBC-TC (/cumm) was 8767 and 8622 and 8122 and 8245, BUN (mg/ml) was 8.5 and 8.7 and 8.3 and 9.1, creatinine was 0.81 and 0.83 and 0.72 and 0.75, AST (units/L) was 27.4 and 27.3 and 25.6 and 23.1, ALT (units/L) was 30.2 and 29.5 and 30.7 and 29.4, ϒ-GT (units) was 30.5 and 33.4 and 24.7 and 26.3, Alk. Phos (units/ml) was 135.2 and 143.2 and 134.6 and 129.3, bilirubin (mg/dl) was 0.93 and 0.92 and 0.95 and 0.82, total cholesterol (mg/dl) was 167.3 and 163.2 and 168.4 and 162.4 and QT-Interval was 0.32 and 0.31 and 0.45 and 0.47 respectively. The difference was significant ($P < 0.05$).

Table IV: Adverse effect of therapy

Adverse effect	Group I / Itopride Group (n=30)	Group II/Levosulpiride group (n=30)
Diarrhoea	0	1(3.33%)
Headache	2(6.67%)	0

Discussion

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The common causes of non-ulcer dyspepsia are gastroesophageal reflux disease (GERD), where acid from the stomach flows back into the oesophagus, causing irritation.[7,8]

Sores in the lining of the stomach or the first part of the small intestine, inflammation of the stomach lining, use of nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, and certain antibiotics, chronic dyspepsia without an identifiable cause, overeating, fatty or spicy foods, alcohol, and caffeine can trigger symptoms, and Helicobacter pylori infection can contribute to dyspepsia.[9,10]

The present study was conducted to compare itopride and levosulpiride in patients suffering from non-ulcer dyspepsia. We found that the itopride group had 17 males and 13 females, and the levosulpiride group had 16 males and 14 females. There was a male preponderance in the current study, with 27 patients being female and 33 being male. The Sati.11 study, in comparison, found a 1:2 male-to-female ratio with a preponderance of females.

We found that in the Itopride group and the Levosulpiride group, responses were marked or complete relief in 18 and 12, moderate relief in 9 and 10, slight relief in 2 and 5, no relief in 1 and 2, and worsening of symptoms in 0 and 1 patient, respectively.

We found that in group I and group II, pre and post mean Hb (mg/dl) was 12.4 and 12.1 and 11.6 and 11.4, FBS (mg/dl) was 82.3 and 85.3 and 82.6 and 83.9, WBC-TC (/cumm) was 8567 and 8622 and 8122 and 8245, BUN (mg/ml) was 8.5 and 8.7 and 8.3 and 9.1, creatinine was 0.81 and 0.83 and 0.72 and 0.75, AST (units/L) was 27.4 and 27.3 and 25.6 and 23.1, ALT (units/L) was 30.2 and 29.5 and 30.7 and 29.4, ϒ-GT (units) was 30.5 and 33.4 and 24.7 and 26.3, Alk. Phos (units/ml) was 135.2 and 143.2 and 134.6 and 129.3, bilirubin (mg/dl) was 0.93 and 0.92 and 0.95 and 0.82, total cholesterol (mg/dl) was 167.3 and 163.2 and 168.4 and 162.4 and QT-Interval was 0.32 and 0.31 and 0.45 and 0.47 respectively.

In their study, Huang et al.[12] included nine RCTs enrolling 2620 FD cases; 1372 cases received itopride treatment, and 1248 cases received placebo or other drugs (control groups). Compared with control groups, itopride had superior RR values of 1.11 [95%CI: (1.03, 1.19), P = 0.006], 1.21 [95%CI: (1.03, 1.44), P = 0.02], and 1.24 [95%CI: (1.01, 1.53), P = 0.04] for global patient assessment, postprandial fullness, and early satiety, respectively. For the Leeds Dyspepsia Questionnaire score, the weighted mean deviation was -1.38 [95%CI: (-1.75, -1.01), P < 0.01]. The incidence of adverse effects was similar in the itopride and control groups. The funnel plots for all indicators showed no evidence of publication bias. Itopride has good efficacy in terms of global patient assessment, postprandial fullness, and early satiety in the treatment of patients with FD and shows a low rate of adverse reactions. Itopride can greatly improve the FD syndrome score.

In the present study, one patient in each group reported two adverse events: headache by a patient receiving Itopride and diarrhoea by one patient receiving Levosulpiride. Both were mild and subsided without interfering with the continuation of the treatment. Saxenaet al.[14] observed that only 4% of patients taking itopride had adverse effects. Abdominal cramps were 1%, constipation was 1%, and 2% had an allergic reaction in the form of itching after the drugs were stopped. While patients were taking levosulpiride, 13% had adverse effects such as loose motion (4%) and obsolescence (4%). Less common adverse effects noted were headache, weight gain, and galactorrhea. Gerald Hotmanet al.[15] observed in 2006 that abdominal pain, diarrhoea, nausea, and constipation are the most common adverse effects of the use of itopride. Gupta et al. [16] have reported various side effects of levosulpiride, such as abnormal limb and facial movements, hyperprolactinemia, neuroleptic malignant syndrome, tardive dyskinesia, and others. We observed that levosulpiride and itopride were equally effective in treating the symptoms of non-ulcer dyspepsia. Clinically and biochemically, both medications were well tolerated. Saxena et al.[14] observed that levosulpiride consistently showed statistical and clinical superiority over placebo and other prokinetic drugs in reducing the symptoms.

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Hassan et al.[17] compared the efficacy and safety of levosulpiride and itopride in patients with gastroesophageal reflux disease. He observed that levosulpiride was superior to itopride in terms of early effects and better quality of life in these patients.

Limitations of the study: The shortcoming of the study is small sample size and short duration of the study.The place of the study was localised at one tertiary centre

Conclusion

Authors found that Levosulpiride and itopride were equally effective in treating the symptoms of non-ulcer dyspepsia. Clinically and biochemically, both medications were well tolerated.

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