Effectiveness of Polyethylene glycol (PEG) combined with linaclotide regimen for adequacy of bowel preparation in high-risk and chronic constipated patients undergoing colonoscopy: A Double -blinded randomized controlled trial (sages2026.21b09f4)

Vijayakumar C[1], Kishore U[1], [1]Uday Shamrao Kumbhar [1], Senthamizh Selvan K[2] Oseen HS [1]

Department of Surgery[1] and Medical Gastroenterology [2], Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry , India- 605006

INTRODUCTION

- Successful completion of colonoscopy depends largely on the quality of bowel preparation. Polyethylene glycol (PEG) is a commonly used preparation for colonoscopy.
- The timing of bowel preparation has evolved, and single dose and split-dose regimen are being used. However, in high-risk patients, additional adjunctive substrates might be required for adequate bowel preparation.
- Hence, we designed a randomized controlled trial (RCT) to evaluate the effectiveness, tolerability, safety of combining PEG with bisacodyl and PEG with linaclotide for bowel preparation in high-risk patients.

AIM

- The aim of this research study was to evaluate the effect of using linaclotide as an adjunctive agent with 2L PEG for adequate bowel preparation in high risk and chronic constipated patients undergoing colonoscopy .

MATERIALS AND METHODS

Methodology

Study type: Prospective, Double blinded, double arm randomized control trial.
Study period: July 2023 to June 2025:Dept of Surgery and Medical Gastroenterology.

Inclusion criteria
1. All Consecutive consenting patients planned for elective colonoscopy for various indications with history of chronic constipation and high-risk patients (Bristol stool form scale 1&2)
2. Prior history of inadequate bowel preparation

Exclusion criteria
1. Bristol stool form scale (3-7)
2. History of colorectal surgery
3. Patients with history of bowel obstruction or resection
4. History of taking linaclotide within 7 days or known linaclotide allergy
5. Pregnant or lactating women

Sample size calculation:
- Assuming the success **rate of adequate** bowel preparation in PEG+L to be **87.9%** compared to **77%** in the control group * with α error of 5% and a power of 80%.
- Total number of participants required in both group was 430. (215 each group)

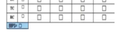
*Zhang M et al: Polyethylene glycol combined with linaclotide is an effective and well-tolerated bowel preparation regimen for colonoscopy: an endoscopist-blinded, randomized,controlled trial. Eur J Gastroenterol Hepatol 2021.

Study Parameters

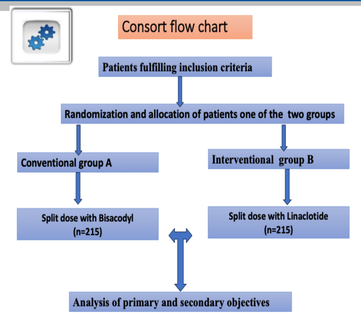
Before colonoscopy (questionnaire survey filled by the blinded endoscopy nurse)
- Compliance of bowel preparation (PEG)
- Patients' acceptability and tolerability of bowel preparation
- Drug compliance
- Sleep disturbance

During colonoscopy (Blinded Colonoscopist and endoscopy nurse)
- Quality of bowel preparation by using Boston Bowel Preparation Scale (BBPS)
- Endoscopic findings
- Caecal intubation time in minutes
- Withdraw time in minutes
- Total duration of procedure in minutes will be recorded
- Surgeons satisfaction with the quality of bowel preparation

After colonoscopy
- Patients' satisfaction rate, acceptability and tolerability of procedure performed
- Willingness to repeat the same preparatory regimen
- Incidence of adverse events
- Polyp /Adenoma/ Malignancy detection rate
- Patients' satisfaction with the whole bowel preparation and colonoscopy



Consort flow chart



RESULTS

Baseline parameters between the groups

Baseline Characteristics		PEG + Bisacodyl (n=215)	PEG + Linaclotide (n=215)	P-value
Age	(in years)	44.5 ± 33.5	46 ± 30	0.32
Sex	Female	86	93	0.79
	Male	131	120	
BMI (kg/m²)	<18.5	16	15	0.47
	18.5 - 22.9	150	172	
	23 - 24.9	34	21	
	25 and more	17	5	
Smoking	Yes	81	50	0.31
	No	134	165	
Alcohol	Yes	76	49	0.27
	No	139	166	
Comorbidities	Diabetes mellitus	85	99	0.29
	Diabetes mellitus and Hypertension	38	53	

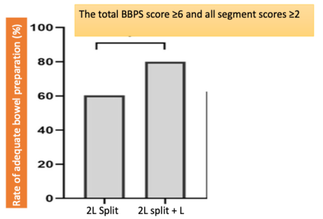
Comparison of the quality of bowel preparation

S.no	Variables	Split dose with Bisacodyl (n=215)	Split dose with Linaclotide (n=215)	P value
1.	Right side of colon (mean ± SD)	1.78 ±0.67	2.20 ±0.54	<0.001
2.	Mid-colon (mean ± SD)	2.23 ±0.70	3.50 ±0.54	<0.001
3.	Left colon (mean ± SD)	1.99 ±0.66	2.19 ±0.77	<0.001
4.	**Total BBPS score (mean ± SD)**	6.1 ±1.61	8.78 ±0.32	<0.001
5	Cecal intubation time (min, mean ± SD)	7.67 ±0.63	7.78 ±0.67	,0.076
6.	Withdrawal time (min, mean ± SD)	8.75 ±4.27	7.65 ±2.24	,0.026
7.	Total examination time (min, mean ± SD)	15.37 ±0.67	14.78 ±0.67	,0.003
8.	The first time of defecation (h, mean ± SD)	1.28) ±0.77	1.18 ±0.95	,0.001
9.	Defecating frequency	8.02 ±1.99	10.78 ±3.15	<0.001
10.	Preparation-to-colonoscopy interval (h, mean ± SD)	4.72 ±0.88	4.76 ±0.76	,0674
11.	**Polyp detection rate, n (%)**	27(16%)	44(21%)	<0.001
12.	**Adenoma detection rate, n (%)**	41(20%)	62(32%)	<0.001

Comparison of primary outcome between the two groups.

Parameters		PEG + Bisacodyl (n=215)	PEG + Linaclotide (n=215)	p-value
Mean Boston Bowel Preparation Scale (BBPS) Score		6.1 ± 0.9	**8.7 ± 0.8**	<0.001
Bowel Preparation Adequacy	**Excellent**	138 (63.49%%)	**160 (74.42%)**	< 0.93
	Good	67 (31.86%)	45 (20.93)	
	Fair	8 (3.72%)	9 (4.19%)	
	Poor	2 (0.93%)	1 (0.47%)	
Colonoscopy Success Rate	**Completed**	190 (88%)	**205 (95%)**	0.59
	Incomplete	25 (12%)	10 (5%)	

The rate of adequate bowel preparation between the two groups



Comparison of secondary outcome between the two groups

Secondary outcome		PEG + Bisacodyl (n=215)	PEG + Linaclotide (n=215)	p-value
Patient Satisfaction	**Very Satisfied**	173 (80.47%)	**192 (89.31%)**	1.0
	Moderately Satisfied	42(19.53%)	23 (10.69%)	
	Moderately Dissatisfied	0 (0.0%)	0 (0.0%)	
	Very Dissatisfied	0 (0.0%)	0 (0.0%)	
Patient Tolerability	Well tolerated	6 (2.8%)	5 (2.3%)	<0.05
	Mild discomfort	63 (29.3%)	104 (48.4%)	
	Moderate discomfort	**120 (55.8%)**	**81 (37.7%)**	
	Severe discomfort	26 (12.1%)	25 (11.6%)	
Compliance of Bowel Preparation	Excellent	73 (34.0%)	**92 (42.8%)**	0.03
	Good	125 (58.1%)	135 (62.8%)	
	Poor	0 (0.0%)	0 (0.0%)	
Overall Satisfaction	Excellent	6 (2.8%)	0 (0.0%)	<0.05
	Very Good	104 (48.8%)	**7 (2.9%)**	
	Good	107 (49.8%)	**208 (96.7%)**	
	Poor	0 (0.0%)	0(0.0%)	

The rate of patient adverse events and tolerance

Variables		Split dose with Bisacodyl (n=215)	Split dose with Linaclotide (n=215)	p - value
Adverse events, n (%)	Total	143(66%)	123(57%)	0.158[d]
	Nausea , n (%)	140(65%)	135(57%)	0.688[d]
	Vomiting , n (%)	150(69%)	165(76%)	0.188[d]
	Bloating n (%)	191(88%)	168(78%)	0.002[d]
	Abdominal Pain	193(89%)	150(70%)	0.071[d]
Willingness to repeat the colonoscopy, n (%)		165(76%)	203(94%)	**<0.001[d]**
Poor sleep , n (%)		153(71%)	166(77%)	0.688[d]

d Anova test

CONCLUSION

Our study demonstrates that the PEG + Linaclotide regimen is **superior** to PEG + Bisacodyl in achieving adequate BP in high-risk and chronically constipated patients.

ACKNOWLEDGMENTS AND FUNDING

This project was in part funded by JIPMER intramural Grant no. JIP 45 APR-JUNE 2023-24.