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Original Research Article

Efficacy and safety of prucalopride in the treatment of chronic constipation

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ABSTRACT

Background: Chronic constipation is a common condition that significantly impacts health care utilization, productivity, and quality of life. Laxatives are commonly used, although often insufficient in restoring normal bowel function or providing adequate relief. There remains a significant need for the development of novel agents to optimize treatment of this condition. Prucalopride, a selective, high-affinity 5-hydroxytryptamine 4 receptor agonist, stimulates gastrointestinal and colonic motility and alleviates common symptoms of chronic constipation. Here authors are evaluating efficacy and safety study of this drug in chronic constipation patient.
Methods: This is a prospective observational study where chronic constipation patient treated with prucalopride 2 mg daily once were enrolled during 6 month period. Data at one week and four weeks were observed along with adverse effects. Efficacy assessed by the number of Spontaneous Complete Bowel Movements (SCBMs) per week recorded by patient diaries. Patients were defined as responders when they had a mean of three or more SCBMs per week over the whole treatment period. The primary efficacy end point was proportion of responders after 1 week and after 4 weeks of treatment.
Results: A total of 43 patients diagnosed with chronic constipation and treated with prucalopride were included in study. The proportions of patients in the present study with at least three SCBMs per week (responders) were 44.2% (19 out of 43 patients) at 1 week and 46.5% (20 out of 43 patients) at 4 weeks. Treatment was well tolerated with minimal side effects. Common adverse effects reported in our study were gastrointestinal disorders like diarrhea, nausea and abdominal pain and nervous system disorders like headache and dizziness.
Conclusions: Prucalopride is effective, has a good safety profile, and is well tolerated in chronic constipation treatment.

Keywords: Chronic constipation, Prucalopride, Responders

INTRODUCTION

Constipation is a common, often chronic, gastrointestinal motility disorder characterized by a diversity of symptoms including bloating, straining, abdominal pain, lumpy or hard stools, sensation of incomplete evacuation, and infrequent defecation (fewer than three bowel movements per week).[1-3] The estimated global prevalence of chronic constipation is 14% and it is more common in women and the elderly.[4,5] Prevalence of constipation by the Rome II criteria is 16.8% in India.[6]

Initial management of chronic constipation includes lifestyle modifications such as increased fluid intake, exercise and changes in diet. If these measures fail to normalise bowel habit, pharmacological therapy is needed. Initial started with fibre supplementation or bulking agents followed by the use of osmotic laxatives, which may

include polyethylene glycol (PEG)-based laxatives, magnesium salts, and poorly absorbed carbohydrates (eg, sorbitol and lactulose). For those with a suboptimal response to these drugs, stimulant laxatives, including bisacodyl or senna, may be effective as a supplementary agent. The majority of these agents are available over-the-counter without a prescription and are relatively inexpensive.[7,8]

A large proportion of patients are not satisfied with traditional treatment options for constipation (e.g., prescription and over-the-counter laxatives, and fibre), mainly owing to lack of efficacy.[9]

Prokinetic agents targeting 5-hydroxytryptamine receptor-4 (5-HT4) and motilin receptors have also been considered as a therapeutic approach for constipation, although most are not easily available or costly.[10]

Prucalopride is a selective, high-affinity, 5-hydroxytryptamine receptor-4 agonist with gastrointestinal prokinetic properties. The high affinity and selectivity for 5-hydroxytryptamine receptor-4 differentiates prucalopride from older generation compounds, such as cisapride and tegaserod, and minimizes the potential for target-unrelated side effects.[11,12] Phase 3 clinical trials have shown prucalopride to be effective in improving stool frequency and it is also effective in reducing abdominal and stool-related symptoms associated with constipation.[13-15]

Studies have been done using various drugs in treatment of chronic constipation in India. But there are very few studied on efficacy and safety of prucalopride in the treatment of chronic constipation in India. Hence authors have undertaken this study to know the efficacy and safety of prucalopride in the treatment of chronic constipation in India.

METHODS

This is a prospective observational study conducted at Basavershwara Teaching and General Hospital attached to M.R. Medical College, Kalaburagi. Ethical clearance was obtained from Ethics committee, M.R. Medical College, Kalaburagi. Study was conducted according to Good Clinical Practice.

Inclusion criteria

Patients of both sexes with age more than 18 years suffered from chronic constipation attending Medicine department at Basavershwara Teaching and General Hospital between 1stJuly 2017 to 31stDecember 2017 and treated with prucalopride for four weeks were included in the study. Written consent was taken before enrollment.

The diagnosis of chronic constipation was based on presence for at least three months of less than three stools per week and/or straining at stool.

Exclusion criteria

- Patients taking concomitant medications which could modify bowel habit
- Patients suffering from severe liver, renal, or cardiac diseases were excluded
- Pregnant and breast-feeding women.

Data collection

Patients of both sexes with age more than 18 years suffered from chronic constipation on prucalopride 2 mg once daily during study period were included in the study. Most of the patients were out patients. Patients were asked to keep daily diaries for the duration of the study to record bowel movement frequency. All patients were reviewed after 1 week and 4 weeks of starting treatment. No other treatments for constipation were allowed during the study.

Efficacy assessed by the number of Spontaneous Complete Bowel Movements per week (SCBMs). Patients were defined as responders when they had a mean of three or more SCBMs per week over the whole treatment period. The primary efficacy end point was proportion of responders after 1 week and after 4 weeks of treatment.

Safety assessed by evaluating treatment related adverse effects during study period.

Statistical analysis

Data on demographics, baseline characteristics, and adverse effects were presented descriptively. Proportion of responders after 1 week and after 4 weeks of treatment was calculated. Microsoft Excel sheet was used for statistical analysis.

RESULTS

A total of 43 patients suffered from chronic constipation and treated with prucalopride 2 mg once daily for four weeks were enrolled in the study during 6 month period (1stJuly 2017 to 31stDecember 2017). A total of 43 patients diagnosed with chronic constipation and treated with prucalopride were included in study.

The demographic characteristics of patients are presented in Table 1. In the present study, mean age of patients included in study was 57 years.

Table 1: Demographic characteristics of study population.

Characteristics		N=43 [n (%)]
Age (years)	≤65	27 (62.8)
	>65	16 (37.2)
Sex	Male	08 (18.6)
	Female	35 (81.4)

Table 2: Efficacy parameters.

	At least three SCBMs per week (Responders)
1 week	44.2% (19/43)
4 weeks	46.5% (20/43)

The proportions of patients in the present study with at least three SCBMs per week (responders) were 44.2% (19 out of 43 patients) at 1 week and 46.5% (20 out of 43 patients) at 4 weeks.

Table 3: Adverse effects.

	N=43 [n (%)]
Diarrhea	3 (6.9%)
Nausea	4 (9.3%)
Abdominal pain	2 (4.7%)
Headache	4 (9.3%)
Dizziness	1 (2.3%)

Common adverse effects reported in our study were gastrointestinal disorders like nausea (9.3%), diarrhea (6.9%), and abdominal pain (4.7%) and nervous system disorders like headache (9.3%) and dizziness (2.3%).

DISCUSSION

In this study, authors analyzed the efficacy and safety of prucalopride 2mg once daily in treatment of chronic constipation.

Mean age of patients were mean age of patients included in study was 57 years. About 27 (62.8%) patients were aged ≤65 and rest 16 (37.2%) were above 65 years. Study conducted by Yiannakou Y et al, had same age distribution as our study.[16]

Most of the patients were females (81.4%). Sex wise distribution of patient was similar to previous studies.[4,16]

The proportions of patients in the present study with at least three SCBMs per week (responders) were 44.2% (19 out of 43 patients) at 1 week and 46.5% (20 out of 43 patients) at 4 weeks.

A study conducted by Müller-Lissner S et al, involving 300 patients had shown similar results (Responders at week 1: 43.8% and week 4: 37.5%).[17]

Another study conducted by Emmanuel A et al, had shown responder rate of 42% at 4 weeks which is similar to our study.[18]

Prucalopride had a good safety profile and was well tolerated in this study. Common adverse effects reported in our study were gastrointestinal disorders like diarrhea, nausea and abdominal pain and nervous system disorders like headache and dizziness. No SAEs occurred. This is also consistent with previous studies.[19,20]

The reported adverse events following the use of prucalopride included abdominal cramps, abdominal pain, nausea, vomiting, dizziness, diarrhea, rash, headache, constipation, skin disorders, and flatulence.[19,20]

A potential limitation of this study is that small sample size and that the trial was restricted to 4 weeks.

However, this is the one of few studies on prucalopride use in chronic constipation in India.

One of main limitation of use of prucalopride in chronic constipation treatment is its high cost compared to other drugs. It cost about approximately 23 rupees per tablet.

CONCLUSION

On the basis of these findings, it can be concluded that prucalopride 2 mg once daily, taken for 4 weeks, is effective in the treatment of chronic constipation. Main limitation for usage prucalopride in treatment of chronic constipation is its high cost. However, there is need for further studies to evaluated efficacy and safety of this drug after prolong used and in larger patient population.

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