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Comparing Bowel Preparation Quality in Chronic Kidney Disease Patients: Low-Dose Polyethylene Glycol (PEG) vs. Low-Dose PEG with SenaGraph

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ABSTRACT

Background: Renal failure presents a critical concern in patients requiring colon preparation for colonoscopy, particularly in those with chronic kidney disease (CKD). In contemporary practice, polyethylene glycol (PEG) serves as a widely employed agent, while herbal alternatives like SenaGraph, standardized dry extract of Senna leaves (*Cassia angustifolia L.*), have demonstrated satisfactory efficacy. This study aimed to compare the quality of bowel preparation in CKD patients using low-dose PEG with and without Sena Graph.

Methods: This randomized clinical trial enrolled 122 patients with CKD who underwent colonoscopies at Imam Hussein Hospital in Tehran, Iran, during 2018 and 2019. Patients were randomly assigned to receive either PEG with SenaGraph or PEG alone. Comparative assessments included the Ottawa Score and measurements of sodium, potassium, urea, and creatinine levels.

Results: The study findings revealed that the mean Ottawa score was deemed acceptable (Ottawa score 0 or 1) in 90.2% of patients receiving PEG with SenaGraph and in 78.7% of patients in the PEG-only group, with statistically significant difference ($P = 0.049$). Alterations in sodium, potassium, urea, and creatinine levels showed no significant differences between the two groups ($P > 0.05$).

Conclusion: This investigation suggests that, in CKD patients requiring colonoscopy, the addition of Sena Graph to PEG could improve the efficacy of PEG. Furthermore, both agents exhibit a comparable safety profile for bowel preparation.

Keywords: PEG, Sena grafin, CKD, Colonoscopy.

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Introduction

Colonoscopy stands as the primary diagnostic tool for a variety of lower gastrointestinal lesions within the colorectal region. Typically, endoscopy is employed to evaluate patients with gastrointestinal bleeding or for malignancy screening (2, 3). This method is invaluable in diagnosing numerous gastrointestinal lesions (4) and ruling out certain differential diagnoses (5). Colonoscopy boasts a high diagnostic value and excellent safety profile (6). Proper colon preparation is a pivotal prerequisite for this procedure, as the absence of adequate preparation may necessitate repeating the colonoscopy in nearly twenty percent of cases (7). Key attributes of effective colon preparation encompass high safety, tolerability, cost-effectiveness, and efficient removal of colonic residues (8).

Given the rising incidence of colorectal cancer and the increasing demand for colonoscopy, primarily for screening purposes, it has evolved into a commonplace diagnostic procedure (6, 7). To enhance diagnostic success rates, effective colon preparation is paramount. The most frequently employed agent for this purpose is polyethylene glycol (PEG), an osmotic agent that does not undergo absorption but requires a substantial volume of water for optimal use (9). However, concerns regarding acute renal failure in individuals with chronic kidney disease (CKD) have prompted exploration of alternative agents such as SenaGraph (Iran Darouk company; Iran), a standardized dry extract of Senna leaves (Cassia angustifolia L.). Additionally, the use of a lower dose of PEG (two liters) compared to the standard dose (four liters) may reduce the risk of renal adverse effects but could also compromise colon preparation quality in some patients (10). Renal adverse effects are particularly concerning, especially in elderly subjects who may be at risk of renal failure (11).

The literature presents conflicting findings on the efficacy and safety of SenaGraph compared to PEG. While some studies report similar efficacy alongside additional adverse effects (11), others indicate reduced efficacy (12), which has limited its use. Conversely, occasional reports highlight the superior efficacy of SenaGraph over PEG (13, 14), further complicating the choice of preparation agent. The cost-effectiveness of SenaGraph represents an additional appealing aspect (15). SenaGraph, contains Hydroxyanthracene glycosides (16) that enhances colonic motility, resulting in alterations in absorption and excretion processes (17). Furthermore, Sena exhibits antimicrobial, anti-cancer, and antioxidant properties (18).

Thus, this study aims to compare the quality of bowel preparation in patients with chronic kidney disease using low-dose PEG and low-dose PEG with SenaGraph. If this combination proves effective without exacerbating renal failure, it may offer a viable option for patients with renal failure requiring colonoscopy.

Methods

In this triple-blind randomized clinical trial, we enrolled 122 consecutive patients diagnosed with CKD who underwent colonoscopy at Imam Hussein Hospital in Tehran, Iran, during the years 2018 and 2019. Inclusion criteria comprised individuals aged 18 years or older, a glomerular filtration rate (GFR) below 60, no history of colectomy, absence of contraindications for colonoscopy, absence of severe mental retardation, and non-pregnant/non-breastfeeding status. Exclusion criteria encompassed patients requiring dialysis with a GFR less than 15, an increase in creatinine exceeding 0.3 GFR or a reduction of over 50% in the last 3-4 days, oliguria, and symptoms of dehydration (urine output < 0.5 cc/kg/h) within the preceding six hours.

This study adhered to the principles of the Helsinki Declaration and received approval from the local ethics committee (IR-SBMU-MSP-REC.1398.803). Informed consent was obtained from all participating subjects. Patients were randomly assigned, using block randomization in groups of four cases, to receive either PEG with SenaGraph or PEG alone. The triple-blind design ensured that patients, physicians, statistical analysts, and healthcare staff remained unaware of the administered drug.

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We assessed and compared the Ottawa Score, as well as levels of sodium, potassium, urea, and creatinine among the groups. Colon preparation commenced 24 hours prior to the scheduled colonoscopy. Simultaneously, all nephrotoxic medications, including angiotensin receptor blockers (ARB)/angiotensin-converting enzyme (ACE) inhibitors, diuretics, and aminoglycosides, were discontinued. Urinary intake/output was meticulously recorded, and patients were continually monitored for hydration status, acute kidney injury (AKI), and the need for dialysis. The dietary regimen consisted of a homogenous fluid intake starting 24 hours before the colonoscopy. From 24 hours prior to the procedure, one group received a fluid containing Senozoid 90 mg and PEG 1000 ml (a total of 1100 ml), while the other group received 100 ml of water and PEG 1000 ml (also totaling 1100 ml). Both solutions were provided in identical, unlabeled containers.

Creatinine, urea, potassium, and sodium levels were assessed both before and after colonoscopy, with post-procedure assessments continuing daily for 48 hours. We utilized the Ottawa grading system for colon preparation classification, categorizing preparations into grades ranging from 0 to 4. Grades 0 and 1 indicated good preparation, while other scores denoted suboptimal preparation. Data analysis was performed by SPSS (version 25.0) statistical software. Utilized tests were Kolmogorov-Smirnov, Chi-square, Fisher, Independent-Sample-T, and Repeated-Measure ANOVA and the P values less than .05 were considered statistically significant.

Results

As depicted in Figure-1, the mean Ottawa score indicated "good" preparation in 90.2% of patients who received PEG with SenaGraph, compared to 78.7% in those who received PEG alone, and this difference was statistically significant (P=0.049). Notably, there were no significant differences in preparation quality based on age, as illustrated in Table 1. Furthermore, when examining the data by gender, no statistically significant disparities emerged, as detailed in Table 2. The presence of comorbid conditions such as diabetes and hypertension, as indicated in Figure 2, did not yield significant differences in preparation quality.

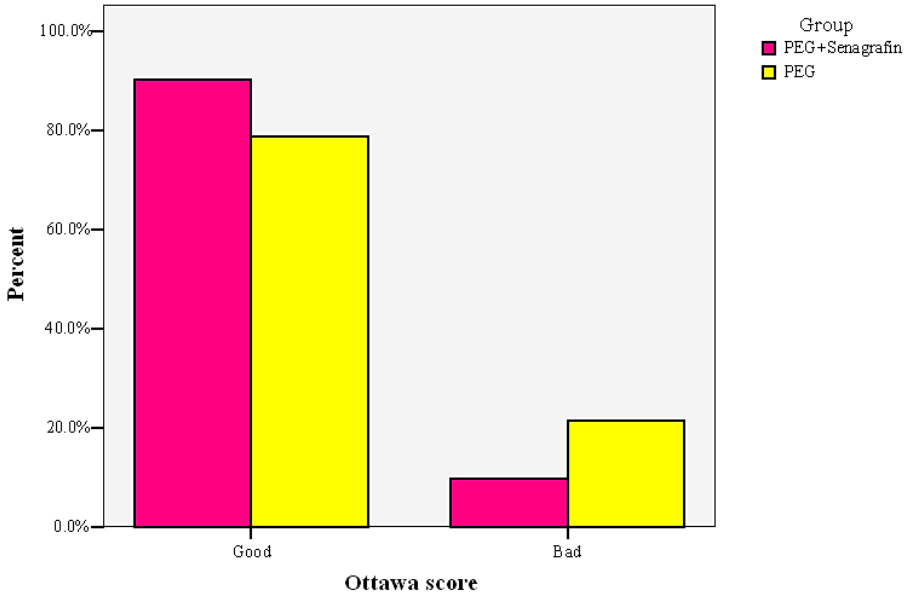

Figure 1. Bowel preparation quality in two groups

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Table 1. Bowel preparation quality according to age in groups

Group				Ottawa score		
				Good	Bad	Total
PEG+Senagafin	Age	<60	Count	21	4	25
			% within Age	84.0%	16.0%	100.0%
		>60	Count	34	2	36
			% within Age	94.4%	5.6%	100.0%
	Total		Count	55	6	61
			% within Age	90.2%	9.8%	100.0%
PEG	Age	<60	Count	23	5	28
			% within Age	82.1%	17.9%	100.0%
		>60	Count	25	8	33
			% within Age	75.8%	24.2%	100.0%
	Total		Count	48	13	61
			% within Age	78.7%	21.3%	100.0%

Table 2. Bowel preparation quality according to sex in groups

Group				Ottawa score		
				Good	Bad	Total
PEG+Senagafin	Sex	Male	Count	23	2	25
			% within Sex	92.0%	8.0%	100.0%
		Female	Count	32	4	36
			% within Sex	88.9%	11.1%	100.0%
	Total		Count	55	6	61
			% within Sex	90.2%	9.8%	100.0%
PEG	Sex	Male	Count	20	7	27
			% within Sex	74.1%	25.9%	100.0%
		Female	Count	28	6	34
			% within Sex	82.4%	17.6%	100.0%
	Total		Count	48	13	61
			% within Sex	78.7%	21.3%	100.0%

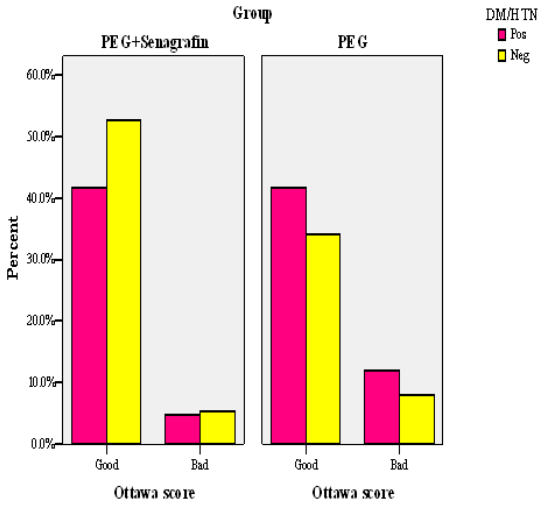

Figure 2. Bowel preparation quality according to background disease in groups

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Analysis of preparation quality in relation to patients' smoking status, as presented in Table 3, revealed no significant variations between the groups. Additionally, a patient's history of angiotensin receptor blocker (ARB) or angiotensin-converting enzyme inhibitor (ACEI) use did not exhibit a statistically significant association with Ottawa scores, as demonstrated in Figure 3 (P > 0.05). Importantly, the levels of creatinine, urea, sodium, and potassium remained consistent across both study groups, as indicated in Figure 4.

Table 3. Bowel preparation quality according to smoking in groups

Group				Ottawa score		
				Good	Bad	Total
PEG+Senagafin	Smoking History	Pos	Count	8	1	9
			% within Smoking History	88.9%	11.1%	100.0%
		Neg	Count	47	55	52
			% within Smoking History	90.4%	9.6%	100.0%
	Total		Count	55	6	61
			% within Smoking History	90.2%	9.8%	100.0%
PEG	Smoking History	Pos	Count	8	2	10
			% within Smoking History	80.0%	20.0%	100.0%
		Neg	Count	40	11	51
			% within Smoking History	78.4%	21.6%	100.0%
	Total		Count	48	13	61
			% within Smoking History	78.7%	21.3%	100.0%

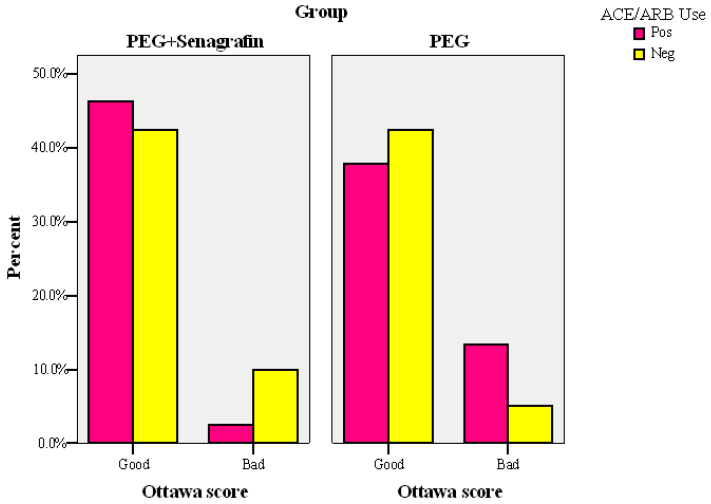
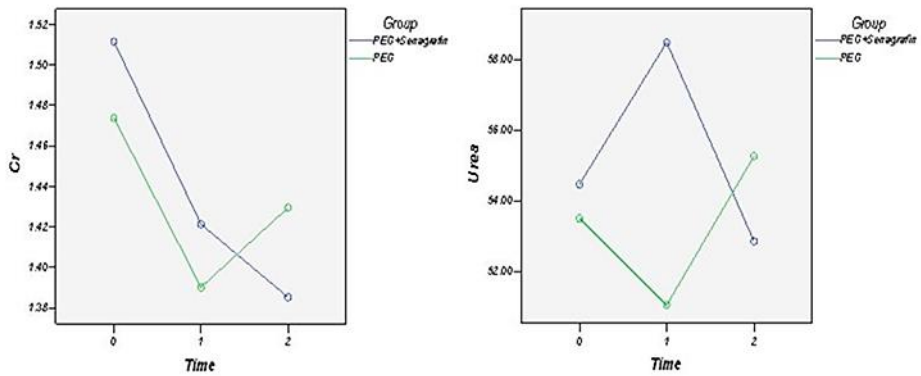


Figure 3. Bowel preparation quality according to ARB/ACEI in groups



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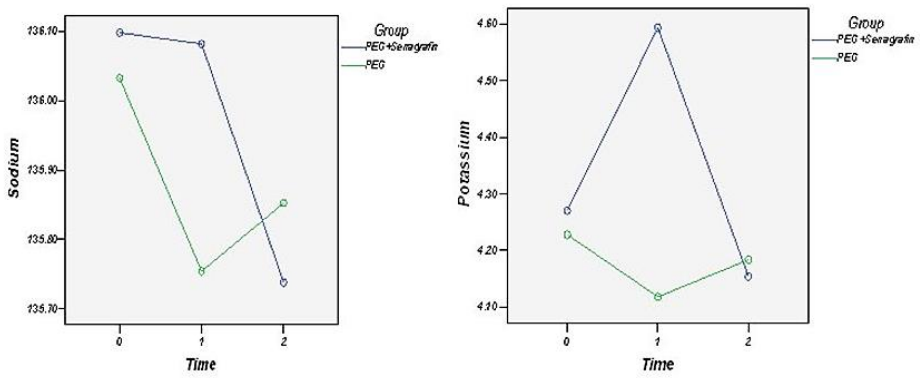

Figure 4. Alterations in creatinine, urea, sodium, and potassium level in two groups

Discussion

This study unveiled a noteworthy and statistically significant difference in bowel preparation quality when comparing the combination of PEG (polyethylene glycol) and SenaGraph to PEG alone. An impressive 90.2% of patients receiving PEG with SenaGraph achieved a "good" preparation status, as opposed to 78.7% in the PEG-alone group. Surprisingly, despite this disparity in bowel preparation quality, there were no discernible distinctions in creatinine, urea, sodium, or potassium levels between the two study groups. Moreover, various background factors had no discernible impact on the overall preparation status. These results strongly suggest that the utilization of SenaGraph can notably enhance bowel preparation quality without introducing additional renal adverse effects.

Our finding contrasts with the findings of Terri et al. (10), who compared SenaGraph to PEG in a pediatric population and reported a preparation status of 29% with SenaGraph versus 88% with PEG, indicating a lower efficacy of SenaGraph, although the safety profile remained consistent. Likewise, Poyrazoglu et al. (14) compared SenaGraph to sodium phosphate for bowel preparation and reported a lower efficacy for SenaGraph. However, both above studies, like ours, found no significant differences in safety profiles between the groups. In another study, Khorasanynejad et al. (8) compared SenaGraph (c-lax) to PEG for bowel preparation and observed no significant differences between the groups. Conversely, Alghamry et al. (19), like our study, compared PEG alone to PEG plus acarbose and found that the combination modality exhibited better efficacy in elderly subjects. Notably, our study, with a similar age distribution across groups, revealed that age did not exert a significant influence on the outcomes.

Zakeri et al. (20) conducted an animal model study comparing PEG, SenaGraph, and their combination, reporting no discernible effects on serum levels of various markers indicative of abnormal levels. Likewise, Avizeh et al. (21) compared PEG and SenaGraph in animal models, attesting to the same efficacy for both agents and similar safety profiles, aligning with our current study's findings. Furthermore, Shafaghi et al. (22) reported no significant alterations in sodium, calcium, and phosphate levels following PEG use in 50 colonoscopy cases, which paralleled our own study's results, where no significant differences in serum markers were observed between the groups. Moreover, Agah et al. (23) compared the effects of various PEG doses for bowel preparation among 117 cases and, conteart to our findings, found no significant differences.

Consequently, our study suggests that SenaGraph could be a beneficial addition to PEG for bowel preparation in patients with CKD requiring colonoscopy. Nonetheless, it is crucial to acknowledge the limitations of this study, which include non-compliance among some patients with regard to enrollment and the single healthcare center assessment, potentially limiting the generalizability of the findings. Future studies involving larger and more diverse sample populations, conducted across multiple centers,

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may provide further insights and enhance our ability to make informed decisions regarding the optimal modality for bowel preparation in this patient population.

This study showed that in patients with CKD needing colonoscopy the PEG with SenaGraph versus without had a better efficacy and therefore addition of SenaGraph to PEG is recommended. The main limitations in this study were lack of compliance for enrollment in the study by some patients and also assessment in one health care center that led to lower generalization capability. Further studies with larger sample population and multi-canter sampling can help to better decision making about the best modality for bowel preparation.

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Competing Interests: The authors declare no conflicts of interest .

Data availability: The data that supports the findings of this study are available from the corresponding author upon reasonable request.

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