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Original Research Article

Understanding functional dyspepsia and its subtypes and the role of prokinetics in its management: a cross-sectional clinician-based survey

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ABSTRACT

Background: This survey evaluated opinions of consulting physicians or gastroenterologists on functional dyspepsia (FD) in the Indian population and the management of FD with prokinetics, especially itopride.
Methods: A total of 243 clinicians involved in the clinical practice of FD were invited to complete an internet-based, structured survey questionnaire. Questionnaire comprised 29 questions on the diagnosis and treatment options for FD.
Results: Majority of the clinicians opined that females were more affected by FD than males in both hospital-based (53.4%) and community-based (56.6%) practices. As per 33.3% of clinicians each, the age group of 21-40 years and 41-60 years were the two most commonly affected groups. FD symptoms were present for >6 months before patients seek consultation as reported by 62.6% of the clinicians. The participating clinicians preferred using detailed patient history (77.7%) and ROME IV criteria (71.1%) for diagnosing FD. Prokinetics were regarded as the therapy of choice primarily because of their efficacy in reducing FD symptoms. Among all prokinetics used, itopride was most preferred for postprandial distress syndrome (64.2% clinicians) and for epigastric pain syndrome in combination with PPIs (66.7% clinicians). Itopride was reported by 93.6% clinicians to be well tolerated, with the leading advantage being absence of extrapyramidal or cardiac side effects according to 40% of clinicians.
Conclusions: The clinicians considered itopride to be most preferred to reduce FD symptoms and to be well-tolerated when taken alone or in combination with PPIs.

Keywords: Functional dyspepsia, Postprandial fullness, Itopride, Proton pump inhibitors, Prokinetics

INTRODUCTION

Functional dyspepsia (FD), also known as non-ulcer dyspepsia, can significantly impact quality of life, including multiple physiological and social factors.[1] The global prevalence of FD is projected to range from 4.5% to 11%.[2-5] Rapid socioeconomic development in Asia over the last 20 years has led to a transition in the health and environmental status of the general population. Cohort-based studies on FD in India are still sparse. As per the Rome III and IV criteria, FD falls under the category of functional gastrointestinal disorders.[6-8]

Many Asian studies report FD to be more common in younger adults; however, in India, FD was predominantly observed in the age group >40 years.[2,3,9] A meta-analysis reports that the majority of patients with FD are females, non-steroidal drug abusers, smokers and those diagnosed with *Helicobacter pylori* infection.[10] In terms of physiological significance, esophagitis and peptic ulcer are the two most common symptoms in dyspeptic patients.[11]

FD is mainly divided into two sub-types based on the type of cardinal symptoms, namely, postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS).

Patients with PDS experience early satiation or feeling of fullness, and those with EPS experience epigastric burning or pain.[12] Patients with PDS experience fluctuations in symptom severity depending on alterations in food consumption, whereas EPS symptoms are independent of food intake.[13]

Dyspepsia is diagnosed in the presence of symptoms expected to originate from the gastro-duodenal circumference; if no organic cause is identified after investigations, the patient is classified as having FD.[14] Usually, initiation of diagnosis begins with the exclusion of organic causes using laboratory tests like metabolic panel, blood count, inflammatory markers, and thyroid function.[15] Further diagnostic evaluation is performed by instrumental examinations like esophagogastroduodenoscopy alongside biopsy and abdominal ultrasonography.[16] For holistic diagnosis, medical history of long-standing postprandial fullness and early satiety is considered to be sufficient; however, esophagogastroduodenoscopy could be often required.[16] Electrogastrography (EGG) is an efficient tool used for diagnosis in patients with FD as it is a minimally invasive diagnostic method for measuring gastric myoelectrical movement.[17] It predominantly measures gastric slow waves, giving a detailed pathophysiological clinical analysis of FD and can guide optimal treatment regimes.

The treatment and management of FD can be challenging in that the main goal is symptom control; the initial approach could be a diagnosis breakdown and discussion about the various treatment options.[18] If FD is suspected, the first treatment is *H. pylori* eradication, which reduces the risk of gastric cancer and peptic ulcers.[19,20] Prokinetics are predominantly used for treating patients with PDS or ulcer-like dyspepsia, while proton pump inhibitors (PPIs) are used for treating EPS. [21] Itopride, a prokinetic, is a vertamide hydrochloride derivative and acts as a D2 receptor antagonist and acetylcholinesterase inhibitor.[22] Itopride has shown efficacy in terms of early satiety and postprandial fullness and good tolerability based on patient assessment.[23]

The aim of this questionnaire-based survey was to garner clinicians' opinions on FD and its subtypes in the Indian population and the role of itopride in the management of FD in terms of treatment outcomes.

METHODS

Survey questionnaire

This was a cross-sectional, questionnaire-based survey conducted from July to September 2022 to understand the clinical perspectives, diagnosis, and treatment options for FD and its subtypes in the Indian clinical setting. A focus-group discussion was held among the 3 authors to identify the need gap based on diagnosis and management practices for FD and its subtypes across India, choice of various prokinetics currently available in India, and safety information on and choice of itopride vis-à-vis other prokinetics like levosulpiride and domperidone. Based on the discussion, the survey questions were framed keeping in mind the need to garner Indian clinician perspective on the diagnosis and management of FD and its subtypes. A total of 243 consulting physicians or gastroenterologists involved in the clinical practice of FD participated in the survey. Participants were invited to complete the web-based, survey questionnaire, which comprised 29 questions on the clinical perspectives, diagnosis, treatment options, and role of prokinetics and itopride in the management of FD (Table 1). This survey was performed in accordance with the protocol of the international conference on harmonization-good clinical practice (ICH-GCP) guidelines. Informed consent was obtained from the participating clinicians. Because this survey did not entail any direct patient intervention, ethical clearance by an external ethics review board was not obtained. The confidentiality and identity of the participating clinicians were preserved throughout the survey and data processing.

Table 1: Survey questionnaire.

S. no.	Questionnaire			
Section 1	**To understand clinical perspectives on functional dyspepsia and its subtypes in Indian population**			
Q1	How many patients with functional dyspepsia have symptoms for more than 6 months?			
	a) <30%	b) 30%-49%	c) 50%-69%	d) >70%
Q2	How many patients have uncomfortable fullness after regular-sized meals or are unable to finish regular-sized meals for 6 months or longer?			
	a) <30%	b) 30%-49%	c) 50%-69%	d) >70%
Q3	How many patients have epigastric pain or burning after meals for 6 months or longer?			
	a) <30%	b) 30%-49%	c) 50%-69%	d) >70%
Q4	What is proportional percentage split of patients with functional dyspepsia across age groups? (n=100%)			
	a) <20 years _____%	b) 21-40 years _____%	c) 41-60 years _____%	d) >60 years _____%
Q5	What is the gender-wise percentage breakup of patients with functional dyspepsia based on where you practice? (Please select based on your area of practice)			
	Gender	Hospital based practice	Community based practice	
	Male	_____%	_____%	
	Female	_____%	_____%	

Continued.

S no.	Questionnaire			
Section 1	**To understand clinical perspectives on functional dyspepsia and its subtypes in Indian population**			
Q6	How long do patients typically suffer from symptoms of FD before they consult you?			
	a) > 6 months	b) >1 year	c) >2 years	d) > 5 years
Q7	How commonly do you see patients with FD having bothersome postprandial fullness or early satiation at least 3 days per week?			
	a) Less than 30%	b) 30%-49%	c) 50%-69%	d) More than 70%
Q8	How commonly do you see patients with FD having bothersome epigastric pain or burning at least 1 day a week?			
	a) Less than 30%	b) 30%-49%	c) 50%-69%	d) More than 70%
Q9	Do your patients try dietary changes to relieve their symptoms before coming to you?			
	a) Yes		b) No	
Section 2	**To understand the diagnosis of FD and its subtypes in the Indian population**			
Q10	How do you diagnose FD (tick all the options that apply)			
	a) Detailed history	b) ROME IV criteria	c) PPI trial	d) Endoscopic evaluation
Q11	If your answer is Yes to the above question, please answer which of the following guidelines you use for managing FD in your patients			
	a) American college of gastroenterology	b) Canadian association of gastroenterology	c) Asian guidelines	d) Any other _____
Section 3	**To understand the role of prokinetics in the management of FD and its subtypes**			
Q12	In patients suffering from FD, what is your treatment of choice?			
	a) PPIs	b) Prokinetics	c) Combinations	d) Others_____
Q13	Which of the following parameters make prokinetics the therapy of choice in FD? Rank the criteria in order of importance with 1=most important to 4=least important			
	a) CNS and cardiac safety	b) Symptom resolution and efficacy	c) Cost of therapy	d) Studies and evidence
Q14	To what % of patients with FD do you prescribe the following (enter % wherever applicable):			
	a) Itopride_____%	b) Acotiamide_____%	c) Domperidone____%	d) Levosulpiride___%
	e) Cinitapride_____%	f) Mosapride_____%	g) PPI_____%	h) PPI+prokinetic__%
Q15	In your clinical practice, on average what is the duration of therapy for an FD patient prescribed the following (You may select more than one alternative):			
	Drug	<2 weeks 2-4 weeks	4-8 weeks	>8 weeks
	Itopride			
	Levosulpiride			
	Domperidone			
	Acotiamide			
	Cinitapride			
	Mosapride			
	PPI			
	PPI + prokinetic			
Q 16 and 17	How would you rate the Q16) efficacy and Q17) tolerability of the following to reduce FD symptoms?			
	Drug	Good	Average	Poor
	Itopride			
	Levosulpiride			
	Domperidone			
	Acotiamide			
	Cinitapride			
	Mosapride			
	PPI			
	PPI + prokinetic			
Q18	Which is the prokinetic of choice in the postprandial distress syndrome (PDS) subtype of FD? (Select one)			
	a) Itopride	b) Levosulpiride	c) Domperidone	d) Acotiamide
	e) Cinitapride	f) Mosapride	g) Any other	
Q19	What is the reason for your selection of the prokinetic in your practice vs other options for treating PDS? (Please specify the reason for answering the selection basis question)			
	a) Efficacy	b) CNS safety	c) CVS safety	d) Guideline recommendation

Continued.

S. no.	Questionnaire			
Section 3	**To understand the role of prokinetics in the management of FD and its subtypes**			
Q20	Along with PPIs, which is the prokinetic of choice in EPS with overlap? (Select one)			
	a) Itopride	b) Levosulpiride	c) Domperidone	d) Acotiamide
	e) Cinitapride	f) Mosapride	g) Any other	
Q21	Which are the factors that decide a choice of drugs for safety and efficacy in early satiety and postprandial fullness/bloating? (Rank in order of preference from 1= most common to 5= least common)			
	a) Clinical efficacy data	b) Duration of action	c) Clinical safety profile	
	d) Cost of therapy	e) Drug interactions		
Q22	How frequently do you have to stop a prokinetic because of its side effects/adverse effects profile?			
	a) Less than 10%	b) 10%-40%	c) 40%-70%	d) More than 70%
Q23	After how many days of prokinetics therapy, do patients get a positive response?			
	Drug		Days	
	Itopride			
	Levosulpiride			
	Domperidone			
	Acotiamide			
	Cinitapride			
	Mosapride			
Section 4	**To understand the role of itopride in the management of FD and its subtypes.**			
Q24	In which subtype of FD, do you find Itopride useful (tick all that apply)?			
	a) EPS	b) PDS	c) EPS–PDS overlap	d) All the subtypes
Q25	What according to you are the advantages of itopride? (Tick all that apply)			
	a) High efficacy	b) No EPS/CVS effects	c) ROME IV recommended	
	d) Useful in all subtypes of FD	e) All the above		
Q26	How commonly do you use itopride in patients to reduce bothersome postprandial fullness/bloating?			
	a) 10%-20%	b) 20%-40%	c) 40%-60%	d) More than 60%
Q27	How many percentages of patients effectively respond to itopride when treated for postprandial fullness/bloating?			
	a) 10%-20%	b) 20%-40%	c) 40%-60%	d) More than 60%
Q28	In your clinical practice, how will you rank the efficacy of safety and efficacy of itopride for managing PDS and EPS overlap? (Rank in order of preference from 1=most satisfied, 5=least satisfied)			
		EPS	PDS	
	Safety			
	Efficacy			
Q29	In your clinical practice, on a scale of 1 to 10, how is your experience in terms of patient convenience and acceptability of itopride for managing patients with EPS and PDS?			
	1 2 3 4 5 6 7 8 9 10			

CNS=central nervous system; CVS=cardiovascular system; EPS=epigastric pain syndrome; FD=functional dyspepsia; PPI=proton pump inhibitor; PDS=postprandial distress syndrome

Data analysis

No formal sample size calculation was performed; however, a respondent: question ratio of grater than seven was achieved.[24] The procedure for data quality check was performed along with the query resolution.

The data were analyzed as well as summarized using the counts or the percentages, as appropriate. The rank data were analyzed by the weighted linear combination method, in which for each question, the most preferred choice as an answer can be determined. Data were analyzed using the (Statistical package for the social sciences (SPSS) software the version was 25.0 (IBM Corp., Armonk, NY, USA) and the Microsoft excel (Microsoft corporation 2019).

RESULTS

Clinicians' perspectives on FD and its subtypes in the Indian population

Table 2 summarizes the participating clinicians' opinions on the FD and its subtypes in Indian clinical practice. The findings revealed that gender distribution of FD patients was similar regardless of the type of practice setting. Female predominance was observed in both hospital-based practice (53.4%) and the community-based practice (56.6%). When asked about FD preponderance by age group, 11.9%, 33.3%, 33.3%, and the 21.6% of the clinicians reported that patients with FD belonged to the age groups of <20, 21-40, 41-60, and the >60 years, respectively.

Majority of the clinicians reported that FD as a symptom was present for >6 months in 30%-69% of their patients (69.5%), 30%-69% of their patients experienced uncomfortable fullness or inability to finish a regular-size meal for ≥6 months (69.9%), 30%-69% of their patients experienced epigastric pain or burning after meals for ≥6 months (72.4%; Table 2).

Table 2: Clinicians' opinions on FD in Indian clinical practice.

Parameters	Overall clinicians, n (%)
Proportion of patients with FD as a symptom for >6 months (%)	
<30	23 (9.5)
30-49	85 (35.0)
50-69	84 (34.6)
>70	51 (21.0)
Proportion of patients with uncomfortable fullness after/unable to finish regular-sized meals for ≥6 months (%)	
<30	55 (22.6)
30-49	111 (45.7)
50-69	59 (24.3)
>70	18 (7.4)
Proportion of patients with epigastric pain/burning after meals for ≥6 months (%)	
<30	56 (23.0)
30-49	120 (49.4)
50-69	56 (23.0)
>70	11 (4.5)
Duration for which patients suffer from FD before medical consultation (In years)	
>6 months	152 (62.6)
>1	71 (29.2)
>2	15 (6.2)
>5	5 (2.1)
Proportion of patients with bothersome post-prandial fullness/early satiation for ≥3 days/week (%)	
<30	36 (14.8)
30-49	125 (51.4)
50-69	60 (24.7)
>70	22 (9.1)
Proportion of patients with bothersome epigastric pain/burning for ≥1 day/week (%)	
<30	48 (19.8)
30-49	113 (46.5)
50-69	68 (28.0)
>70	14 (5.8)

FD=functional dyspepsia; PPIs=proton pump inhibitors

Duration for which patients suffer from FD before seeking medical consultation was >6 months according to 62.6% of clinicians; in contrast, only 2.1% clinicians reported that this duration was >5 years. According to majority of the clinicians, 30%-69% of patients experienced bothersome postprandial fullness or bothersome early satiation for ≥3 days/week (76.1%) and bothersome epigastric pain or bothersome epigastric burning for ≥1 day/week (75.5%). According to 90.5% clinicians, patients with FD attempt dietary changes to alleviate their symptoms before seeking medical consultation.

Clinicians' perspectives on diagnosis of FD in the Indian population

Detailed patient history was the most common technique used by participating clinicians for diagnosing FD (77.7%), followed by ROME IV criteria (71.1%), endoscopic evaluation (40.5%), and PPI trial (36%). Among all survey participants, 190 (78.2%) clinicians followed the American college of gastroenterology guidelines for the management of FD symptoms, 34 (14%) followed Asian guidelines, and 2 (0.8%) followed Canadian association of gastroenterology guidelines. Only 15 (6.2%) clinicians reported following other guidelines (Table 3).

Table 3: Clinicians' perspectives on diagnosis of FD.

Variables	N (%)
Diagnosis of FD, n=242	
Detailed history	188 (77.7)
ROME IV criteria	172 (71.1)
PPI trial	87 (36.0)
Endoscopic evaluation	98 (40.5)
National/international guidelines followed for managing FD, n=243	
American college of gastroenterology	190 (78.2)
Canadian association of gastroenterology	2 (0.8)
Asian guidelines	34 (14.0)
Any other	15 (6.2)

FD=functional dyspepsia; PPI=proton pump inhibitor

Clinicians' perspectives on the role of prokinetics in the management of FD and its subtypes

In terms of drug class of choice, 58 (23.9%) clinicians stated that they preferred prokinetics, 43 (17.7%) preferred PPIs, 138 (56.8%) preferred combination therapies, and only 1 (4.0%) clinician preferred other options.

In terms of choice of drug, clinicians prescribed a PPI to an average of 59.2% of their patients, PPI + prokinetic to an average of 55.5% of patients and itopride to an average of 38.5% of patients. Among all the prokinetics, itopride was the preferred prokinetic for PDS according to 64.2% of clinicians and itopride in combination with PPIs preferred treatment for EPS according to 66.7% of clinicians. Mean (SD) response duration of PPI + prokinetic was 4.88 (2.29) days (Table 4).

Among the prokinetics, acotiamide was the preferred prokinetic for PDS according to 18.5% clinicians, with a mean (SD) response duration of 5.57 (2.50) days. Along with a PPI, domperidone was the preferred prokinetic for EPS according to 13.2% clinicians, with a mean (SD) response duration of 5.04 (2.34) days.

Table 4: Clinicians' practices for the management of FD and its subtypes.

Drug	Proportion of patients prescribed therapy (%)	Prokinetic of choice in PDS (%)	PPI + prokinetic of choice in EPS with overlap (%)	Time to response after therapy, mean (SD)
Itopride	38.5	64.2	66.7	4.88 (2.29)
Acotiamide	20.6	18.5	5.8	5.57(2.50)
Domperidone	26.6	4.1	13.2	5.04 (2.34)
Levosulpiride	16.8	6.2	8.2	4.48 (2.31)
Cinitapride	16.0	5.3	4.5	5.01 (2.34)
Mosapride	5.3	0.4	-	5.27 (2.49)
PPI	59.2	-	0.4	
PPI+prokinetic	55.5	-	-	

FD=functional dyspepsia; PDS=postprandial distress syndrome; PPI=proton pump inhibitor; SD=standard deviation.

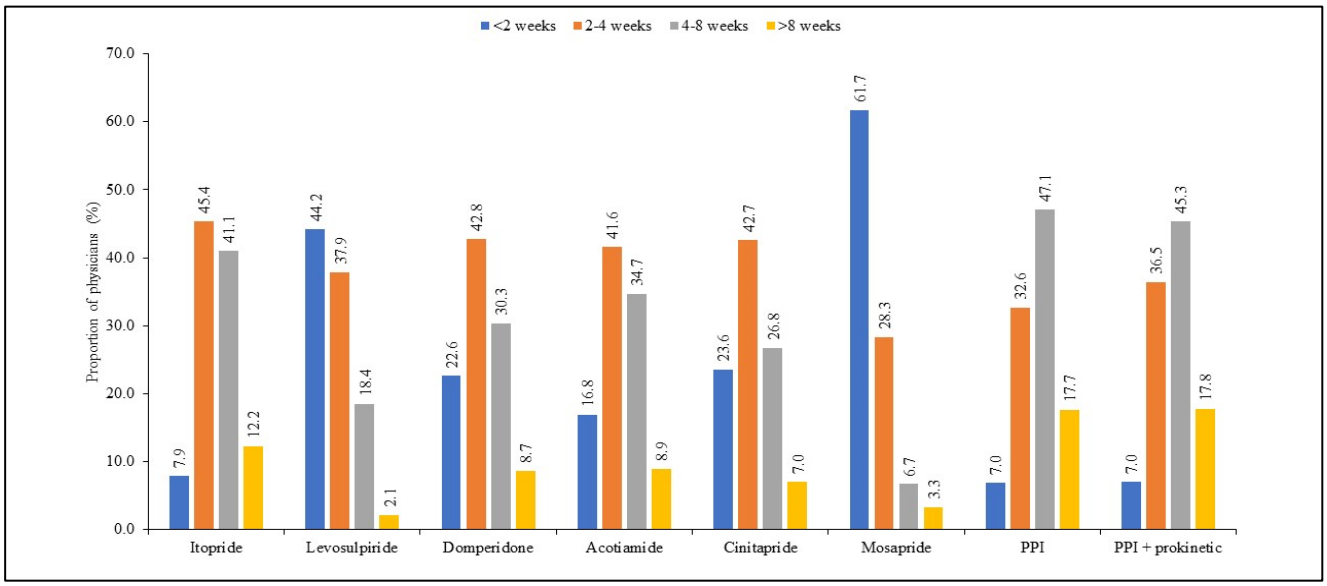

Figure 1: Average duration of therapy of various therapies for FD as reported by participating clinicians.

The most important factor for selecting a prokinetic as a treatment for PDS over other options was efficacy according 56.9% of respondents, followed by concerns related to central nervous system (CNS) safety (25.9%), guideline recommendations (14.2%) of cases, and cardiovascular safety (2.9%).

Figure 1 illustrates the clinician-reported average duration of treatment with various therapeutic modalities for patients with FD. The results show that among clinicians surveyed, 45.4% prescribed itopride for a duration of 2-4 weeks, 41.1% prescribed it for 4-8 weeks, 12.2% clinicians prescribed it for >8 weeks, and 7.9% prescribed it for <2 weeks.

Figure 2 depicts clinicians' perspectives on the efficacy and safety of different therapies. Based on the survey results, itopride was reported to have good efficacy by 86.6% of clinicians, followed by PPI + prokinetics (86.0%). Itopride was reported to have good tolerability as per 93.6% of clinicians. Mosapride was found to have poor efficacy according to 25.3% clinicians and poor tolerability according to 29.6% clinicians.

According to the survey findings, 69.5%, 21.4%, 5.8%, and 2.1% of the clinicians reported that they had to discontinue a prokinetic medication because of its side effects/adverse events profile in <10%, 10%-40%, 40%-70%, and >70% of patients, respectively.

According to the participating clinicians, symptom resolution and efficacy was the most important parameter for prokinetics as the therapy of choice, followed by CNS and cardiac safety, studies and evidence, and cost of therapy.

Clinicians' perspectives on the role of itopride in the management of FD and its subtypes

Clinical efficacy ranked first as the most important factor that influenced the choice of drugs for safety and efficacy in early satiety and postprandial fullness/bloating in FD patients. Clinical safety profile was the second most important factor, followed by the duration of action in third place, the cost of therapy in fourth place, and drug interaction being the least important factor.

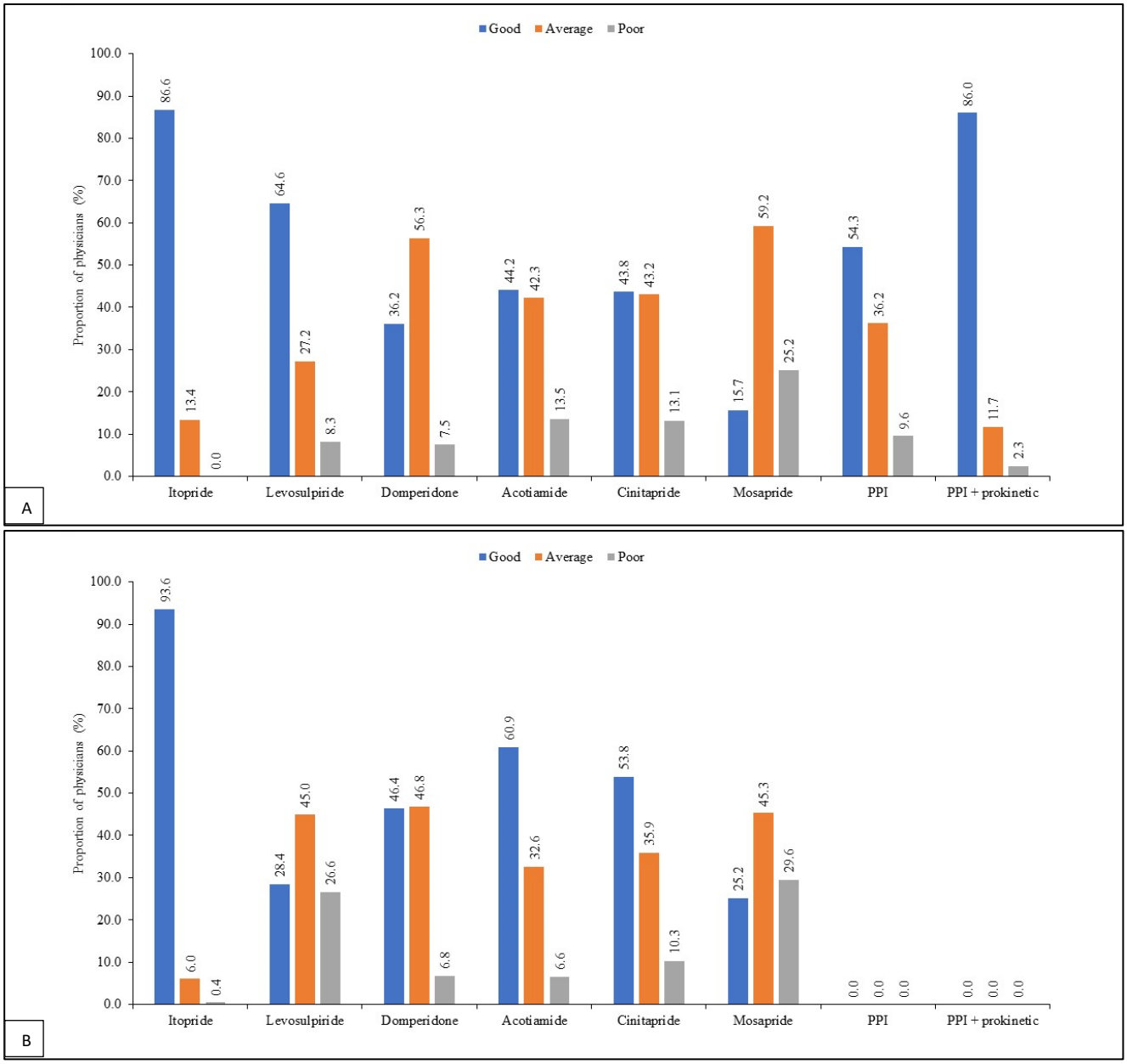

Figure 2 (A and B): Clinicians' rating of efficacy and tolerability of various therapies for patients with FD.

Table 5: Itopride in bothersome post-prandial fullness/bloating.

Proportion of clinicians (%)	Overall clinicians, n=243 (%)
Proportion of patients prescribed itopride for bothersome postprandial fullness/bloating	
0	2 (0.8)
10-20	25 (10.3)
20-40	73 (30.0)
40-60	83 (34.2)
>60	58 (23.9)
Missing	2 (0.8)
Proportion of patients showing effectiveness in reducing postprandial fullness/bloating with itopride treatment	
10-20	10 (4.1)
20-40	48 (19.8)
40-60	102 (42.0)
>60	81 (33.3)
Missing	2 (0.8)

Among the clinicians surveyed, 83 (34.2%) used itopride to alleviate bothersome postprandial fullness/bloating in 40%-60% of their patients, 73 (30.0%) used it in 20%-40% of patients, and 58 (23.9%) used it in >60% of patients. Itopride was thought to effectively reduce postprandial fullness/bloating in 40%-60% of patients according to 102 (42.0%) clinicians, in >60% of patients according to 81 (33.3%) clinicians, and in 20%-40% of patients according to 48 (19.8%) clinicians (Table 5).

The leading advantage of itopride as reported by the participating clinicians was absence of extrapyramidal or cardiovascular effects (40.0%), followed by high efficacy (36.2%), usefulness in all subtypes of FD (20.8%), and ROME IV recommended drug (18.7%; Table 6). According to the survey findings, 52.7% of clinicians found itopride treatment to be beneficial in all subtypes of FD, 38.2% found it to be useful in PDS, 27.4% in EPS-PDS overlap, and 15.8% in EPS.

Clinicians were asked to rank the efficacy and safety of itopride in EPS and PDS on a scale of 1-5, with a score of one being the most satisfied and 5 being the least satisfied.

Itopride was marked 1 or 'most satisfactory' in terms of safety and efficacy for EPS and PDS both. Among the participant clinicians, itopride was ranked highest for efficacy in EPS by 100 clinicians, for safety in EPS by 161 clinicians, for efficacy in PDS by 126 clinicians, and for safety in PDS by 154 clinicians. When asked to rate patient convenience and acceptability of itopride for managing EPS and PDS on a scale of 1-10 (10 being the highest), 66.7% of clinicians rated itopride in the range 7-10, 8.3% rated it in the range 4-6, and 25.0% rated it in range 1-3.

Table 6: Clinicians' perspectives on the response with and advantages of itopride.

Proportion of clinicians (%)	Overall clinicians, n=241
Subtypes of FD where itopride is useful	
EPS	15.8
PDS	38.2
EPS-PDS overlap	27.4
All subtypes	52.7
Advantages of itopride, n=240	
High efficacy	36.2
Absence of extrapyramidal or cardiac side effects	40.0
ROME IV recommended	18.7
Useful in all subtypes of FD	20.8

DISCUSSION

Alterations in gastrointestinal sensory function and motility are believed to exacerbate symptoms of FD.[21,22] The main goal of this survey was to understand Indian clinicians' perspectives on the role of prokinetics and especially itopride in FD via a structured questionnaire. Consistent with a previous retrospective review by Cheddie et al clinicians in this survey reported that FD is more prevalent in women than in men.[23]

In this survey, majority of the clinicians stated that patients with FD belonged to the age group of 21-60 years. In a study by Alwahaibi et al 56.8% of patients with dyspepsia were between the age of 34 and 64 years.[25] Factors like age, sex and education levels play a key role in manifestation of FD symptoms.[26] However, it was suggested that researchers should focus on female patients above the age of 60 years because they are more susceptible to FD symptoms than men.[27]

Participating clinicians largely agreed that their patients experience FD symptoms for >6 months before seeking medical consultation and that they experience bothersome postprandial fullness or early satiation falling under the PDS type of FD for ≥3 days/ week and bothersome epigastric pain or burning falling under the EPS type of FD for ≥1 day/week. This was in agreement with a Delphi consensus study by Lucas et al that reported predominance of cardinal symptoms such as postprandial fullness, early satiation, epigastric pain and epigastric burning in patients with FD.[27] Per ROME IV criteria, FD encompasses these four symptoms and are commonly employed in clinical trials of definitive diagnosis of FD.[8,28,29] Therefore, majority of the clinicians in this survey agreed to the use of ROME IV criteria for diagnosis of FD.

In this survey, treatment regimens used by the clinicians' treating patients with FD were also explored. The most common medications prescribed to FD patients were PPIs, followed by PPI + prokinetic, and itopride. PPI inhibits and irreversibly binds the hydrogen-potassium ATPase pump to effectively block gastric secretion.[30] The prescription patterns identified in this survey are aligned with those of an open-label trial by Takeshi et al where positive efficacy of PPI with prokinetics was found.[31] Furthermore, a review by Maria et al that examined results of 25 randomized controlled trials in which PPI was given in combination with a prokinetic to improve the overall symptoms of FD, it was found that a PPI was more effective in the treatment of FD patients with EPS and a prokinetic was more effective in the treatment of FD patients with PDS.[32] However, a combination of a PPI and prokinetic can help reduce both EPS and PDS symptoms in patients with FD.[33] It is noteworthy to understand that the majority of the clinicians in this survey reported itopride to be the optimum prokinetic for treatment of patients with FD considering that the proportion of patients who were prescribed itopride was higher than those prescribed acotiamide and domperidone. These practices are consistent with findings from a study by Takeshi et al wherein 97.3% of patients with PDS were found to benefit from itopride.[31]

Overall, itopride monotherapy was found to be the preferred prokinetic for FD with PDS, and it was the preferred prokinetic for EPS when used in combination

with a PPI. Itopride is a dopamine D2 receptor antagonist and an acetylcholinesterase inhibitor that is used for treating FD symptoms like vomiting and nausea.[34,35] Itopride is highly polar in nature, which prevents it from crossing the blood-brain barrier and elevate levels of prolactin; thus, it is not expected to have any CNS-related adverse drug reactions (ADRs).[35] This helps prevent side effects like hyperprolactinemia and other extrapyramidal symptoms like akinesia and Parkinsonism in patients with FD.[21,36] In a prospective study conducted at a tertiary care center, duration of treatment with levosulpiride, a prokinetic used for gastric motility disorders, was found to have a significant positive correlation (r=0.8295, p=0.0154) with the occurrence of extrapyramidal side effects commonly manifested as tremor, stiffness, dystonia, pain in the neck or back, dysarthria, and abnormal sensations.[37] In this survey, clinicians believed that itopride shows higher efficacy in the reduction of FD symptoms, which was in agreement with a meta-analysis by Huang et al reporting patient assessment scores for EPS, PDS and EPS-PDS overlap patients.[30] Itopride was shown to have better therapeutic outcomes in patients with early satiation and postprandial fullness. Domperidone was prescribed to 26.6% of patients, which aligns with the results of a single-blinded study conducted by Chen et al, where 17.7% of FD patients were prescribed domperidone.[32]

Safety is a key factor when selecting a prokinetic.[28] Itopride has less risk of extrapyramidal side effects and ADRs in comparison with mosapride and domperidone.[35] In India, domperidone and levosulpiride are usually prescribed in combination with a PPI for the treatment of FD.[36] However, this survey highlights a notable preference among clinicians for itopride over other prokinetics when managing symptoms of EPS and PDS in patients with FD. Nevertheless, treatment with prokinetics has shown better efficacy in reducing FD symptoms.[30]

This survey had two main limitations. First, as no direct patient intervention was possible in the survey, the effect of treatment adherence on side effects of prokinetics could not be assessed. This can create bias in understanding the overall scope of prokinetic treatment in FD patients. Another limitation of the study was the absence of reported data on specific prokinetic used for treating PDS and EPS overlap. This can cause information bias leading to dis-aligned results for the PDS and EPS overlap endpoints.

CONCLUSION

In this cross-sectional pan-India survey, FD was reported by clinicians to be a significantly prevalent gastrointestinal disorder with more female patients being affected. Treatment of FD using itopride was reported by clinicians to have optimum efficacy and safety, as it is not expected to have extrapyramidal or cardiac side effects. Nevertheless, clinicians were largely of the opinion that itopride treatment in combination with PPI is efficacious in treating EPS and PDS in patients with FD. However, prospective studies involving itopride are needed to validate these findings.

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