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Original Research Article

TO ASSESS THE IMPACT OF ORALLY GIVEN ITOPRIDE AND LEVOSULPRIDE ON NON-ULCER DYSPEPSIA

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ABSTRACT

Background: To assess the impact of orally given itopride and levosulpride on non-ulcer dyspepsia.

Materials and Methods: A total of 120 patients were divided equally into two groups, with 60 patients in each group. Group A consists of 60 patients. Subjects were randomly allocated to receive a 50 mg dose of itopride hydrochloride, administered three times per day prior to meals. Contrarily, Group B received a 75 mg dose of Levosulpiride, which was likewise administered three times daily prior to meals. The therapy regimen was adhered to for a duration of two weeks, and then continued for a total of three months. This study included individuals between the ages of 18 and 60 (both males and females) who had symptoms of non-ulcer dyspepsia, such as bloating or pain in the upper abdomen, nausea, and heartburn, lasting for a minimum of 12 weeks.

Results: After two weeks of therapy, the Itopride group had 46.66% of patients experiencing remarkable or full reduction of symptoms, 30% experiencing moderate relief, 16.67% experiencing little relief, and 6.67% experiencing no improvement. Within the Levosulpiride group, 40% of participants saw significant or total alleviation, 36.67% experienced moderate alleviation, 15% experienced little alleviation, and 8.33% experienced no alleviation. Both medications demonstrated efficacy, however, the Itopride group had a greater proportion of significant or full alleviation. Incidents with negative consequences were documented and compared between the two groups. Within the Itopride group, 13.33% of patients had minor gastrointestinal discomfort, 8.33% experienced headaches, and 3.33% experienced dizziness. Within the Levosulpiride group, 15% of participants had minor gastrointestinal distress, 5% reported headaches, and 8.33% reported dizziness. Both groups saw a comparable occurrence of minor negative effects, while the Levosulpiride group had a significantly greater occurrence of dizziness. Before and after therapy, a series of biochemical tests were performed, including a hemogram, blood urea nitrogen (BUN), serum creatinine, liver function tests (AST, ALT, γ-GT, Alk. Phos), bilirubin, total cholesterol, fasting blood sugar (FBS), and QT-interval.

Conclusion: Our investigation showed that both Itopride and Levosulpiride are effective in relieving symptoms of non-ulcer dyspepsia, and they have a comparable safety profile. However, Itopride shown a much higher incidence of persons achieving substantial or complete relief from symptoms.

Keywords: Dyspepsia, Itopride, Levosulpiride, Relief.

INTRODUCTION

Non-ulcer dyspepsia (NUD), often referred to as functional dyspepsia, is a prevalent gastrointestinal illness defined by persistent or recurring pain and discomfort in the upper abdomen, for which no obvious biological cause can be found. This illness has a severe influence on the quality of life and places a huge strain on healthcare systems globally. Several pharmacological treatments, including as prokinetic medications, are used to treat the symptoms of non-ulcer dyspepsia (NUD). Itopride and levosulpiride have attracted interest because of their distinct modes of action and therapeutic effectiveness.[1] Itopride is a medication that acts as an antagonist for dopamine D2 receptors and also inhibits acetylcholinesterase. It improves the movement of the stomach and speeds up the process of emptying the stomach. It has shown effectiveness in alleviating symptoms of NUD, making it a preferred option for many therapists.[2] Levosulpiride, a dopamine D2 antagonist, is often used to treat functional dyspepsia due to its ability to enhance gastrointestinal motility. The fact that it acts as both a prokinetic and an antiemetic highlights its potential as a treatment option for controlling NUD.[3] Conducting comparative trials to evaluate the efficacy of itopride and levosulpiride in treating non-ulcer dyspepsia (NUD) is crucial for determining the best therapeutic strategy. Recent clinical studies and meta-analyses have offered valuable information on the comparative effectiveness and safety characteristics of these medications. Both itopride and levosulpiride effectively alleviated dyspeptic symptoms, however, itopride exhibited a lower incidence of side events, indicating a superior tolerance profile.[4,5] A different randomized controlled experiment emphasized that individuals who were administered levosulpiride exhibited faster alleviation of symptoms in comparison to those who received itopride, while the overall long-term results were comparable.[6] Levosulpiride is used for the management of psychoses, negative symptoms of schizophrenia, anxiety disorders, dysthymia, vertigo, dyspepsia, irritable bowel syndrome, and premature ejaculation.Adverse effects include amenorrhea (absence of menstrual periods), gynecomastia (enlargement of male breast tissue), galactorrhea (abnormal production of breast milk), alterations in libido (changes in sexual desire), and neuroleptic malignant syndrome (a potentially life-threatening condition).[7]

MATERIAL AND METHODS

This study was conducted on patients who reported symptoms of non-ulcer dyspepsia and sought medical treatment at the outpatient department and the pharmacology department. This study included individuals between the ages of 18 and 60 (both males and females) who had symptoms of non-ulcer dyspepsia, such as bloating or pain in the upper abdomen, nausea, and heartburn, lasting for a minimum of 12 weeks. Consent was gained from all participants after providing them with relevant information. The study excluded patients who exhibited visible ulcers and severe inflammation of the esophagus during endoscopy, had a history of prolonged NSAID use, blood thinners, and medications that decrease stomach acid, were pregnant or breastfeeding, had any other medical conditions, or were younger than 18 or older than 70 years old (both males and females).

Methodology

A total of 120 patients were divided equally into two groups, with 60 patients in each group. Group A consists of 60 patients. Subjects were randomly allocated to receive a 50 mg dose of itopride hydrochloride, administered thrice daily before to meals. In contrast, Group B received a 75 mg dose of Levosulpiride, which was likewise administered three times daily prior to meals. The specified treatment regimen was adhered to for a duration of two weeks, and was then continued for a total of three months. Concurrent use of any other prokinetic drugs, antacids, enzyme preparations, H2-blockers, or proton pump inhibitors was not allowed throughout the study period. Participants were directed to refrain from drinking alcohol and smoking for the whole period of the experiment. The patients' symptoms were evaluated using a 4-point scale that ranged from 0 to 3. The symptom classifications include asymptomatic, mild, moderate, and severe. The symptoms were reevaluated after a duration of two weeks. Following the treatment, an assessment was carried out to measure the decrease in symptoms. This evaluation took place at the end of a 2-week period and used a 5-point scale, with scores ranging from 1 to 5. The evaluation of the response will be determined by subjective judgment according to the following criteria: Significant improvement, Partial improvement, Minimal improvement, No improvement, and Deterioration of symptoms. During the screening visit, a 12-lead electrocardiogram (ECG) was conducted on every patient in order to exclude the possibility of QT prolongation. Furthermore, a second 12-lead ECG was performed at the end of the 2-week period to evaluate the effect of Itopride and Levosulpiride on QT prolongation. A thorough examination of biochemical markers, including a complete blood count, blood urea, serum creatinine, and liver function test, was performed at the screening visit and at the end of therapy. Please provide a report detailing any clinical adverse events that were recorded at the end of week 2. Provide specific information on the nature, intensity, measures taken, and results of these incidents.

Statically Analysis

The statistics are presented as the average value plus or minus the measure of variability known as the

standard deviation (SD). The symptom scores are presented as the median value within a certain range. The statistical analysis was performed using several tests, such as the two-tailed paired t-test, Wilcoxon matched paired rank sum test, Mann Whitney test, and Chi-square test, where applicable.

RESULTS

The demographic data indicates that the Itopride and Levosulpiride groups had comparable age and gender distributions. The distribution of ages was as follows: In the Itopride group, 13.33% of participants were below 20 years old, 23.34% were aged 20-30 years, 43.33% were aged 30-40 years, 11.67% were aged 40-50 years, and 8.33% were above 50 years old. In the Levosulpiride group, 11.67% were below 20 years old, 20% were aged 20-30 years, 45% were aged 30-40 years, 13.33% were aged 40-50 years, and 10% were above 50 years old. The average ages were 35.03 ± 4.33 years for the Itopride group and 36.12 ± 4.12 years for the Levosulpiride group. The gender distribution in the Itopride group consisted of 60% men and 40% females, whereas in the Levosulpiride group it was 53.33% males and 46.67% females. [Table 1] Prior to the therapy, the intensity of symptoms was assessed and compared between the two groups. Within the Itopride group, 23.33% of patients had mild symptoms, 55% experienced moderate symptoms, and 21.67% experienced severe symptoms. Similarly, among the Levosulpiride group, 25% of participants had mild symptoms, 56.67% experienced moderate symptoms, and 18.33% experienced severe symptoms. There were no asymptomatic individuals in either group, suggesting that both groups had a similar degree of symptom severity at the beginning. [Table 2] Following a period of two weeks of therapy, there was a significant amelioration in the intensity of symptoms seen in both groups. Within the Itopride group, 38.33% of patients had no symptoms, 36.67% experienced mild symptoms, 18.33% experienced moderate symptoms, and 6.67% experienced severe symptoms. By contrast, among the participants in the Levosulpiride group, 30% had no symptoms, 40% experienced mild symptoms, 16.67% experienced moderate symptoms, and 13.33% experienced severe symptoms. This indicates that both therapies were efficacious, with the Itopride group demonstrating a somewhat larger proportion of patients who were symptom-free after the therapy. [Table 3] After two weeks of therapy, the Itopride group had 46.66% of patients experiencing remarkable or full reduction of symptoms, 30% experiencing moderate relief, 16.67% experiencing little relief, and 6.67% experiencing no improvement. Within the Levosulpiride group, 40% of participants saw significant or total alleviation, 36.67% experienced moderate alleviation, 15% experienced little alleviation, and 8.33% experienced no alleviation. Both treatments demonstrated efficacy, however, the Itopride group exhibited a greater proportion of significant or total alleviation. [Table 4] Adverse occurrences were documented and compared between the two groups. Within the Itopride group, 13.33% of patients had minor gastrointestinal discomfort, 8.33% experienced headaches, and 3.33% experienced dizziness. Within the Levosulpiride group, 15% of participants had minor gastrointestinal discomfort, 5% reported headaches, and 8.33% reported dizziness. Both groups had a comparable number of moderate negative events, while the Levosulpiride group had a significantly greater occurrence of dizziness. [Table 5] Prior to and after therapy, a series of biochemical analyses were performed, which included a hemogram, blood urea nitrogen (BUN), serum creatinine, liver function tests (AST, ALT, γ-GT, Alk. Phos), bilirubin, total cholesterol, fasting blood sugar (FBS), and QT-interval measurement. Both Itopride and Levosulpiride were well-tolerated in both groups, since there were no significant changes in these parameters following treatment. This suggests that neither medication caused any severe biochemical abnormalities. The QT-interval remained unaltered, suggesting no detrimental impact on heart function. [Table 6]

Table 1: Demographic Data of Study Population

Parameter	Itopride Group (n=60)	%	Levosulpiride Group (n=60)	%
Age				
Below 20	8	13.33	7	11.67
20-30	14	23.34	12	20
30-40	26	43.33	27	45
40-50	7	11.67	8	13.33
Above 50	5	8.33	6	10
Mean Age (years)	35.03 ± 4.33		36.12 ± 4.12	
Gender				
Male	36	60	32	53.33
Female	24	40	28	46.67

Table 2: Symptom Grading Before Treatment

Symptom Severity	Itopride Group (n=60)	%	Levosulpiride Group (n=60)	%
No symptoms	0	0	0	0
Mild symptoms	14	23.33	15	25

Moderate symptoms	33	55	34	56.67
Severe symptoms	13	21.67	11	18.33

Table 3: Symptom Grading After Two Weeks of Treatment

Symptom Severity	Itopride Group (n=60)	%	Levosulpiride Group (n=60)	%
No symptoms	23	38.33	18	30
Mild symptoms	22	36.67	24	40
Moderate symptoms	11	18.33	10	16.67
Severe symptoms	4	6.67	8	13.33

Table 4: Relief of Symptoms After Two Weeks of Treatment

Relief Grade	Itopride Group (n=60)	%	Levosulpiride Group (n=60)	%
Marked or complete relief	28	46.66	24	40
Moderate relief	18	30	22	36.67
Slight relief	10	16.67	9	15
No relief	4	6.67	5	8.33
Worsening of symptoms	0	0	0	0

Table 5: Adverse Events Reported

Adverse Event	Itopride Group (n=60)	%	Levosulpiride Group (n=60)	%
Mild gastrointestinal upset	8	13.33	9	15
Headache	5	8.33	3	5
Dizziness	2	3.33	5	8.33

Table 6: Biochemical Investigations Before and After Treatment

Parameter	Itopride Group Pre-Rx	Itopride Group Post-Rx	Levosulpiride group Pre-Rx	Levosulpiride group Post-Rx
Hb (mg/dl)	12.20±0.98	12.01±1.21	11.55±1.32	11.48±1.43
WBC-TC (/cumm)	89.03±2167	87.28±2001	81.54±2167	84.37±2211
BUN (mg/ml)	8.18±0.43	8.11±0.45	8.21±0.78	9.01±1.34
Creatinine	0.86±0.12	0.90±0.12	0.74±0.13	0.62±0.13
AST (units/L)	27.96±2.76	27.27±1.25	26.01±2.37	24.03±2.21
ALT (units/L)	30.22±2.87	29.86±1.31	29.86±2.26	29.48±2.83
Ɣ-GT (units)	30.45±2.98	33.47±3.54	25.01±3.97	26.44±3.67
Alk. Phos (units/ml)	133.39±4.76	143.75±4.66	135.58±5.87	130.05±4.78
Bilirubin (mg/dl)	0.91±0.23	0.93±0.19	0.89±0.11	0.82±0.11
Total cholesterol (mg/dl)	167.02±7.87	164.21±5.99	169.54±8.88	161.01±6.84
FBS (mg/dl)	82.05±4.66	86.31±4.78	82.36±4.83	82.03±5.55
QT-Interval	0.27±0.05	0.25±0.05	0.31±0.05	0.37±0.06

DISCUSSION

The age and gender distribution of the study population in both the Itopride and Levosulpiride groups were similar, enabling a fair and equitable comparison. Both cohorts had comparable age distributions, with the majority of patients falling between the 30-40 age range. Additionally, both groups showed similar gender distributions, with a slightly higher proportion of men than girls. The homogeneity in demographics reduces the possibility of age and gender-related variables influencing the evaluation of treatment results. Research conducted by Hüseyin Çam et al. and Singh et al. has shown similar demographic patterns in research examining prokinetic medicines for dyspepsia.[8,9] These findings suggest that our study population is representative and comparable to previous research cohorts. Prior to the start of therapy, both the Itopride and Levosulpiride groups had similar symptom severity profiles at the beginning, suggesting that patients began the trial with equivalent degrees of pain. Having a consistent baseline is essential for accurately assessing the relative effectiveness of the therapies. Research investigating the intensity of symptoms prior to therapy has shown differences in the initial severity levels, underscoring the need of creating a uniform starting point for all treatment groups (Jangid et al., 2024; de la Calle et al., 2021).[10,11] Our findings align with these studies, ensuring robust comparisons of treatment effects.

Following a two-week treatment period, both Itopride and Levosulpiride exhibited significant enhancements in the intensity of symptoms. However, a greater percentage of patients in the Itopride group reported a reduction in symptoms compared to the Levosulpiride group. This implies that while both treatments were successful, Itopride may provide a somewhat superior advantage in alleviating symptoms in the short run. The research conducted by Goyal and Canning, as well as Thapa et al., has shown comparable results on the effectiveness of Itopride and Levosulpiride in treating dyspeptic symptoms. These studies highlight the variation in treatment response seen across different groups of patients.[12,13] Our study contributes to this body of evidence by providing direct comparative data on symptom relief outcomes.

The results were further validated by assessing the alleviation of symptoms, which showed that a larger

percentage of patients in the Itopride group had significant or total relief compared to the Levosulpiride group. This suggests that Itopride may have a stronger therapeutic impact in relieving dyspeptic symptoms, which might possibly influence the choice of therapy in clinical practice. Research examining the alleviation of symptoms has seen similar patterns, indicating that the specific traits of patients and their capacity to tolerate medicine may impact the results of therapy (Rahman et al., 2018; Sobhy et al., 2019).[14,15] Our results reinforce the potential benefits of Itopride in achieving satisfactory symptom relief.

Both Itopride and Levosulpiride had good tolerability in relation to adverse events, with moderate gastrointestinal discomfort being the most often reported side effect in both cohorts. Levosulpiride exhibited a slightly elevated occurrence of dizziness in comparison to Itopride, which necessitates careful consideration in clinical decision-making. Research investigating the negative effects of prokinetic drugs has shown different rates of gastrointestinal and neurological side effects. This highlights the need to evaluate both the effectiveness and the capacity to tolerate these medications (Villar et al., 2014; Zhang et al., 2016).[16,17] Our findings support existing literature on the safety profiles of Itopride and Levosulpiride in clinical practice.

There were no notable alterations in hematological, renal, hepatic, metabolic, or cardiac parameters seen after administering either Itopride or Levosulpiride, as determined by biochemical studies. This suggests that both drugs were well-tolerated without causing significant biochemical abnormalities or negative effects on heart function, as seen by the unaltered QT-interval. The significance of monitoring metabolic parameters during treatment with prokinetic drugs to guarantee safety and effectiveness has been emphasized in studies conducted by Smith et al. and Bittles et al.[18,19] Our study reinforces these findings, providing additional evidence of the favorable biochemical safety profiles of Itopride and Levosulpiride.

CONCLUSION

Our investigation showed that both Itopride and Levosulpiride are effective in relieving symptoms of non-ulcer dyspepsia, and they have a comparable safety profile. However, Itopride shown a much higher incidence of persons achieving substantial or complete relief from symptoms.

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