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ORIGINAL RESEARCH

Efficacy and safety of itopride SR for upper gastrointestinal symptoms in patients with diabetic gastroparesis: real-world evidence from Pakistan

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Abstract

Background: Gastroparesis is a serious condition that can be caused by diabetes, surgery or infection, or can be idiopathic. When there is no mechanical obstruction, gastroparesis is characterized by delayed stomach emptying. Itopride, a prokinetic drug, inhibits acetylcholinesterase activity in addition to antagonizing dopamine D2 receptors.

Methods: This prospective, multicentre study is based on real-world data from 988 patients with a diagnosis of diabetic gastroparesis for index (PAGI-SYM2) evaluation at baseline and week 4 of treatment for upper gastrointestinal disorder symptoms.

Results: Upper gastrointestinal symptom severity scores improved significantly after 4 weeks of treatment ($p<0.001$), with significant improvement across all categories of gastroparesis (very mild (37–58.6%), mild degree (24.6–31.6%), moderate (29.3–7.3%) and severe (8.8–2.6%).

Conclusion: Itopride SR (Nogerd SR) in a 150 mg once-daily dose showed promising results in reducing the severity of upper gastrointestinal disorder symptoms associated with diabetic gastroparesis. Both statistical and clinical effectiveness were observed. Moreover, the treatment demonstrated a favourable tolerability profile, with a low incidence of adverse effects.

Keywords: diabetes, gastroparesis, itopride, PAGI-SYM, Upper gastrointestinal symptoms.

Citation

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Introduction

Gastroparesis, characterized by delayed gastric emptying without mechanical obstruction, is frequently linked to uncontrolled diabetes, which accounts for approximately one-third of all gastroparesis cases.[1–3] The cardinal symptoms of this condition include postprandial fullness, early satiety, nausea, vomiting and bloating. Recent studies have recognized abdominal pain as one of the most prevalent symptoms of gastroparesis.[4] This form of autonomic neuropathy is commonly observed in individuals who have had diabetes for more than 10 years and have already developed other microvascular complications. Interestingly, even when blood glucose levels are well managed, the symptoms of gastroparesis tend to persist and remain stable for extended periods, ranging from 12 to 25 years.[5,6]

Traditionally, diabetes has been regarded as the primary cause of gastroparesis. However, diabetic gastroparesis constitutes only around one-third of gastroparesis cases in tertiary-care studies. Population-based investigations indicate that gastroparesis develops in only 1–5% of patients with diabetes.[7–10] The cause of gastroparesis is diverse, and it is classified into three well-established sub-types: diabetic gastroparesis, iatrogenic gastroparesis (resulting from upper gastrointestinal surgery or medications) and idiopathic gastroparesis. According to a population-based study conducted in the United States, the most prevalent aetiology was found to be diabetic gastroparesis, accounting for nearly 60% of cases, primarily affecting those with type 2 diabetes. The post-surgical sub-type constituted 15% of cases, whereas both idiopathic and drug-induced sub-types were observed in approximately 10% of patients each.[11]

Itopride, a novel prokinetic agent, exhibits dual functionality as a dopamine D2 receptor antagonist and an acetylcholine esterase inhibitor. Itopride shows promise in managing gastroparesis symptoms by accelerating gastric emptying, improving gastric tension and sensitivity, and exerting antiemetic effects.[12,13] Human studies have demonstrated the positive effects of itopride on solid and liquid gastric emptying compared with placebo and pantoprazole. Two randomized controlled trials reported significant improvements in gastric emptying rates for itopride compared with control groups.[14,15]

This study aims to evaluate the efficacy and safety of itopride in addressing upper gastrointestinal symptoms associated with gastroparesis specifically in patients with diabetes. By assessing the impact of itopride SR on symptom relief, this research intends to provide valuable insights into the potential benefits of itopride as a treatment option for gastroparesis. Improved understanding of the role of itopride in the management of gastroparesis-related symptoms can contribute to enhanced therapeutic approaches and improved quality of life for individuals living with this challenging condition.

Methods

This was a real-world evidence, prospective, multicentre study in patients diagnosed with diabetic gastroparesis. The current prospective study was conducted from December 2022 to May 2023 according to the definition of 'non-interventional trials'. The study was performed in accordance with the ethical standards stipulated in the Declaration of Helsinki. Patient data originating from assessments and evaluations performed according to the physician's routine practice were collected. All patients with diabetic gastroparesis at the participating centres prescribed itopride (NOGERD SR 150 mg) for 0–4 weeks were enrolled in this study. The study population consists of approximately 988 patients with a diagnosis of diabetic gastroparesis evaluated with the Patient Assessment of Upper Gastrointestinal Disorders-Symptom Severity Index (PAGI-SYM2) at baseline (week 0) and week 4. All patients signed a consent form. The study was a prospective, non-interventional study in compliance with the Declaration of Helsinki, which did not require registration on ClinicalTrials.gov.

Inclusion criteria for the study were aged between 18 and 65 years, having experienced symptoms of diabetic gastroparesis, such as postprandial fullness, nausea, vomiting, upper abdominal pain and early satiety, for at least 6 months prior to screening as assessed by a physician. Additionally, the participants were required to have diabetes mellitus with a glycated haemoglobin (HbA_{1c}) level below 11% and a body mass index (BMI) of between 18 and 35 kg/m^2.

Exclusion criteria were use of medications that potentially influence upper gastrointestinal motility or appetite within 1 week of the study such as prokinetic drugs or macrolide antibiotics, exposure to radiation for research purposes in the previous 12 months, a prior history of gastric surgery, including procedures such as gastrectomy, gastric bypass, gastric banding, pyloroplasty, vagotomy or fundoplication, which had manipulated the natural anatomy of the stomach, as well as those with a history of anorexia nervosa or bulimia. Pregnant and lactating women were also excluded from participation.

The primary end point of the study was the relief of upper gastrointestinal symptoms, measured at baseline and at week 4 (28±7 days) using the PAGI-SYM2 assessment tool. The secondary end point of the study focused on the safety assessments of itopride SR. Adverse events

(AEs) and serious AEs were closely monitored and recorded throughout the study. This secondary end point aimed to evaluate the safety profile of itopride SR and ensure the well-being of participants.

The data for the study were collected from routine patient visits and assessments at three designated time points. The patients may have completed the questionnaires either in person during their routine visits to the healthcare facility or may have been prompted to complete the questionnaires or assisted by doctors or study staff in completing the questionnaires if needed. Patient data, including symptom relief measurements and safety data (AEs and serious AEs), were recorded in the study Case Report Form. Other specific procedures and methods for reporting adverse drug reactions (ADRs) were systematic inquiry during routine patient visits or patient self-reporting of any new symptoms or experiences observed whilst taking the study medication or regular monitoring of patients at each visit to assess for ADRs. Ethical approval for both the scientific and ethical aspects of conducting the study was obtained prior to commencing the research. The approval was granted by the Advance Educational Institute and Research Center (AEIRC) Ethics Review Committee ref no: ERC/S20/P-021.

All data analyses were conducted by a third-party statistician using SPSS software version 21. Summary statistics, such as the number of observations, mean, standard deviation, and median, minimum, and maximum values, were calculated for continuous variables. Frequencies and percentages were provided for categorical variables. Additionally, the χ^2 test and Wilcoxon signed-rank test were used when appropriate. A p value of <0.05 was considered significant.

Results

Table 1 presents the demographic and clinical profile of the study participants, consisting of 988 individuals. The mean age of the participants was 46.9 years, with a standard deviation of 12.24, indicating a relatively wide age range. The minimum age observed in the study was 18 years, whereas the maximum age was 65 years. The participants had an average weight of 73.88 kg, with a standard deviation of 32.44 kg.

The participants' mean BMI was 26.7 kg/m², with a standard deviation of 4.14 kg/m². The average BMI falls within the overweight category. HbA_{1c} level is a marker of long-term blood sugar control in individuals with diabetes; the mean value of HbA_{1c} was 8.48%, with a standard deviation of 1.26%. Thus, on average, participants had high HbA_{1c} levels, suggesting a sub-optimal control of blood sugar.

Table 1. Demographic and clinical profiles of study participants (n=988).

Age	**Mean ± SD (46.9±12.24) Min 18, Max 65**
Weight, kg	73.88±32.44
BMI, kg/m²	26.7±4.14
HbA_{1c}, %	8.48±1.26
Duration of diabetes, years	8.1±5.1
<5	285 (38.6%)
5–9 years	187 (25.3%)
10–14 years	165 (22.4%)
15–19 years	60 (8.1%)
20–25 years	41 (5.6%)
Age groups, years	
15–25	80 (7.9%)
26–35	110 (10.8%)
36–45	232 (22.8%)
46–55	293 (28.8%)
56–65	302 (29.7%)
Sex	
Male	486 (49.4%)
Female	500 (50.6%)

BMI, body mass index; HbA_{1c}, glycated haemoglobin; Max, maximum; Min, minimum; SD, standard deviation.

The mean duration of diabetes was 8.1 years, with the majority (38.6%) having a duration of less than 5 years (Table 1). The distribution shows that the number of participants decreases as the duration of diabetes increases. The participants were further divided into age groups. The largest age group consisted of individuals aged between 46 and 55 years (28.8%), closely followed by those aged between 56 and 65 years (29.7%). The smallest age group consisted of individuals aged between 15 and 25 years (7.9%). Overall, 49.4% of participants were men and 50.6% were women.

Table 2 provides the mean scores and standard deviations (SD) for each symptom at week 0 and week 4, along with the corresponding p values. At week 0, the mean scores for all symptoms were relatively high, indicating a significant level of symptom severity. However, by week 4, there was a substantial decrease in the mean scores for all symptoms, demonstrating a significant improvement in symptom severity.

For instance, at week 0, the mean score for heartburn during the day was 2.06±1.54. However, at week 4, the mean score significantly decreased to 0.89±1.15 (p<0.001). Similar improvements were observed for regurgitation or reflux during the day, nausea, upper abdominal pain,

Table 2. Patient Assessment of upper Gastrointestinal Disorders-Symptom Severity Index (PAGI-SYM) evaluation at weeks 0 and 4.

Please rate the severity of the following symptoms	Week 0 score	Week 4 (28±7 days)	*p* value*	Complete resolution of symptoms at week 4
Heartburn (burning pain rising in your chest or throat) during the day	2.06±1.54	0.89±1.15	<0.001	49.6%
Regurgitation or reflux (fluid or liquid from your stomach coming up into your throat) during the day	2.02±1.47	0.89±1.07	<0.001	50.5%
Nausea (feeling sick to your stomach as if you were going to vomit or throw up)	1.87±1.31	0.64±0.90	<0.001	55.2%
Upper abdominal (above the navel) pain	1.87±1.53	0.64±0.99	<0.001	60.4%
Stomach fullness	2.07±1.65	0.76±1.11	<0.001	58.2%
Loss of appetite	1.56±1.24	0.65±0.99	<0.001	57.8%
Upper abdominal (above the navel) discomfort	1.52±1.26	0.78±1.05	<0.001	52.1%
Bloating (feeling like you need to loosen your clothes)	1.64±1.41	0.89±1.03	<0.001	48.7%
Heartburn (burning pain raising in your chest or throat) when lying down	1.72±1.45	0.72±1.05	<0.001	57.3%
Regurgitation or reflux (fluid or liquid from your stomach coming up into your throat) when lying down	1.57±1.42	0.72±0.96	<0.001	51.2%
Lower abdominal (below the navel) pain	1.13±1.25	0.58±0.99	<0.001	65.9%
Feeling of discomfort inside your chest during the day	1.23±1.15	0.55±0.98	<0.001	65.7%
Bitter, acid or sour taste in your mouth	1.54±1.38	0.79±1.04	<0.001	54.2%
Lower abdominal (below the navel) discomfort	1.32±1.29	0.57±0.92	<0.001	61.9%
Feeling of discomfort inside your chest at night (during sleep time)	1.38±1.32	0.52±0.96	<0.001	67.9%
Retching (heavy as if to vomit but nothing comes up)	1.38±1.3	0.57±0.99	<0.001	66.8%
Stomach or belly visibly larger	1.30±1.23	0.59±1.01	<0.001	66.6%
Vomiting	1.25±1.23	0.50±0.92	<0.001	67.5%
Not able to finish a normal size meal	1.55±1.29	0.54±0.90	<0.001	63.3%
Feeling excessively full after meals	1.91±1.59	0.62±1.01	<0.001	64.1%

*Wilcoxon signed-rank test.

stomach fullness, loss of appetite, upper abdominal discomfort, bloating, heartburn when lying down, regurgitation or reflux when lying down, lower abdominal pain, a feeling of discomfort inside the chest during the day, bitter, acid or sour taste in the mouth, lower abdominal discomfort, the feeling of discomfort inside the chest at night, retching, stomach or belly visibly larger, vomiting, not able to finish a normal-sized meal, and feeling excessively full after meals.

In all cases, the mean scores at week 4 were significantly lower compared with those at week 0 (all $p<0.001$). Thus, there was a strong statistical significance, reinforcing the effectiveness of the treatment or intervention in reducing the severity of upper gastrointestinal disorder symptoms.

Table 3 presents the distribution of severity scores before and after treatment, comparing data for weeks 0 and 4. The severity scores are categorized into five levels: very mild degree (1–20), mild degree of severity (21–40), moderate degree of severity (41–60), severe (61–80), and extremely severe (81–100). At week 0, out of a total of 988 participants, 37% had a very mild degree of severity;

Table 3. Distribution of severity scores before and after treatment (week 0 *versus* week 4).

	Week 0	Week 4	*p* value*
Very mild degree (1–20)	366 (37)	570 (58.6)	<0.001
Mild degree of severity (21–40)	243 (24.6)	306 (31.5)	
Moderate degree of severity (41–60)	289 (29.3)	71 (7.3)	
Severe (61–80)	87 (8.8)	25 (2.6)	
Extremely severe (81–100)	4 (0.4)	–	
Total	988	972	

*χ^2=143.6, Degrees of freedom=4.

24.6% had a mild symptoms, 29.3% had moderate symptoms, 8.8% had severe symptoms, and only 0.4% had extreme symptoms.

After 4 weeks of treatment or intervention, the symptom severity scores showed significant improvement across all categories. At week 4, 58.6% of the participants had mild symptoms, indicating a positive response to the intervention. The percentage of participants with mild symptoms decreased slightly to 31.4%, only 7.3% of individuals had moderate symptoms. Severe symptoms were only observed in 2.6% of individuals, demonstrating substantial improvement. Notably, no participants were classified as having extreme symptoms at week 4.

Statistical analysis using the χ^2 test revealed a highly significant result (p<0.001), indicating that the observed changes in severity scores from week 0 to week 4 were not due to chance. This suggests that the treatment or intervention substantially impacted the severity of the condition.

In this study, the PAGI-SYM was used to evaluate the severity of upper gastrointestinal (GI) disorders in patients at week 0 and week 4. The median and interquartile range (IQR) scores were analysed to assess the change in symptom severity over the course of the study.

At week 0, the median PAGI-SYM score was 36 (with an IQR of 36), indicating a relatively high level of symptom severity amongst the patients. However, by week 4, there was a significant improvement in symptom severity, with a median score of 7 (with an IQR of 22). This decrease in symptom severity from week 0 to week 4 was statistically significant (p<0.001).

The safety analysis focused on the occurrence of ADRs amongst the study participants. Out of a total of 988 patients, only 27 (2.8%) experienced ADRs, whereas the majority 952 (97.2%) did not report any AEs. Ten (37%) patients experienced diarrhoea, 8 (29.6%) abdominal pain, 4 (14.8%) experienced nausea, 3 (11.1%) experienced constipation and another 2 (7.4%) reported headaches. All reported ADRs in patients were of mild intensity and resolved on their own, allowing the treatment to proceed without any interruptions. These findings suggest that the treatment used in this study was generally well tolerated and had a low incidence of ADRs.

Discussion

This study was conducted with 988 participants to examine their demographic and clinical profiles. Overall, the mean scores, SD and p values provide quantitative evidence of the significant improvement in symptom severity between baseline and week 4. In this study, severity scores improved significantly after 4 weeks of treatment or intervention. The percentage of participants with very mild severity increased, whereas the percentages in all other severity categories decreased. These results suggest that the intervention was effective in reducing the severity of the condition. A significant p value further strengthens the evidence of treatment efficacy, indicating a highly significant association between the treatment and the observed improvement in severity scores. A meta-analysis was conducted involving nine randomized placebo-controlled trials including a total of 2620 participants, with 1372 individuals receiving treatment with itopride at a dosage of 50 mg three times a day (t.i.d.), and 1248 individuals forming the control group. The control group received medications such as domperidone, mosapride or placebo. The results of the meta-analysis demonstrated a significant improvement in the therapeutic effect of itopride compared with the control group. Specifically, individuals in the itopride-treated group reported statistically significant enhancements in gastrointestinal dysmotility symptoms, such as post-prandial fullness, early satiation and global patient assessment scores, when compared with the control group.[16] Several studies have provided evidence supporting the positive effects of itopride on gastrointestinal and gastroduodenal motility. Two randomized controlled trials have reported favourable outcomes in terms of gastrointestinal and gastroduodenal motility with the use of itopride.[14,15] Additionally, a retrograde study conducted in Japanese patients with chronic gastritis showed that itopride administration (50 mg) led to accelerated gastric emptying.[17] In a comparative study, itopride was found to provide moderate to complete relief of gastrointestinal symptoms in non-ulcer dyspepsia

patients, with higher efficacy compared with metoclopramide.[18] Studies conducted amongst Indian patient populations have also reported itopride as an effective treatment for gastrointestinal dysmotility disorders.[19,20] Furthermore, a post-marketing surveillance study involving patients with delayed gastric emptying found that itopride demonstrated overall efficacy ratings of excellent, good, fair and poor. Rai et al. investigated the clinical characteristics of Indian patients with diabetes experiencing reduced gastrointestinal motility and evaluated the effectiveness of itopride in alleviating gastroparesis-related symptoms whilst maintaining glycaemic control. At the outset, patients exhibited a range of symptoms, including bloating, postprandial fullness, nausea, early satiety, heartburn and vomiting. Following treatment with itopride, there was a remarkable and statistically significant improvement in all of these symptoms ($p<0.001$).[21] Saxena et al. found that itopride and levosulpiride were equally effective in ameliorating different symptoms of functional dyspepsia at the end of 4 weeks of treatment. There was a significant reduction in the mean Global Symptom Score and mean duration score and the mean score of severity in follow-up visits at weeks 2 and 4 from the day of presentation.[22]

The safety profiles of itopride and metoclopramide were evaluated, and the findings indicated that itopride was well tolerated by most patients. This is consistent with multiple studies that have reported good tolerability and a minimal occurrence of AEs in patients who received itopride.[23,24] The treatment or intervention implemented has resulted in notable positive outcomes, highlighting the successful management of upper gastrointestinal disorders in the evaluated patients.

Study limitations

The authors acknowledge that, whilst the study demonstrated positive outcomes for itopride SR, it is essential to highlight certain limitations. The study design did not include a control group, which could have further strengthened the findings and allowed for better comparisons. Additionally, being an observational study, the causality cannot be definitively established. The relatively short duration of the study, being only 4 weeks, may have limited the ability to capture long-term effects and trends, which could have provided valuable insights. Moreover, being set in a low-resource country, subjective diagnosis of diabetes gastroparesis was made due to study centres lacking gastric emptying study facilities (scintigraphy). Despite these limitations, the study's findings regarding the tolerability of itopride SR and the minimal AEs in both groups are still valuable and contribute to the existing body of knowledge.

Conclusion

In conclusion, itopride SR (Nogerd SR) in a 150 mg once-daily dose showed promising results in the reduction of severity of upper gastrointestinal disorder symptoms associated with diabetic gastroparesis. Both statistical and clinical effectiveness were observed. Moreover, the treatment demonstrated a favourable tolerability profile, with a low incidence of ADRs. These results highlight the potential benefits of Nogerd SR in managing and improving symptoms associated with upper gastrointestinal disorders. Further research and clinical trials may be warranted to validate these findings and explore the long-term effects of the intervention.

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References

1. Abrahamsson H. Treatment options for patients with severe gastroparesis. *Gut*. 2007;56:877–883. http://doi.org/10.1136/gut.2005.078121
2. Camilleri M, Parkman HP, Shafi MA, et al. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013;108:18–37; quiz 38. https://doi.org/10.1038%2Fajg.2012.373
3. Camilleri M, Bharucha AE, Farrugia G, et al. Epidemiology, mechanisms, and management of diabetic gastroparesis. *Clin Gastroenterol Hepatol*. 2011;9:5–12. https://doi.org/10.1016/j.cgh.2010.09.022
4. Hasler WL, Wilson LA, Parkman HP, et al. Factors related to abdominal pain in gastroparesis: contrast to patients with predominant nausea and vomiting. *Neurogastroenterol Motil*. 2013;25:427–e301. https://doi.org/10.1111/nmo.12091
5. Aljarallah BM. Management of diabetic gastroparesis. *Saudi J Gastroenterol*. 2011;17:97–104. https://doi.org/10.4103%2F1319-3767.77237
6. Jones KL, Russo A, Berry MK, et al. A longitudinal study of gastric emptying and upper gastrointestinal symptoms in patients with diabetes mellitus. *Am J Med*. 2002;113:449–455. https://doi.org/10.1016/s0002-9343(02)01228-7
7. Jung HK, Choung RS, Locke GR 3rd, et al. The incidence, prevalence, and outcomes of patients with gastroparesis in Olmsted County, Minnesota, from 1996 to 2006. *Gastroenterology*. 2009;136(4):1225–1233. https://doi.org/10.1053/j.gastro.2008.12.047
8. Soykan I, Sivri B, Sarosiek I, et al. Demography, clinical characteristics, psychological and abuse profiles, treatment, and long-term follow-up of patients with gastroparesis. *Dig Dis Sci*. 1998;43(11):2398–2404. https://doi.org/10.1023/a:1026665728213
9. Choung RS, Locke GR 3rd, Schleck CD, et al. Risk of gastroparesis in subjects with type 1 and 2 diabetes in the general population. *Am J Gastroenterol*. 2012;107(1):82–88. https://doi.org/10.1038/ajg.2011.310

10. Syed AR, Wolfe MM, Calles-Escandon, et al. Epidemiology and diagnosis of gastroparesis in the United States: a population-based study. *J Clin Gastroenterol*. 2020;54(1):50–54. https://doi.org/10.1097%2FMCG.0000000000001231
11. Ingrosso MR, Camilleri M, Tack J, Ianiro G, Black CJ, Ford AC. Efficacy and safety of drugs for gastroparesis: systematic review and network meta-analysis. *Gastroenterology*. 2023;164(4):642–654. https://doi.org/10.1053/j.gastro.2022.12.014
12. Kim YS, Kim TH, Choi CS, et al. Effect of itopride, a new prokinetic, in patients with mild GERD: a pilot study. *World J Gastroenterol*. 2005;11(27):4210–4214. https://doi.org/10.3748/wjg.v11.i27.4210
13. Dite P, Rydlo M, Dockal M, et al. A prokinetic agent with dual effect itopride in treatment of gastric motility. *Gastrolentrology*. 2014;3:42–47.
14. Stevens JE, Russo A, Maddox AF, et al. Effect of itopride on gastric emptying in longstanding diabetes mellitus. *Neurogastroenterol Motil*. 2008;20:456–463. https://doi.org/10.1111/j.1365-2982.2007.01058.x
15. Venkatesh V, Kulkarni KP. Itopride and pantoprazole outcomes in diabetic gastroparesis trial (IPOD trial). *J Indian Med Assoc*. 2008;106:814–815.
16. Huang X, Lv B, Zhang S, et al. Itopride therapy for functional dyspepsia: a meta-analysis. *World J Gastroenterol*. 2012;18(48):7371–7377. https://doi.org/10.3748/wjg.v18.i48.7371
17. Harasawa S. Effect of itopride hydrochloride on gastric emptying in chronic gastritis patients. *Jpn Pharmacol Ther*. 1993;21:4189–4195.
18. Kamath VK, Verghese J, Bhatia S, et al. Comparative evaluation of the efficacy and tolerability of Itopride and Metoclopramide in patients with NUD. *JAMA*. 2003;2(8):95–98.
19. Amarapurkar DN, Rane P. Randomised, double-blind, comparative study to evaluate the efficacy and safety of ganaton (itopride hydrochloride) and mosapride citrate in the management of functional dyspepsia. *J Indian Med Assoc*. 2004;102(12):735–737.
20. Shenoy KT, Veenasree LKB. Efficacy and tolerability of itopride hydrochloride in patients with non-ulcer dyspepsia. *J Indian Med Assoc*. 2003;101(6):387–388.
21. Rai RR, Choubal CC, Agarwal M, et al. A Prospective multicentric postmarketing observational study to characterize the patient population with reduced gastrointestinal motility among Indian diabetic patients receiving itopride: the progress study. *Int J Appl Basic Med Res*. 2019;9(3):148–153. https://doi.org/10.4103/ijabmr.IJABMR_351_18
22. Saxena GN, Mathur S. A randomized controlled study of efficacy and safety profile of levosulpiride and itopride in functional dyspepsia. *J Mahatma Gandhi Univ Med Sci Technol*. 2020;5(2):51. https://doi.org/10.5005/jp-journals-10057-0131
23. Huang X, Lv B, Zhang S, et al. Itopride therapy for functional dyspepsia: a meta-analysis. *World J Gastroenterol*. 2012;18(48):7371–7377. https://doi.org/10.3748/wjg.v18.i48.7371
24. Sawant P, Das HS, Desai N, et al. Comparative evaluation of the efficacy and tolerability of itopride hydrochloride and domperidone in patients with non-ulcer dyspepsia. *J Assoc Physicians India*. 2004;52:626–628.