

Original Article**High dose Senna or Poly Ethylene Glycol (PEG) for elective colonoscopy preparation: a prospective randomized investigator-blinded clinical trial**

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Abstract

BACKGROUND: The aim of this study was to determine the efficacy of two methods of colon preparation for colon cleansing in a randomized controlled trial.

METHODS: In this prospective randomized investigator-blinded trial, consecutive outpatients indicated for elective colonoscopy were randomized into two groups. Patients in Senna group took 24 tablets of 11 mg Senna in two divided doses 24 hour before colonoscopy. In Poly Ethylene Glycol (PEG) group they solved 4 sachets in 4 liters of water the day before the procedure and were asked to drink 250 ml every 15 minutes. The overall quality of colon cleansing was evaluated using the Aronchick scoring scale. Difficulty of the procedure, patients' tolerance and compliance and adverse events were also evaluated.

RESULTS: 322 patients were enrolled in the study. There was no significant difference in the quality of colon cleansing, patients' tolerance, compliance and the difficulty of the procedure between two groups ($p > 0.05$). The incidence of adverse effects was similar between two groups except for abdominal pain that was more severe in Senna group ($p < 0.05$) and nausea and vomiting that was more common in PEG group ($p < 0.05$)

CONCLUSIONS: In conclusion we deduce that Senna has the same efficacy and patient's acceptance as Polyethylene glycol-electrolyte solution (PEG-ES) and it could be prescribed as an alternative method for bowel preparation.

KEYWORDS: Senna, Poly ethylene glycol, Colon preparation, Colon cleansing, Clinical trial, Adverse effects.

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Nowadays colonoscopy has become an essential procedure for detection and treatment of colonic lesions and investigating the bowel. Preparing a clean colon before colonoscopy is essential to obtain an accurate diagnosis and meaningful visualization during colonoscopy.¹

An ideal colon preparation should meet the following criteria: 1) easy on patients; 2) need little time; 3) have few adverse reactions; 4) clean colon mucosa adequately; and 5) have the best cost-effectiveness profile.²

In the past decades, several studies have been performed and various bowel prepara-

tion methods have been proposed including castor oil, anthraquinones, Diphenylmethanes, Phenolphthalein, Magnesium Citrate, Poly Ethylene Glycol (PEG), Sodium Phosphate (NaP).³⁻⁷ PEG and NaP preparations are the most popular regimens for colon cleansing worldwide.⁸

But despite their proven efficacy, they are still far from ideal.

The unpleasant taste and large volume of PEG frequently lead to poor compliance with recommended dosing regimens, often causing patients significant dissatisfaction with the procedure.⁹⁻¹¹

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Most of studies that have been conducted to compare NaP and PEG solutions have suggested a superiority or equivalence of NaP in preparing mechanical bowel adequately and safely.¹²⁻¹⁵

In other hand, considering the financial aspects, NaP is more beneficial and increases the patient's compliance.^{13,14,16}

However NaP has several limitations in the application such as fluid shifts and precipitating intravascular volume depletion and could not be used in patients with congestive heart failure, renal failure, and decompensate cirrhosis.¹⁷

Stimulant laxatives, such as Bisacodyl and Senna (an herb), and Anthraquinones, were widely used for colonoscopy preparation in past decades and now they are commonly used for treatment of constipation.^{4,17} However experiences are limited and results are conflicting on their use as single oral agents for colon cleansing.¹⁸⁻²⁰ There are some studies that counteracted previous investigations and revealed that bowel preparation with Senna was more effective than PEG in achieving a successful preparation for elective colonoscopy and could be tolerated better.^{17,18,20} All of these show that the use of Senna in single for preparation is a controversial issue.

In this study we aimed to compare the colon cleansing, difficulty of procedure and patient's compliance in patients who used Senna or PEG in preparation for colonoscopy.

Methods

Trial Design and Participants

This study was an investigator blinded randomized clinical trial which carried out in the tertiary referral gastroenterology centers (Noor, Aliasghar Hospital and Al-Zahra Hospital), in Isfahan, Iran.

During a period of 18 months consecutive outpatients who referred to the gastroenterology clinic indicated for colonoscopy were enrolled in the study. Patients were excluded from the study if each of the following criteria were existed: 1) age under eighteen; 2) previous colon resection; 3) presence of any contraindications for colonoscopy (uncontrolled con-

gestive heart failure [American heart society class 3 and 4]); 4) major psychiatric disease; 5) pregnancy or breastfeeding; and 6) refusal to give consent.

All endoscopies were performed at Al-Zahra Hospital in the evening under the conscious sedation (Midazolam and Meperidine) by two expert gastroenterologists.

Sample size was calculated using statistical formula according to recent similar studies. The $\alpha = 0.05$ and power was 80% ($\beta = 0.2$).

Intervention

The eligible patients were randomized according to random allocation software and one of the project investigators sequentially determined the assigned bowel preparation using closed envelopes. Detailed written instructions regarding the assigned bowel preparation were given to all patients.

Patients assigned to Senna group were instructed to take 24 tablets in divided doses, the first twelve at 2 P.M. and the other twelve at 10 P.M. the day before the colonoscopy. They were also advised to drink clear liquids. Each Senna tablet (Senamed, Iran Darvak, Tehran, Iran) contains 9-11 mg of Sennoside A and B.

In the PEG group, patients received 4 sachets in 4 liters of water the day before the procedure and were asked to drink 250 ml every 15 minutes beginning at 5 P.M. in the evening until 4 l were consumed. They were also instructed to begin a clear liquid diet on the morning of the day before colonoscopy and to fast after midnight.

The drug product which was used in this group was Pidrrolax (produced by Sepidaj drug company, Tehran, Iran); each sachet contains 70 g of PEG.

Outcomes

Primary outcome in this study was quality of overall colon cleansing; this was assessed using validated Aronchick scale²¹ that has been used in previous studies for the same purpose.

Secondary outcomes included difficulty of the procedure, patients' tolerance and compliance, and severity of adverse events.

Table1. Demographic and patients characteristics in both Senna and PEG groups

	PEG	Senna	P value
Male, No (%)	84 (51.5)	79 (48.5)	p > 0.05
Age, Mean ± SD	45.16 ± 16.19	44.23 ± 15.61	p > 0.05
Weight, Mean ± SD	68.12 ± 13.73	67.31 ± 13.44	p > 0.05
Indication for colonoscopy, No (%):			
Rectoragia	70(41.18)	56(36.84)	
Chronic diarrhea	26(15.30)	23(15.13)	p > 0.05
Iron deficiency anemia	22(12.94)	23(15.13)	
Colon cancer	15(8.82)	10(6.57)	
Others	37(21.76)	40(26.31)	

Difficulty of the procedure was rated by the endoscopist (1 = easy, 2 = fairly easy, 3 = difficult, 4 = failure to complete the examination).

Patients' tolerance was determined using a questionnaire. They were asked to rate their tolerance of the preparation with a scale from 1 to 4 (1 = very comfortable, 2 = comfortable, 3 = uncomfortable, 4 = very uncomfortable).

Compliance of the patients to the regimen was assessed by asking the patients if they completed the dosing regimen as prescribed or not.

In order to assess safety, patients were asked to rank the severity of side effects of the drugs, including nausea, abdominal pain, vomiting, dizziness, or headache during the preparation period, as follows: 1 = absent, 2 = mild, 3 = moderate, 4 = severe.

All outcomes were gathered by a questionnaire which completed by the study co-investigators and a data collection form that was fulfilled by the endoscopists. In this study participants were aware of the preparation methods and only the endoscopist was blinded about the method. To prevent unbinding of endoscopist patients were also advised not to discuss about their preparation method with the endoscopist during the procedure.

Informed consents were obtained from all patients and the protocol was approved by the

ethical committee of Isfahan University of Medical Sciences.

Statistical analysis was performed using the statistical software SPSS XV. Comparison between groups was done with Mann-Whitney, Chi square and t-test as needed. Statistical difference considered significant if p < 0.05.

Results

Patients' Characteristics

A total number of 322 patients (163 men, 159 women) were enrolled in the study and randomized into 2 groups: 152 patients were assigned in Senna group and 170 in PEG group.

The mean age of the patients was 44.37 year (SD = 15.9, range: 18 to 86). All of them took the study product and included in the analysis.

As it is shown in table 1, there was no statistically significant difference between two groups regarding age, gender, weight and indication for colonoscopy.

Effectiveness of Colon Cleansing

Overall colon cleansing (primary outcome) was compared between study groups using Mann-Whitney test; there was no statistically significant difference (p > 0.05). Detailed information on colon cleansing in PEG and Senna groups is presented in table 2.

Table2. Colon cleansing in PEG and Senna group

Kind of drug	Mean rank	The colon cleansing power, No (%)				P value
		Excellent	Good	Fair	Inadequate	
PEG (n = 170)	162.27	69 (40.6)	48 (28.2)	37 (21.8)	16 (9.4)	p = 0.83
Senna (n = 152)	160.81	64 (42.1)	37 (24.3)	33 (21.7)	18 (11.8)	

Table 3. Tolerability of the preparation method in each group

Kind of drug	Mean rank	Tolerability, No (%)				P value
		Very comfortable	Comfortable	Uncomfortable	Very uncomfortable	
PEG (n = 170)	161.56	89 (52.4)	46 (27.1)	27 (15.9)	8 (4.7)	p = 0.97
Senna (n = 152)	161.45	80 (52.6)	42 (27.6)	18 (11.8)	12 (7.9)	

Twenty procedures (9 in Senna group and 11 in PEG group) were failed due to insufficient bowel preparation; the difference was not significant (p > 0.05).

Patients' Compliance and Adverse Events

Compliance to the preparation was not statistically different in two groups: 81.5% patients in Senna group and 73.6% in PEG group (p > 0.05).

Regarding patients' tolerance, 19.7% in Senna group and 20.6% in PEG group reported that the preparation method was uncomfortable and very uncomfortable for them. Detailed data are shown in table 3 (p > 0.05).

The frequency of adverse events and their severity were compared. Patients in Senna group suffered from abdominal pain more than those in PEG group (p < 0.05). On the other hand nausea and vomiting had higher rates in PEG group (p < 0.05). Headache and

vertigo was the same in both groups (p > 0.05). More details are shown in table 4.

Investigator Blindness

We evaluated our investigator blindness using this question that what was his estimation for preparation agent in that colonoscopy. The analysis of results showed that our endoscopist's answers were true in 50%.

Discussion

As it is known the success of colonic examination mainly depends on the quality of bowel cleansing and the patient's acceptance.^{17,22} There are several methods for bowel preparation before colonoscopy; however the ideal method is still a controversial issue.²³ Nowadays, NaP and PEG-ES have widely been used for bowel preparation but there are problems in compliance and safety with these regiments.^{8,23}

Table 4. Frequency and severity of adverse events in each preparation group

	Mean rank	None n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	P value
Nausea:						
PEG	172.94	91 (53.5)	57 (33.5)	11 (6.5)	11 (6.5)	p = 0.0070
Senna	148.71	104 (68.4)	35 (23)	7 (4.6)	6 (3.9)	
Vomiting:						
PEG	167.9	148 (87.1)	14 (8.2)	3 (1.8)	5 (2.9)	p = 0.0090
Senna	154.34	145 (95.5)	5 (3.3)	2 (1.3)	0	
Headache:						
PEG	167.03	117 (68.8)	35 (20.6)	7 (4.1)	11 (6.5)	p = 0.1430
Senna	155.32	115 (75.7)	26 (17.1)	6 (3.9)	5 (3.3)	
Dizziness:						
PEG	164.08	132 (77.6)	27 (15.9)	5 (2.9)	6 (3.5)	p = 0.4590
Senna	158.62	123 (80.9)	21 (13.8)	5 (3.3)	3 (2)	
Abdominal pain:						
PEG	126.44	118 (69.4)	37 (21.8)	9 (5.3)	6 (3.5)	p = 0.0001
Senna	200.71	45 (29.6)	48 (31.6)	24 (15.8)	35 (23)	

Previous studies showed that PEG is a fast, effective and safe diet but it had been reported that some patients did not complete the preparation procedure with this method because of poor palatability, large volume or adverse effects such as nausea and vomiting.^{24,25} Senna laxative is another method for bowel preparation but fear of adverse effects might be responsible for its underuse. However it should be considered that these adverse effects are uncommon and result of long term and large amount usage.

There are studies performed by Farca Bel-saguy et al, Chilton et al, and Valverde et al showed that Senna solution alone or in combination with other cathartics was more effective than PEG.^{18,25,26} On contrary, other studies by Dahshan et al and Arezzo et al showed that those other laxatives were better than Senna.^{27,28} Also Radaelli et al compared an oral high dose of Senna (24 tablets of 12 mg) with standard 4 l PEG-ES lavage solution in 388 patients undergoing elective colonoscopy. They found that high dose of Senna was more effective than PEG in achieving a successful preparation for elective colonoscopy.¹⁷ Our study revealed that 24 Senna tablets of 11 mg had no significant difference in colon cleansing results, and the overall colon cleansing was the same between two study groups.

However there is an important point to be considered; the bowel cleansing may be affected by other factors such as gender, age, race, and previous abdominal surgeries.²⁸

Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

AS and MK designed the study. GT, AN, MH, BS, FM, FR and PN collected the data and interviewed the patients. AS and MM performed the colonoscopies. MK, BS, GT and AN analyzed the data. MK, GT, AN, BS, FR, PN, MH and FM drafted the manuscript and it has been revised by AS, AN, MK, GT and MM. All authors have read and approved the content of the manuscript.

The data in table 4 show the frequency of adverse effects in both study groups. We found that the occurrence of adverse reactions was similar in both groups except for abdominal pain which was more severe in Senna group and nausea and vomiting that were more in PEG group. These were similar to other studies except for abdominal pain which was higher in Senna group in our study (23%). This might be in relation with race difference.

Also, we noticed that, despite adverse effects, patient convenience the day before colonoscopy in Senna group was better than PEG. The majority of patient could work or perform usual activities the day before colonoscopy in Senna group.

The limitation of this study was that we evaluated outpatients administered for elective colonoscopy and the result therefore cannot be generalized to other population or practice setting like urgent colonoscopy.

Conclusions

In conclusion we deduce that Senna has the same efficacy and compliance and adverse events as PEG solution and it could be prescribed as an alternative method for bowel preparation.

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