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Addition of Prucalopride to Standard Bowel Preparation Does Not Improve Colonic Mucosa Visualization—A Retrospective Observational Cohort Study

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Abstract

Background Colonoscopy is currently gold standard for visualizing colonic mucosa. Presence of constipation is generally associated with poor bowel preparation. We compared effect on colonic cleansing when prucalopride was used as adjunct with polyethylene glycol (PEG) in patients of constipation.

Methods A retrospective study was conducted at our center. One 70 patients with constipation were enrolled in two groups of who took only PEG and other of prucalopride plus PEG+ for bowel preparation. They underwent colonoscopy by a single-blinded experienced endoscopist. Bowel preparation quality was reported by Boston bowel preparation scale prior to washing or suctioning. The groups were analyzed for bowel preparation quality and side effects in either groups based on preformed questionnaire.

Results Mean Boston Stool preparation Score (BSS) in PEG group (5.33 ± 1.43) was slightly higher than PEG+ ($5.16 + 1.37$) (p-value $=0.44$). The total number of patients with side effects was higher in PEG+ group than PEG group. ($p < 0.05$).

Conclusion We conclude addition of prucalopride has no additional benefit when added with standard bowel preparation in patients of constipation. It may rather lead to noncompliance and inferior bowel preparation due to increased side effects.

Keywords
- Boston stool preparation score
- bowel preparation
- colonoscopy
- constipation
- polyethylene glycol
- prucalopride

Introduction

Colonoscopy is currently the gold standard for visualization of colonic mucosa. It is an integral part of all colorectal screening programs given its ability to detect high-risk lesions like adenoma and cancer.[1,2] Poor bowel preparation results in a longer procedure duration and incomplete colonoscopy, leading to need of repeat colonoscopy and missed lesions[3] and has been regarded as one of the most common causes for failure to achieve good mucosal visualization.[4] Despite technological advances in colonoscopies, ideal bowel preparation still represents one of the most difficult stages of the process.

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Constipation has been associated with poor bowel preparation.[5,6] Davis et al in 1980 introduced the split dosing of polyethylene glycol (PEG) for bowel preparation before colonoscopy. Since its introduction, it is one of the most safest and efficacious bowel preparation regimens available.[7] It has been compared with various other agents like lactulose, bisacodyl, and mannitol-based solution and was found to be more superior and tolerable.[8,9] Prucalopride is a selective stimulator of the serotonin type 4 (5HT4) receptors. These receptors can be found throughout the gastrointestinal tract primarily in smooth muscle cells, enterochromaffin cells, and myenteric plexus that on stimulation release excitatory neurotransmitter acetylcholine, leading to muscle contraction.[10] Prucalopride augments this effect and is currently approved for functional constipation and constipation predominant irritable bowel syndrome.[11] We aim to establish benefit, if any, of combining prucalopride to standard bowel preparation in patients of constipation undergoing colonoscopy. Bloom et al concluded that constipation is one of the predominant factors in relation with poor bowel preparation with PEG.[12]

Materials and Methods

Study Design

The study was done at a tertiary care center in western India after approval from the institutional ethics committee, among the patient who visited the outpatient department of gastroenterology from October 2018 to October 2019 with a history of constipation. It was a retrospective observational cohort analysis of patients who had constipation undergoing colonoscopy. All patients between 18 and 60 years of age who had nonorganic cause of constipation like irritable bowel syndrome—constipation variant and functional constipation—as defined by ROME IV consensus, were included.[13] Pregnancy, history of prior colonic or rectal surgery, history of acute coronary syndrome and ischemic heart disease, congestive heart failure, unstable angina, known or suspected renal failure, ascites, megacolon, known or suspected bowel obstruction, colonic malignancies, or those patients who did not consent for the study were excluded from the study.

The patients were retrospectively divided into two groups. One group that received bowel preparation only by split-dose PEG group, while the other received split-dose PEG along with prucalopride (single dose of 2 mg at 8am) (PEG+ group) a day prior to the colonoscopy. People in either group were explained about the bowel preparation in detail along with information sheet about the same, in their native language. In both groups, low-residue diet 2 days prior to colonoscopy was advocated. Both the groups took PEG solution (PEG 3300) with the following composition: PEG 118 gm, potassium chloride 1.484 g, and sodium bicarbonate 3.37 g. Each packet was dissolved in 2 L of water and divided into two 1-Lter solution to be consumed a day prior to colonoscopy by split-dose method. The participants were given written instructions for the PEG preparation in their own language after comprehensively explaining the same to them. PEG+ group was advised to take prucalopride 2 mg, single tablet at morning 8 am followed by PEG solution (PEG 3300) in the same way as in PEG group. Same brand was used in both groups. A validated questionnaire[8] was administered to the patients in both groups, before and after the colonoscopy, to assess the quantum of adverse effects thus defining tolerability to particular bowel preparation, if any faced by the patients due to the preparation.

Both groups underwent unsedated colonoscopy by an experienced endoscopist (minimum of 200 colonoscopies) who was unaware about the method of bowel preparation. Colonoscopy was performed using Olympus colonoscope Q-150L series (Olympus Optical, Tokyo, Japan). Each endoscopist evaluated the bowel preparation in accordance with Boston Bowel preparation scale[14] (►**Fig. 1**), prior to washing or suctioning in all the three segments.

Statistical Analysis

Data analysis was done in SPSS software version 16. Likelihood ratio was employed in the statistical analysis and *p*-value <0.05 was taken as significant. Total sample size was calculated on the basis of number of patient who underwent colonoscopy in the foresaid period from October 2018 to 2019.This study is registered with the ethical society with reg no LTM/38/19.

Results

The consort diagram in ►**Fig. 2** explains the outline of the study. Two hundred and one patients underwent colonoscopy. Thirty-one patients were excluded in view of incomplete colonoscopy on account of distal obstructing lesion, stricture, or nonachievement of cecal intubation. Thus, 85 patients were included in either group of PEG or PEG+ group. Both the groups were comparable with respect to age, sex, and comorbidity.

The patient demographics have been mentioned in ►**Table 1**. The side effects related to the study drug were examined using a questionnaire and compared in both groups in terms of nausea, vomiting, headache, abdominal discomfort, and abdominal pain. The overall side effects seen in the PEG+ group were shown to be significantly higher when compared with the PEG only group; although the individual adverse events did not achieve statistical significance (►**Table 2)**. None of the patients have any serious adverse event during the course of the study.

Discussion

In this single-center retrospective observational study, *p*-value was not significant for prucalopride usage in bowel preparation. Addition of prucalopride also increases the rate of side effects related to bowel preparation and significantly increases the unwillingness in the patient to repeat the procedure. Both groups had similar frequency of bowel movements demonstrating no additional benefit of the number of bowel movements in bowel cleansing with

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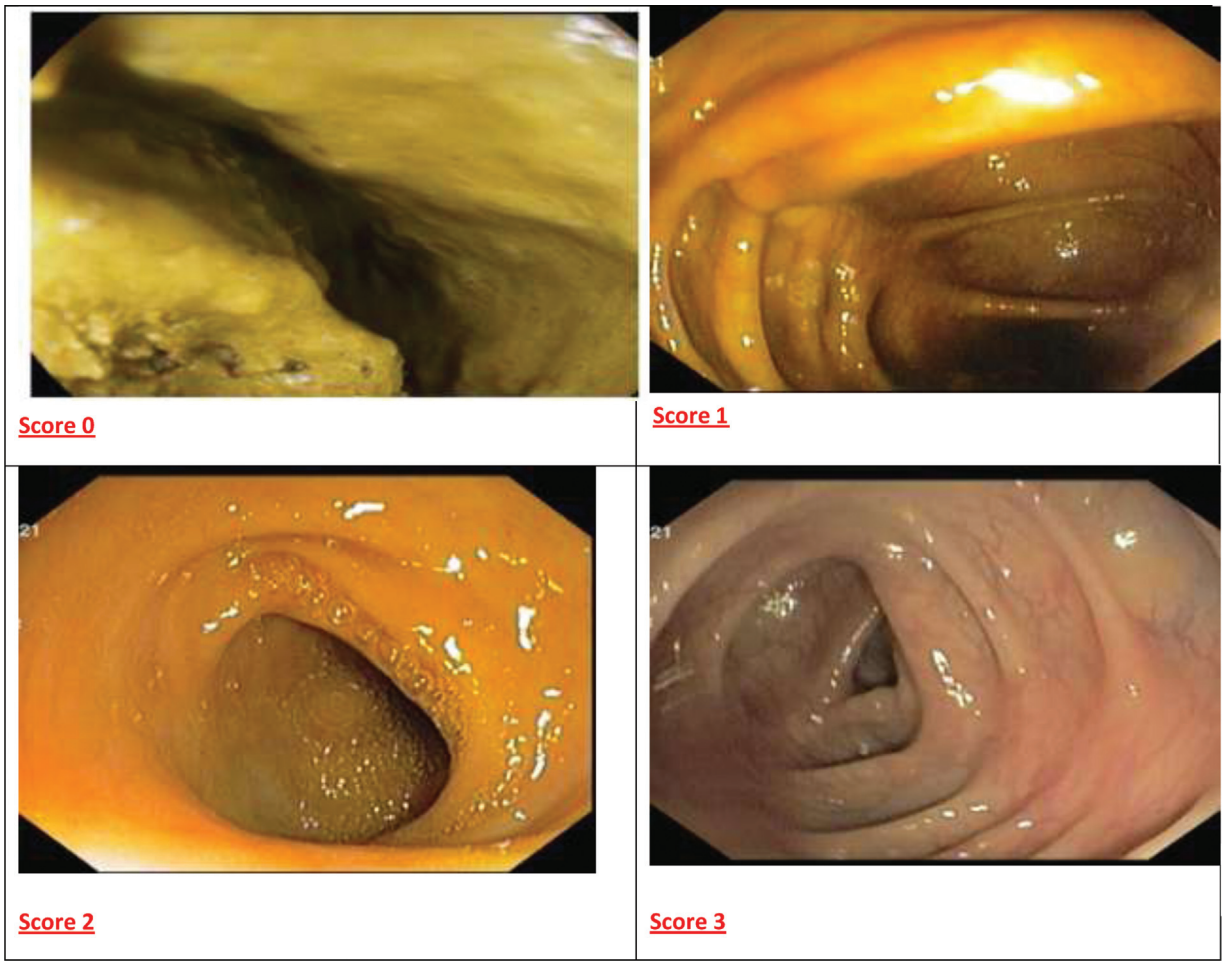

Fig. 1 Boston stool preparation scoring based on preparation. Score 0—Unprepared colon segment with mucosa. Not seen due to solid stools that cannot be cleared. Score 1—Portion of mucosa of colonic segment seen but other areas not well seen due to staining residual stool or opaque liquid. Score 2—Minor amount of residual staining, small fragment of stool or opaque liquid but mucosa of colon seen well. Score 3—Entire mucosa of colonic segment seen well without residual staining.

addition of prucalopride. In this retrospective observational study, we compared the bowel-cleansing effectiveness of prucalopride when used along with PEG than PEG alone for lavage of the bowel in patient of constipation. We showed that addition of prucalopride to PEG in fact significantly increased the side effects post its use and this leads to unwillingness among patients to repeat the procedure if ever needed. This was in accordance with study of Bloom et al where they demonstrated constipation to be one of major determinants in bowel preparation.[12] Multiple studies have evaluated the additional benefits of adding additional laxatives to standard bowel preparation using PEG, but none showed any clinical significance. Lactulose, mannitol, sodium picosulfate, and magnesium citrate have all been used with PEG but did not show any efficacy in achieving bowel cleasning.[8–10] No study has yet been done employing prucalopride as an additional tool in bowel cleansing. Prucalopride is 5HT4 agonist indicated for functional constipation because of its role in enhancing colonic motility. Thus, it would appear as an attractive option as an addition to improve bowel preparation. Our study showed that addition of prucalopride was not associated with improvement in bowel preparation. The tolerability was evaluated by a scale of side effects that was universally involved in all studies using PEG for bowel preparation like nausea, vomiting, bloating headache, or abdominal pain.[8] Our study demonstrated that addition of prucalopride leads to significant increase in the number of these side effects due to the bowel preparation. The increase in side effects might be reason of unwillingness to repeat the procedure if ever required ($p < 0.001$).

Our study has few forthcomings. First, it was not a randomized control trial. Second, absence of measurable parameter in view of educational status of patient was not employed in this study that is very importance in our setup where we tend to lower strata of the patients. Third, patients with comorbidities with different type of drugs may have hindered the bowel cleansing. Four, the questionnaire of willingness to undergo colonoscopy again is subjective and there are no objective criteria for the same and is again dependent on patient education and motivation.

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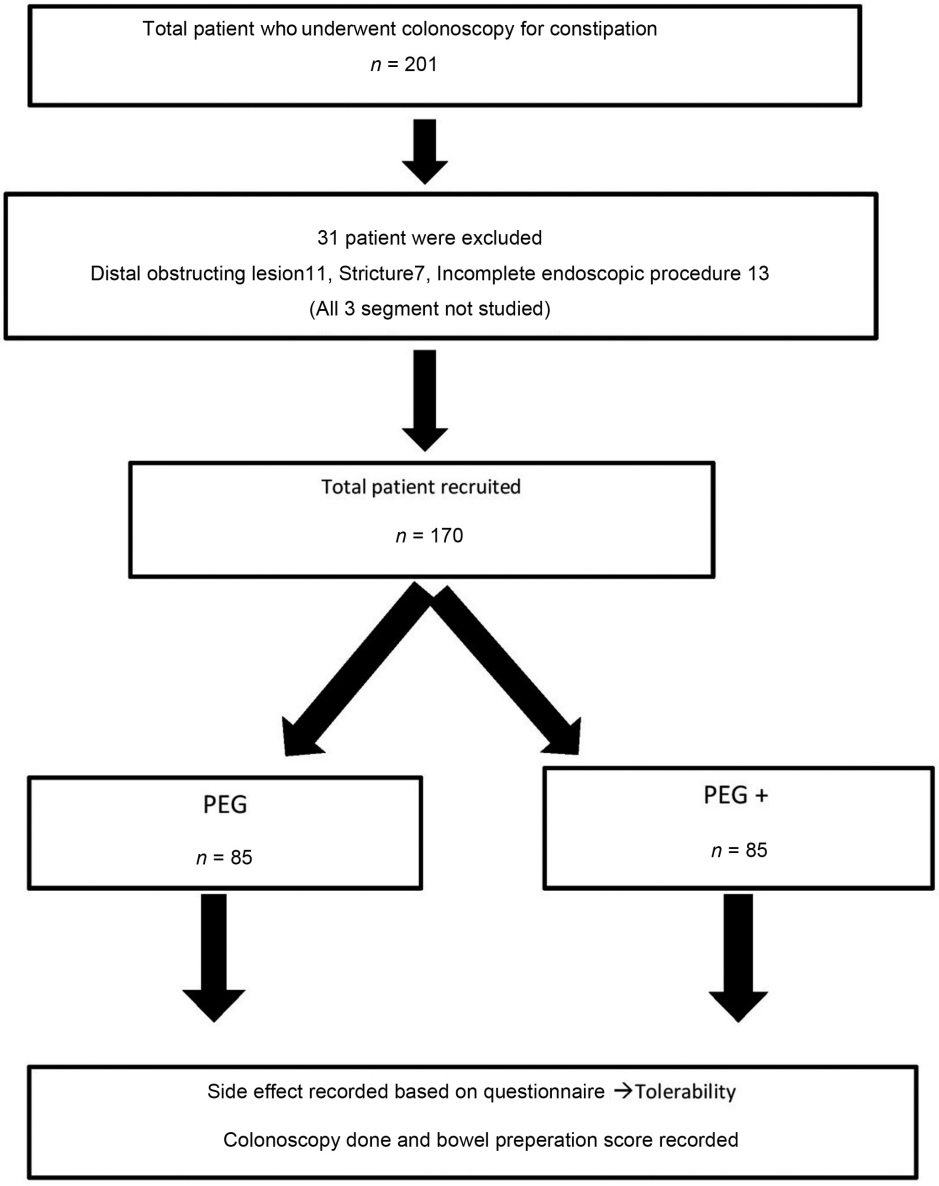

Fig. 2 Consolidated Standards of Reporting Trials (CONSORT) diagram of the study. PEG, polyethylene glycol.

Table 1 Baseline data of the patients from both groups

Parameters	PEG ($n = 85$)	PEG + ($n = 85$)	*p*-Value
Mean age (years)	43 ± 14.7	41 ± 14.6	0.342
Male	43	43	0.561
Female	42	42	0.77
Co-morbidities	21	22	0.76
Diabetes	12	10	0.942
Hypertension	4	5	0.841
Ischemic heart disease	2	3	0.87
Hypothyroidism	3	4	0.74
Frequency of bowel movement	7.88 ± 2.5	8 ± 2.7	0.776
Boston bowel stool preparation score	5.33 ± 1.434	5.17 ± 1.37	0.445

Abbreviation: PEG, polyethylene glycol.

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Table 2 Side effects related to the administered drugs

Adverse events	PEG	PEG+	*p*-Value
Total number	34	68	0.036 (<0.05) Significant
Nausea	33	40	0.196
Vomiting	23	28	0.353
Abdominal pain	13	22	0.064
Headache	6	11	0.153
Bloating	14	18	0.212
Willingness to repeat the procedure	21	3	<0.001

Abbreviation: PEG, polyethylene glycol.

Conflict of Interest

The authors have no financial conflict of interest.

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