

Original Research Article

COMPARISON OF EFFICACY OF PRUCALOPRIDE ALONE & WITH COMBINATION WITH SODIUM PICOSULPHATE IN PATIENTS OF CHRONIC IDIOPATHIC CONSTIPATION

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ABSTRACT

Background: Chronic idiopathic constipation is a frequent gastrointestinal disorder that can have a major impact on bowel function and quality of life. The objective is to evaluate the effectiveness and safety of prucalopride alone versus prucalopride in combination with sodium picosulfate in chronic idiopathic constipation (CIC) patients.

Materials and Methods: A prospective comparative interventional study was carried out at the Department of Gastroenterology, Bahawal Victoria Hospital Bahawalpur, from September, 2025 to February, 2026. 100 patients were randomly allocated into two groups: 50 patients for prucalopride alone and 50 for sodium picosulfate in combination with prucalopride.

Results: There was an improvement in bowel habits and constipation symptoms in both groups. Overall clinical improvement was observed in 68% of patients on prucalopride alone and 82% on combination therapy. The combination group had statistically significant improvement in bowel frequency, stool consistency, straining, and incomplete evacuation, while experiencing only mild additional gastrointestinal adverse effects.

Conclusion: Prucalopride plus sodium picosulfate resulted in greater symptomatic improvement than prucalopride alone and could be a useful alternative to prucalopride in patients with persistent constipation.

Keywords: Chronic idiopathic constipation, prucalopride, sodium picosulfate, bowel movements, laxative, gastrointestinal motility.

INTRODUCTION

Chronic idiopathic constipation (CIC) is a relatively frequent gastrointestinal condition where there is a persistent problem with stool evacuation, infrequent stools, hard stools, excessive straining, or the feeling that the stool has not fully passed. The condition can significantly affect quality of life as symptoms can be chronic, recurrent, and refractory to conventional treatments. Current clinical guidelines focus on a step-wise strategy to treatment, starting with lifestyle and dietary changes and moving to pharmacologic treatment as needed if symptoms are not controlled.^[1]

Conventional laxatives have drawbacks and costs, leading to greater interest in more recent pharmacological methods that target intestinal motility and secretion.

Conventional preparations for the pharmacological treatment of CIC include osmotic and stimulant laxatives, stool-bulking agents. While these treatments may help relieve symptoms, some people still have poor bowel movements or strain, feel bloated, have abdominal discomfort, or do not empty their bowels. Therefore, prescription agents like intestinal secretagogues and prokinetic drugs are recognized to have a role in patients who fail to

respond adequately to over-the-counter agents.^[2] Prucalopride is a highly selective serotonin type 4 (5-HT₄) receptor agonist with a beneficial effect on gastrointestinal coordinated motility and colonic transit and has proven to be an important option. Prucalopride acts on the enteric nervous system to stimulate 5-HT₄ receptors, which may increase spontaneous bowel movement frequency and bowel movement evacuation symptoms.

A recent review has emphasized the growing therapeutic options for CIC beyond the traditional laxatives. Prucalopride, linaclotide, plecanatide, and lubiprostone are effective in appropriately selected patients, and this choice of agent depends on the severity of symptoms, effectiveness of treatment, tolerability, and the characteristics of the patient.^[3] In these indications, prucalopride has special significance in those cases where delayed colonic transit is suspected, as its main therapeutic effect is the stimulation of colonic motor activity. However, even potent prokinetic agents may not be sufficient to completely normalize bowel function in all patients with constipation, especially when there is a problem with stool consistency, fecal retention, or inadequate evacuation. This justifies assessing combination approaches targeting various aspects of constipation. The current study is focused on adults with CIC, but data from the functional constipation literature show that pharmacologic treatment may need to be tailored to the pattern, severity, and response to initial therapy. The same structured approach to treatment, sufficient disimpaction as needed, maintenance therapy, and adjustment of pharmacological treatment based on clinical response are also stressed for pediatric patients.^[4] The principles reflect the general idea that no single therapy works for all patients with constipation. Therefore, a combination of agents with complementary mechanisms in clinical practice may be more effective in patients who are always symptomatic despite treatment with a single agent.

In addition, Brazilian experts have conducted a narrative review that highlights the importance of considering bowel frequency, stool characteristics, evacuation difficulty, associated symptoms, medication history, and possible secondary causes prior to starting treatment for CIC.^[5] The management must then be tailored to the individual, and the choice of medications depends on the predominant symptoms and the response to the previous interventions.^[6] Likewise, the Seoul consensus on functional constipation emphasizes the need for correct diagnosis, lifestyle changes, pharmacologic treatment, and escalation of treatment in case of persistent symptoms.^[7] The recommendations apply to the adult CIC as they reiterate the need to assess the effectiveness of the therapy based on clinically relevant outcomes, not just stool frequency. The ideal treatment should increase stool passage and stool frequency, decrease straining, complete evacuation, improve abdominal symptoms, and increase patient comfort.

Constipation may also be a problem in patients with significant comorbidities such as chronic kidney disease and neurological disease, where several physiological and treatment-related factors may be responsible for the poor bowel function. Dietary restrictions, decreased mobility, fluid restrictions, medication exposure, and gastrointestinal dysfunction can all contribute to constipation in children with chronic kidney disease.^[8] While these observations show that constipation may have multiple mechanisms, and that more than one mechanism may be involved in patients who continue to be constipated. Likewise, recent studies on personalized dietary and microbiome-based interventions indicate that the intestinal function is affected by intricate relationships between nutrition, gut microbiota, and gastrointestinal physiology.^[9] These results are further evidence of the importance of personalized treatment strategies.

There has also been a lot of research on alternative and complementary therapies for functional constipation. A systematic review protocol on alternative therapies emphasizes ongoing research for effective alternatives because current therapies may not be sufficient to alleviate symptoms in all patients.^[10] There has also been a wide range of research on acupuncture and other non-pharmacological treatments, with some studies focusing on particular populations and others being highly varied. For instance, the ACU-PILOT study evaluated the feasibility, safety, and treatment efficacy of acupuncture in children with functional constipation.^[11] and systematic evidence has been reviewed on acupuncture in post-stroke constipation.^[12-14] These studies show the wide therapeutic relevance of constipation and highlight the need for continued investigation of available pharmacologic therapies through carefully designed comparative studies.

Another good example of the need for mechanism-specific management is drug-induced constipation. Management of OIC typically involves interventions targeting the different pathophysiological mechanisms involved in opioid-induced constipation, which is caused by the opioid effect on gastrointestinal motility and secretion.^[12] While CIC is not an opioid-induced constipation, the principle applies – impaired propulsion, altered secretion, altered consistency, or combinations of these factors. Physiological studies with imaging and high-resolution manometry have shown that the structure and motor function of the colon play an important role in the severity of constipation, and that an enlarged colon is correlated with clinically significant abnormalities of colonic function.^[13] This evidence supports the rationale for the treatments, as they both stimulate intestinal propulsion and stimulate bowel movements.

Constipation also occurs in patients with neurological diseases. For instance, gastrointestinal symptoms can be a significant burden of the disease in Parkinson's

disease and may need to be treated specifically.^[15] For those with severe neurological dysfunction, gastrointestinal dystonia and gastrointestinal dysfunction can also play a role in managing constipation.^[16] Dietary changes also may affect bowel movements and symptoms of the gastrointestinal tract. A low-residue diet has been studied in a feasibility trial in adults with mitochondrial disease to assess its impact on gastrointestinal symptoms, tolerability and the gut microbiome, as diet composition is known to interact with gastrointestinal physiology.^[17] But a diet may not be enough to resolve the motility issues associated with CIC.

Therefore, pharmacologic treatment continues to play a major role in the treatment of chronic constipation. The clinical relevance of the combination of prucalopride and sodium picosulfate is that the two drugs have complementary activities in this therapeutic context. Prucalopride is mainly selective 5-HT₄ receptor stimulator and sodium picosulfate is a stimulant laxative that stimulates colonic activity and facilitates stool passage. Thus, a combination regimen may be more effective than prucalopride alone in the treatment of constipation, particularly in patients who continue to have constipation despite prokinetic therapy. But it is essential to compare these directly with the patient because combination therapy can also lead to side effects such as abdominal cramping, diarrhea or urgency. The effectiveness and safety of prucalopride alone versus prucalopride plus sodium picosulfate could therefore provide clinically relevant information to help determine if complementary pharmacologic mechanisms translate to better symptom relief for CIC patients.

Objective: To evaluate the effectiveness and safety of prucalopride alone compared with prucalopride plus sodium picosulfate for the improvement of bowel frequency, stool consistency, evacuation difficulty, and symptoms in patients with chronic idiopathic constipation (CIC).

MATERIALS AND METHODS

Study Design: Comparative prospective interventional study.

Study Setting: Department of Gastroenterology, Bahawal Victoria Hospital Bahawalpur, Pakistan.

Duration of the Study: The study was carried out for 6 months from September, 2025 to February, 2026.

Inclusion Criteria

Patients were included if they met the clinical criteria for chronic idiopathic constipation and were 18 years or older. Persistent constipation symptoms, such as infrequent bowel movements, hard stools, excessive straining, or feeling as if there is something left behind, were deemed eligible. Patients who were willing to participate in the study and provided informed consent were also included. Participants

had to complete the recommended treatment and follow-up evaluations.

Exclusion Criteria

Patients with constipation due to known organic gastrointestinal, metabolic, or structural disease were excluded. Those patients suffering from possible or known intestinal obstruction, colorectal malignancy, inflammatory bowel disease, or significant gastrointestinal bleeding were not included. Patients with severe renal or hepatic impairment, significant cardiovascular disease, or clinically significant hypersensitivity to prucalopride or sodium picosulfate were excluded. Patients using other prescription drugs regularly for constipation, pregnant women, and breastfeeding women were also excluded. Those patients who refused informed consent and those who failed to attend the follow-up were excluded from the study.

Methods

Patients with chronic idiopathic constipation (CIC) were recruited after clinical examination and confirmation of the eligibility criteria. Written informed consent was obtained and participants were randomly allocated to 2 treatment groups. Group A received prucalopride, Group B received prucalopride + sodium picosulfate. Treatment was administered at the standard recommended therapeutic dosage, and was continued during the study follow-up period. A structured data collection proforma was used to obtain baseline demographic and clinical data including age, sex, duration of constipation, frequency of bowel movements, stool consistency, straining, and sensation of incomplete evacuation. Treatment response and tolerability were clinically evaluated in patients. The primary results were an increase in bowel movements and a decrease in constipation. Secondary outcomes included stool consistency, straining, incomplete evacuation, abdominal discomfort, and adverse effects of the treatment. Patients were monitored for abdominal cramps, diarrhea, nausea, urgency and other side effects reported.

RESULTS

A total of 100 patients with chronic idiopathic constipation (CIC) were studied. The patients were randomly allocated to two treatment groups, 50 patients in each group, one group receiving prucalopride only (Group A) and the other group receiving sodium picosulfate in addition to prucalopride (Group B). The baseline demographic data for the two groups were similar. The mean age was 42.6 ± 11.8 years in Group A and 43.1 ± 12.2 years in Group B, with females being a slightly larger proportion of the study population in both groups. The mean duration of constipation was also similar between the groups, suggesting that the two treatment groups had generally similar clinical characteristics at baseline.

Table 1: Baseline demographic characteristics of study participants

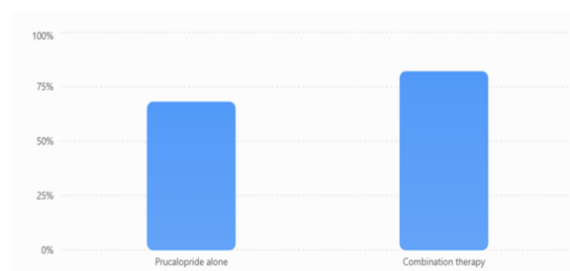
Characteristic	Prucalopride alone (n=50)	Combination therapy (n=50)
Mean age (years)	42.6 ± 11.8	43.1 ± 12.2
Female, n (%)	31 (62.0)	29 (58.0)
Male, n (%)	19 (38.0)	21 (42.0)
Mean duration of constipation (years)	4.8 ± 2.7	5.0 ± 2.9
Baseline bowel movements/week	2.3 ± 0.8	2.2 ± 0.9
Hard stool, n (%)	38 (76.0)	39 (78.0)
Excessive straining, n (%)	41 (82.0)	40 (80.0)

The main symptoms related to constipation were comparable at baseline in both groups. The percentages of patients who reported excessive straining were 82.0% for prucalopride alone and 80.0% for combination therapy. The consistency of stool was hard in 76.0% and 78.0% of cases, respectively. After treatment, both groups showed an

improvement in bowel habits, but the patients who received combination therapy showed a larger improvement. The mean number of bowel movements per week rose from 2.3 ± 0.8 to 4.6 ± 1.3 in Group A, while Group B had a rise from 2.2 ± 0.9 to 5.4 ± 1.5 bowel movements per week.

Table 2: Changes in bowel movement frequency and constipation symptoms

Outcome	Prucalopride alone	Combination therapy
Baseline bowel movements/week	2.3 ± 0.8	2.2 ± 0.9
Post-treatment bowel movements/week	4.6 ± 1.3	5.4 ± 1.5
Improvement in bowel frequency	2.3 ± 1.0	3.2 ± 1.2
Patients with ≥ 3 bowel movements/week, n (%)	34 (68.0)	41 (82.0)
Improved stool consistency, n (%)	32 (64.0)	40 (80.0)
Reduced straining, n (%)	35 (70.0)	42 (84.0)
Reduced incomplete evacuation, n (%)	33 (66.0)	41 (82.0)



The combination group had a higher percentage of patients who reached clinically meaningful improvement. In total, 34 patients (68.0%) on prucalopride alone and 41 patients (82.0%) on combination treatment had at least 3 bowel

movements per week. In addition, 64.0% of patients in Group A improved stool consistency compared with 80.0% in Group B, and 70.0% reduced excessive straining compared with 84.0% in Group B. The improvement in the sensation of incomplete evacuation was reported by 66.0% of patients in Group A and 82.0% in Group B.

Overall clinical improvement by treatment group

In the combination group, 82.0% of patients achieved overall clinical improvement (defined as improvement in bowel frequency and major constipation symptoms) compared to 68.0% in the prucalopride-alone group. Therefore, the use of sodium picosulfate was correlated with a higher rate of satisfactory symptomatic improvement.

Table 3: Overall treatment response

Treatment response	Prucalopride alone (n=50)	Combination therapy (n=50)
Marked improvement, n (%)	20 (40.0)	29 (58.0)
Moderate improvement, n (%)	14 (28.0)	12 (24.0)
Minimal/no improvement, n (%)	16 (32.0)	9 (18.0)
Overall improvement, n (%)	34 (68.0)	41 (82.0)

The combination regimen also gave a larger percentage of patients who experienced significant improvement. There was an improvement in 58.0% of patients in Group B and 40.0% in Group A, moderate improvement in 24.0% of patients in Group B and 28.0% in Group A, and minimal or no improvement in 18.0% of patients in Group B and

32.0% in Group A. These results suggest that the combination treatment shows a favorable clinical response. The tolerability of the treatment was determined by documenting adverse effects during follow-up. The majority of adverse events were mild and did not require discontinuation of treatment.

Table 4: Treatment-related adverse events

Adverse event	Prucalopride alone (n=50)	Combination therapy (n=50)
Abdominal cramping, n (%)	5 (10.0)	9 (18.0)
Diarrhea, n (%)	4 (8.0)	8 (16.0)
Nausea, n (%)	3 (6.0)	4 (8.0)
Abdominal discomfort/bloating, n (%)	5 (10.0)	6 (12.0)
Treatment discontinuation, n (%)	2 (4.0)	3 (6.0)

The combination group reported more adverse events, but these were mostly minor and temporary. There were no serious complications of treatment noted. Overall, both treatment strategies had beneficial effects on the symptoms of chronic idiopathic constipation, with the combination of prucalopride and sodium picosulfate showing greater improvements in bowel frequency, stool consistency, straining, incomplete evacuation, and clinical response. This was accompanied by a small rise in minor gastrointestinal side effects, but treatment discontinuation was low in both groups.

DISCUSSION

In the present study, the efficacy and tolerability of prucalopride alone versus prucalopride combined with sodium picosulfate were compared in patients with CIC. The results showed that both treatments were effective, with the combination treatment showing a higher overall clinical response rate. The combination therapy group experienced a higher rate of improvement in bowel movement frequency, stool consistency, straining, and incomplete evacuation, with 82% in the combination therapy group improving in general compared to 68% in the prucalopride alone group. The guidelines endorse the use of already approved prescription medications such as prucalopride for the proper patient with chronic idiopathic constipation.^[1] Therefore, the effect of prucalopride alone observed in the present study is clinically reasonable, as the drug directly affects gastrointestinal motility. The greater response seen with the combination suggests that patients with ongoing evacuation problems may benefit from a greater therapeutic effect provided by an additional stimulant mechanism.

The results are also consistent with the general literature on pharmacology, which indicates that treatment of chronic idiopathic constipation has moved beyond the use of traditional laxative drugs. Modern treatment strategies include prokinetic agents, secretagogues, and other targeted therapies, depending on symptoms and prior response to treatment.^[3] In the present study, prucalopride + sodium picosulfate was associated with a greater increase in bowel movements per week than prucalopride alone. This suggests that combining colonic propulsive activity with bowel evacuation may have a greater therapeutic effect than colonic propulsive activity alone. While this study was conducted in adults, the lessons learned from managing functional constipation should be taken into account in individualizing treatment and adjustment based on the clinical response.

Pharmacological management should not be regarded as a standard treatment, as the severity and response to constipation may be very different between different patients.^[4] The principle applies to the present findings as the percentage of inadequate responders was lower in the combination therapy group, while about one-third of the patients who

received prucalopride alone did not reach the defined overall improvement. These findings indicate that combination therapy may be helpful, especially when monotherapy is insufficiently effective. Similarly, the Brazilian expert task force has noted that CIC is a heterogeneous condition and that careful clinical evaluation and treatment directed to the predominant symptoms are required.^[5] This is corroborated by the present study, which showed that there was not only an improvement in bowel frequency, but there was an improvement in several symptom domains. The importance of reducing straining and incomplete evacuations is that patients may still feel constipated even with increased stool frequency.

The better improvement of these symptoms in combination therapy patients suggests that the extra stimulant effect may have contributed to the improved evacuation. Current pediatric guidelines also emphasize individualized and structured treatment approaches, adjusting treatment according to treatment response and tolerance.^[6] These recommendations are not directly applicable to adults, but they do support a general therapeutic principle for the management of constipation: If one intervention does not seem to be working, it should be reassessed and, if appropriate, escalated or modified. The present results support this approach as combination therapy resulted in greater overall improvement without a significant increase in treatment discontinuation.

The Seoul consensus on functional constipation also highlights the importance of a comprehensive approach to the management of the condition, which involves a proper assessment, lifestyle modifications and, if necessary, appropriate drug treatment.^[7] In this regard, the uniformity of stools and reduction in the number of strains described in the present study are important findings. The aim of treatment for constipation is to enhance the entire bowel experience, not simply the number of bowel movements. The greater proportion of patients who improved on number of symptoms in the combination therapy group further enhances the clinical relevance of the difference between the treatment groups. For those who have underlying conditions, constipation can occur for more complicated reasons, such as decreased mobility, dietary changes, and medications that impact the gastrointestinal tract. In children with chronic kidney disease, a number of clinical and treatment-related factors have been shown to have an impact on constipation, and these factors are interdependent.^[8]

Such patients were not the primary focus of the present study, but these observations underscore the multifactorial nature of constipation and why a treatment targeting a single physiological mechanism may not be sufficient to relieve the condition in all patients. Recent studies have also investigated the role of diet and gut microbiome in functional constipation. The personalized approach to bowel function improvement through diet intervention is illustrated by a randomized controlled study of

microbiome modulation.^[9] However, drug treatment is still significant for those who have symptoms that have been present for a long time. The current results indicate that pharmacological combination therapy may provide significant symptomatic relief in the context of new dietary and microbiome-based therapies.

Evidence testing alternative treatments also shows that constipation is an area where several treatments are being explored, as conventional treatment is not always effective.^[10] The present findings add to the larger body of evidence showing that a combination of two pharmacological strategies may be more effective in treatment response. The present study should not be interpreted as a universal superiority of combination therapy, but rather as an indication that certain patients might benefit from the combination of the complementary pharmacological mechanisms. Safety findings are also significant. The combination group had slightly more abdominal cramping and diarrhea than the prucalopride-only group, but most side effects were mild, and there was little discontinuation of treatment. This is a typical example of the "efficacy-tolerability" trade-off that occurs when introducing a second bowel stimulant.

Studies on other interventions for constipation, including acupuncture, also highlight the need to assess feasibility and safety in addition to treatment efficacy.^[11] Therefore, the combination therapy should be weighed against the slight additional gastrointestinal side effects. The findings can also be understood in a mechanistic way in relation to the gastrointestinal motility in the presence of specific pharmacological influences. For instance, opioid-induced constipation is associated with impaired intestinal motility and secretion, and targeted therapy of these abnormalities may be needed.^[12] Therefore, the prokinetic effect of Prucalopride may offer a crucial basis for treatment, and sodium picosulfate may add further stimulation of bowel evacuation.

Physiological studies have also shown that the structure and motor function of the colon may affect the severity of constipation. In the RECLAIM study, advanced imaging and high-resolution manometry were employed to explore colonic abnormalities, and it was shown that the enlarged colon is important in constipation.^[13] These results could offer a physiological rationale for the use of treatments that stimulate colonic motor activity. The increased bowel frequency observed in the present study with combination therapy results from the combined effects of improving propulsion and stimulating evacuation. Constipation is also common in neurological disorders, where changes in the autonomic function, decreased activity, contact with drugs, and gastrointestinal dysfunction can also be involved. Therefore, the management of gastrointestinal symptoms is an important aspect of the care of patients with Parkinson's disease.^[15]

The present study did not include patients with major secondary causes of constipation, but the literature reviewed emphasized the importance of optimizing

bowel function and minimizing gastrointestinal symptom burden, not just stool frequency. Likewise, gastrointestinal dystonia and complex disturbances of gastrointestinal function have been associated with severe neurological impairment.^[16] This evidence supports the idea that constipation may be caused by abnormalities of intestinal motility and coordination. Prucalopride may be especially relevant in patients with chronic idiopathic constipation, where impaired propulsion may be a factor in symptoms. The enhancement of clinical response seen with the addition of sodium picosulfate suggests that a complementary mechanism of bowel evacuation may improve clinical response.

Lastly, dietary composition may affect gastrointestinal symptoms and gut microbial properties, as seen in studies of low-residue dietary intervention in mitochondrial disease patients.^[17] While diet and pharmacologic therapy target different components of gastrointestinal function, the results highlight the need to view constipation as a multifactorial disease. In general, the present study suggests that both prucalopride alone and combination therapy with sodium picosulfate are effective for the treatment of chronic idiopathic constipation, with a greater percentage of clinically meaningful responses obtained with combination therapy. The small rise in minor gastrointestinal side effects should be taken into account when choosing treatment. These results should be confirmed in larger randomized trials with longer follow-up to establish the durability of the response and to define the patients who are most likely to benefit from combination therapy.

CONCLUSION

The present study showed that prucalopride alone and prucalopride in combination with sodium picosulfate were effective in relieving the symptoms of chronic idiopathic constipation. Combination therapy, however, yielded the more impressive overall clinical response, with increased improvements in bowel movement frequency, stool consistency, excessive straining, and incomplete evacuation than prucalopride monotherapy. The combination of sodium picosulfate complemented the effect of prucalopride, with the bowel evacuation being stimulated in a complementary manner. Mild gastrointestinal side effects (abdominal cramping and diarrhea) were slightly more common in the combination group but were not severe enough to cause treatment discontinuation in most patients. These results indicate that the combination of prucalopride and sodium picosulfate could be a more effective treatment in patients with chronic idiopathic constipation that is not adequately controlled by prucalopride alone.

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