

## Adding stewed apricot juice to senna improves quality of colon cleansing in preparation for colonoscopy

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### ABSTRACT

**Background:** To achieve optimal colonoscopic examination, the bowel must be sufficiently cleansed. However, none of the currently available colonoscopy preparation regimens is safe, efficient, and comfortable. The aim of this study was to determine whether adding stewed apricot juice to senna increased patient comfort and improved bowel cleansing during colonoscopy preparation.

**Methods:** Outpatients of both genders who were over 18 years old and were referred for elective colonoscopy were randomly allocated to drink stewed apricot juice with senna or senna by itself. The quality of the colon cleansing was evaluated using the Ottawa scale. Patient tolerance and adverse events were evaluated through the completion of a questionnaire.

**Results:** The study included a total of 128 patients in the randomization procedure. A significantly greater cleansing effect was observed using stewed apricot juice plus senna in the right and transverse colon ( $p = 0.038$ ,  $p = 0.037$  respectively). It was also determined that in the stewed apricot juice plus senna group, overall cleansing was superior ( $p < 0.001$ ), total colonoscopy (17.6 min vs. 22.8 min,  $p = 0.048$ ) and cecal intubation (7.4 min vs. 11.2 min,  $p = 0.042$ ) times were shorter, and the colonoscopy procedure was easier (79.4% vs. 49.2%,  $p < 0.001$ ). No differences were observed between the groups with respect to patient acceptance, compliance, and adverse

events. In the stewed apricot juice plus senna group, 91.2% of patients stated their willingness to receive the same regimen in the future compared to 80% of the patients in the senna alone group ( $p = 0.037$ ).

**Conclusion:** The addition of natural, stewed apricot juice to senna significantly improves cleansing outcomes without additional adverse effects.

**Clinical trial registration number** is NCT02665624, and the validity date is 24.01.2016.

**Keywords:** bowel cleansing, colonoscopy, stewed apricot juice, senna.

## BACKGROUND

In the diagnosis of colon cancer and polyps, colonoscopy is the current standard method, a method which can also be used for therapeutic interventions including polypectomy. However, the diagnostic accuracy and therapeutic safety of the procedure depends on the quality of the colonic cleansing [1]. Inadequate bowel preparation may result in missed precancerous lesions, longer colonoscopy time, lower cecal intubation rates, and increased electrocautery risks [2]. It also leads to additional costs because the colonoscopy either has to be re-scheduled or alternative examinations have to be planned [3].

Although polyethylene glycol (PEG) and sodium phosphate (NaP) are the main cleansing solutions used in current practice, they tend to be poorly tolerated. Patient compliance is decreased due to requirement of ingesting a large volume of fluid and the unpleasant, salty taste of PEG [4]. To overcome these limitations, split-dose administration of PEG has been reported to be an effective method which is better tolerated by patients [5]. However, PEG solutions are not available in some countries due to marketing problems. The potential risk for clinically significant alterations in serum electrolyte levels and hemodynamic instability in patients with renal failure, congestive heart failure, uncontrolled hypertension, and ascites also limit the usage of NaP. Moreover, the European Society of Gastrointestinal Endoscopy (ESGE) suggest that oral NaP can only be advised in selected cases, such as when patients are unable to tolerate other agents and within individuals who are at low risks of experiencing NaP-related adverse effects [6]. Unfortunately, insufficient bowel cleansing has been reported in 20% of patients who consume PEG or NaP [7]. Consequently, due to the limitations of NaP and unavailability of PEG solutions, senna is the primary colonoscopy preparation in some countries.

The ideal colonoscopy preparation would reliably empty the colon without causing discomfort within patients. Unfortunately, there is currently no preparation which meets all of these criteria [1]. Thus, numerous clinical trials have assessed prokinetic and spasmolytic agents, ascorbic acid, olive oil, orange juice, and pineapple juice in an effort to improve the effectiveness and tolerance of colonoscopic preparation regimens [8-13]. From these preparations, the use of prokinetic and spasmolytic agents has not had any additive effects. However, some authors have determined that other agents provide better colon cleansing with a higher rate of patient satisfaction.

The direct effect of senna on intestinal mucosa increases colonic motility, enhances colonic transit, and inhibits water and electrolyte secretion [14]. Despite previous cases where senna was successfully used, PEG and NaP solutions are currently used. Senna has a pleasant taste and is well-tolerated, inexpensive and has fewer adverse events, although its efficacy is controversial.

Apricot (*Prunus armeniaca*) has an important place in human nutrition and is widely believed

to improve various gastrointestinal disorders. Apricot consumption results in relief of gastroesophageal reflux symptoms and dyspepsia by improving digestive motility. It was also reported that apricot has a preventive effect on chronic atrophic gastritis by inhibiting *Helicobacter pylori* [15]. Dried apricots have traditionally been used in Mediterranean countries as a remedy for constipation due to their high fiber content. It was shown that fiber from apricot ingestion has a laxative effect by producing fecal fat excretion, which also has a bulking effect, thereby inducing changes in the composition of intestinal flora in a low-fiber, diet-induced constipation rat model [16]. Although this fruit is already widely consumed to the best of our knowledge, there has been no study examining the effects of apricot juice on precolonoscopic preparation. In the current study, we investigated whether stewed apricot juice intake would increase patient comfort and improve bowel cleansing during bowel preparation using senna.

## **METHODS**

This prospective, randomized, investigator-blinded study was conducted at Camlica Erdem and Haydarpaşa Numune Training and Research Hospitals. The study protocol was reviewed and approved by the Haydarpaşa Numune Training and Research Hospital Ethical Committee, Istanbul, Turkey on 26.01.2015 (approval number HNEAH-KAEK 2015/KK/04). Informed consent was obtained from all study participants. The authors had no relationship with either the laxative or apricot manufacturers used. No funding for the study was requested or accepted.

### ***Patients***

The study included outpatients of both genders, aged over 18 years, who were referred for elective colonoscopy. Exclusion criteria included the following: (i) history of renal, cardiac, hepatic or metabolic disease; (ii) diabetes mellitus; (iii) history of colonic resection; (iv) hospitalized patients; (v) pregnancy and breast-feeding; (vi) history of inflammatory bowel disease; (vii) known allergy to senna.

### ***Study Design***

The patients' medical histories, demographic data and indications for colonoscopy were recorded at the time of referral for colonoscopy. During the same clinical examination, patients were randomly assigned to one of two groups using a computer-generated random numbers table. They were instructed by the study nurse on how to drink the bowel preparations. Patients who were assigned to the group with stewed apricot juice intake were also given 300 grams of dried apricots and verbal instructions describing the preparation of the liquid.

### ***Bowel Preparation Protocol***

All patients were instructed to adhere to clear liquid diets one day before the procedure and to only drink water between midnight and the two hours preceding the colonoscopy. Group A patients received 75 ml of senna solution (containing 150 mg sennoside A+B calcium) (X-M solution, Yenisehir Pharmaceuticals, Turkey) at 18:00 on the day before their colonoscopies, and at 06:00 on the morning of the procedure. An additional one liter of stewed apricot juice was required to be consumed at least two hours before the colonoscopy. Group B patients received the above-mentioned senna solutions but no stewed apricot juice. All the patients drank at least an additional 1.5 liters of water and were requested to record the number of cups they drank.

### ***Colonoscopy Procedure and Data Collection***

A nurse-administered questionnaire was completed by the patients on arrival at the endoscopy unit to assess their tolerance and adverse effects experienced during preparation. The questionnaire included 18 items which had been used in similar previous studies [7, 11, 17]. All patients were told not to discuss their regimen with the endoscopy unit staff. To provide consistency, all the colonoscopies were carried out under conscious sedation between 09:00 and 12:30 by the same endoscopist who was blinded to the study groups. Standard white-light adult colonoscopes (Pentax EC-3880 LK colonoscope) were used for all examinations. The cecal intubation, withdrawal and total colonoscopy time, endoscopic diagnosis, and additional therapeutic procedures (including polypectomy) were recorded. At the end of the colonoscopy, the difficulty of the procedure was rated by the endoscopist using the scale (1 = easy, 2 = fairly easy, 3 = difficult, and 4 = failure to complete the procedure) which was previously used by Radaelli et al. [18]. The quality of the colon cleansing was evaluated using the validated Ottawa Bowel Preparation Quality Scale (Table 1) [19]. The score was calculated by adding 0 to 4 ratings for the recto-sigmoid, transverse, and right colon separately and a 0 to 2 fluid quantity rating. The authors performed a calibration exercise before using the scale in this study.

The primary endpoint of the study was the quality of overall colon cleansing. For this purpose, scores of 0, 1, and 2 were accepted as adequate preparations of each colonic segment, whereas scores of 3 and 4 were considered inadequate. Secondary endpoints included the quality of cleansing in the right colon and patient tolerance.

**Table 1.** Ottawa Bowel Preparation Quality Scale

<b>Score</b>	<b>Description</b>
0	No fluid
1	Able to see mucosa without aspiration
2	Able to see mucosa after aspiration
3	Able to see mucosa after both washing and aspiration
4	Solid stool, incapable of aspiration

### ***Statistical Analysis***

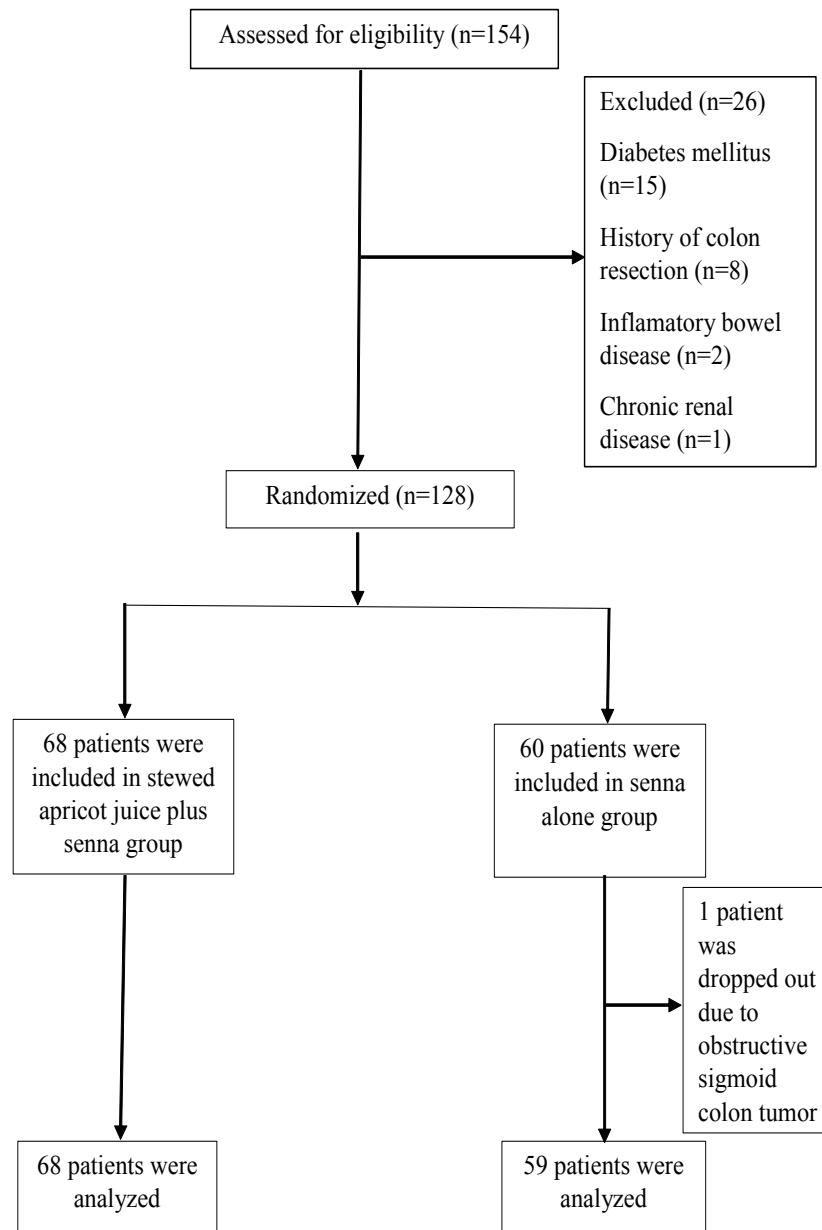
The sample size calculation was based on the primary objective of this study. The primary outcome of this study was the efficacy of bowel preparation measured by the Ottawa Bowel Preparation Quality Scale, which ranges from 0 to 14. Our previous study demonstrated that the values were evenly distributed across the 15-point scale with a mean of 5.0 points and standard deviation (SD) of 1.927 points. We considered a 1-point average difference between groups to be minimally clinically significant. Therefore, we used a 1-point margin of equivalence to test the superiority of the senna plus stewed apricot juice group. It was assumed that with an SD of 2.6 and 48 individuals per arm, a chi-squared test would be performed at a significance level of 0.05, with a required power of at least 95% and an  $\alpha$ -value of 0.025 to detect the stated difference in success rates.

All statistical analyses were performed using SPSS for Windows v. 15 (SPSS Inc., Chicago, IL, USA). Demographic and endoscopic features were classified as continuous or categorical variables. The distribution of the data was evaluated using the Kolmogorov–Smirnov test. The data were expressed as arithmetic mean  $\pm$  standard deviations (SD) since the evaluated variables were Gaussian distributed. Comparisons between the two groups were made using a Student's *t*-test for continuous variables. Categorical variables were compared using a chi-squared test or Fisher's exact test, as appropriate. All reported *p* values were two-tailed, with a value of *p* < 0.05 being considered statistically significant.

**RESULTS**

The eligibility of a total of 154 consecutive patients was assessed. Of these patients, 26 patients were excluded for the following reasons: diabetes mellitus (15), history of colonic resection (8), inflammatory bowel disease (2), and chronic renal disease (1). Thus, 128 patients were included in the randomization procedure: Group A comprised 68 patients assigned senna plus stewed apricot juice while Group B comprised 60 patients assigned senna alone. In Group B, 1 patient was withdrawn from the study due to obstructive sigmoid colon cancer.

A flowchart of the study is shown in Figure 1. No significant differences were determined between the two groups with respect to age, gender, body mass index, and indications for colonoscopy (Table 2).



**Figure 1.** Flowchart of the study.

**Table 2.** Demographic Data and Colonoscopy Indications

	<b>Stewed apricot juice plus senna group (n = 68)</b>	<b>Senna alone group (n= 59)</b>	<b>p value</b>
Age (y), mean $\pm$ SD	51.8 $\pm$ 15.6	48.9 $\pm$ 15.1	0.292
Gender, n (%)			
Male	31 (45.6%)	21 (35.6%)	0.253
Female	37 (54.4%)	38 (64.4%)	
BMI, mean $\pm$ SD, kg/m <sup>2</sup>	26.85 $\pm$ 4.62	27.26 $\pm$ 6.51	0.713
Indication for colonoscopy, n (%)			
Bleeding-anemia	30 (44.1%)	29 (49.2%)	
Abdominal pain	18 (26.5%)	13 (22.0%)	
Change in bowel habits	4 (5.9%)	2 (3.4%)	0.687
Family history of colon cancer/polyp surveillance	4 (5.9%)	6 (10.2%)	
Others	12 (17.6%)	9 (15.2%)	

**Procedure Data**

Cecal intubation was achieved in 100% of patients. Total colonoscopy (17.6 min vs. 22.8 min,  $p = 0.048$ ) and cecal intubation (7.4 min vs. 11.2 min,  $p = 0.042$ ) times were shorter in Group A compared to Group B. No significant differences in endoscopic findings were determined between the groups ( $p = 0.723$ ). However, polyp detection rates were slightly higher in Group A (27.9% vs. 22%) (Table 3). The colonoscopy procedure was performed more easily in Group A than in Group B (79.4% vs. 49.2%,  $p < 0.001$ ).

**Table 3.** Procedure Outcomes

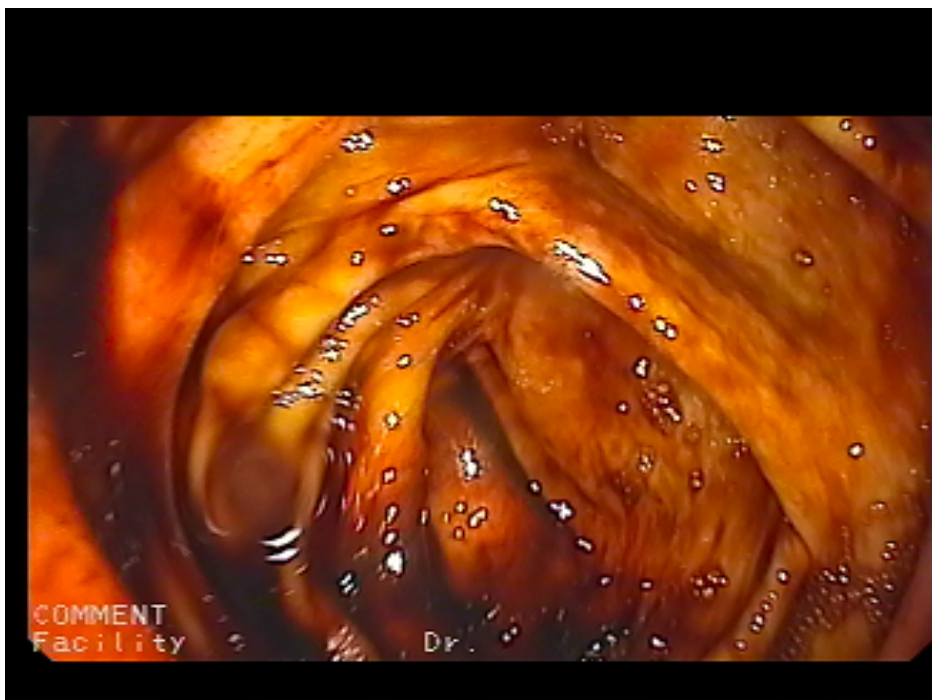
	<b>Stewed apricot juice plus senna group (n = 68)</b>	<b>Senna alone group (n= 59)</b>	<b>p value</b>
Duration of colonoscopy, min	17.69 $\pm$ 3.16	22.85 $\pm$ 3.17	0.048
Cecal intubation time, min	7.45 $\pm$ 2.29	11.26 $\pm$ 2.27	0.042
Endoscopic findings, n (%)			
No mucosal lesions	35 (51.5%)	34 (57.6%)	
Polyps	19 (27.9%)	13 (22.0%)	
Cancer	0 (0%)	2 (3.4%)	0.723
Diverticulosis	3 (4.4%)	3 (5.1%)	
Colitis	8 (11.8%)	5 (8.5%)	
Others	3 (4.4%)	2 (3.4%)	
Technical difficulty, n (%)			
Easy	54 (79.4%)	29 (49.2%)	
Fairly easy	12 (17.6%)	25 (42.3%)	< 0.001
Difficult	2 (2.9%)	5 (8.5%)	

### ***Evaluation of Bowel Cleansing***

The quality of bowel cleansing was evaluated for the left, transverse, and right colon separately. A statistically significant difference was determined between the groups with respect to the right and transverse colon ( $p = 0.038$ ,  $p = 0.037$  respectively). A significantly better cleansing effect was seen in Group A compared to Group B (Figures 2 and 3).



**Figure 2.** Endoscopic view of the cecum. Colon cleansing with senna and stewed apricot juice.



**Figure 3.** Colon cleansing with senna alone.

No statistically significant difference was determined between the groups with respect to the cleansing effects in the left colon ( $p = 0.745$ ). Overall cleansing was adequate in 64 examinations in Group A and in 33 examinations in Group B (94.1% vs. 55.9%,  $p < 0.001$ ) (Table 4).

**Table 4.** The Effectiveness of the Bowel Cleansing Regimes in the Different Segments of the Colon According to the Ottawa Bowel Preparation Scale, n (%)

	Stewed apricot juice senna group (n = 68)	Senna alone group (n = 59)	p value
Left side colon segments			
Adequate	59 (86.8%)		0.745
Inadequate	9 (13.2%)	50 (84.8%) 9 (15.2%)	
Transverse colon segments			
Adequate	62 (91.2%)	46 (78.0%)	0.037
Inadequate	6 (8.8%)	13 (22.0%)	
Right side colon segments			
Adequate	51 (75%)	34 (57.6%)	0.038
Inadequate	17 (25%)	25 (42.4%)	
Overall			
Adequate	64 (94.1%)	33 (55.9%)	< 0.001
Inadequate	4 (5.9%)	26 (44.1%)	

**Patient Acceptance, Compliance and Preference**

Patient acceptability was assessed according to the difficulty of completing ingestion of the regimens. The regimens used were stated to be difficult to drink by 17 patients in Group A (25%) and 18 patients in Group B (30.5%). Compliance was defined as successful consumption of the total amount assigned by the regimens. The total bowel cleansing regimen was completed by 65 (95.6%) patients in Group A and 56 (94.9%) patients in Group B. Neither patient acceptance nor compliance was significantly different between the groups ( $p > 0.05$ ). In Group A, 91.2% of patients stated their willingness to receive the same regimen in the future, compared with 80% of the patients in Group B ( $p = 0.037$ ) (data not shown).

**Adverse Effects**

In both groups, the most common adverse effects experienced were abdominal pain, nausea, anal irritation and sleep disturbance. No significant difference was determined between the groups with respect to adverse effects (Table 5). Since no serious adverse effects developed, no patient terminated the study for this reason.



**Table 5.** Frequency and Severity of Adverse Effects, n

	Stewed apricot juice plus senna group (n = 68)	Senna alone group (n = 59)	<i>p</i> value
Nausea			
Absent	46	39	0.922
Minimal	13	14	
Moderate	8	6	
Severe	1	0	
Vomiting			
Absent	61	53	0.692
Minimal	3	3	
Moderate	2	3	
Severe	2	0	
Abdominal pain			
Absent	43	42	0.065
Minimal	12	13	
Moderate	10	1	
Severe	3	3	
Abdominal bloating			
Absent	53	46	0.312
Minimal	7	9	
Moderate	6	1	
Severe	2	1	
Weakness			
Absent	45	38	0.679
Minimal	13	13	
Moderate	6	6	
Severe	4	1	
Anal irritation			
Absent	28	22	0.972
Minimal	31	28	
Moderate	6	6	
Severe	3	3	
Sleep disturbance			
Absent	14	12	0.920
Minimal	25	25	
Moderate	22	17	
Severe	7	5	

## DISCUSSION

Although there have been some previous reports regarding the addition of pineapple and orange juices to PEG solutions that were found to be effective for bowel cleansing [12, 13], this is the first prospective study evaluating the efficacy of apricot juice combined with senna for the purposes of colonoscopy preparation.

PEG and NaP have been widely used for bowel preparation worldwide, probably due to

conflicting results about senna. Although there are some studies regarding the efficacy of senna in combination regimens, there have been few studies evaluating senna alone. For example, Valverde et al. and Chilton et al. showed that senna either alone or in combination was associated with more effective colonic cleanliness than other regimens [20, 21]. Radaelli et al. concluded that high-dose (288 mg) senna was an effective alternative to a standard 4-liter PEG solution, with overall cleansing reported as excellent or good in 90.6% of the senna group and in 79.7% of the PEG group ( $p = 0.003$ ) [18]. Moreover, Yenidogan et al. claimed that administration of senna on the colonoscopy day was effective as a bowel preparation protocol, since only 9.3% of the patients were asked to repeat the examination [4].

In contrast, three other studies undertaken by Kositchaiwat et al., Dashan et al. and Arezzo et al. reported that NaP and PEG regimens were more effective than senna [22-24]. The latter study showed that only 38% of patients experienced a “good” colon cleansing, while the feasibility of the examination was considered “optimal” in 59% of the procedures. In the current study, 44.1% of patients were found to have inadequate bowel cleansing when senna was used alone, which is a far from ideal outcome. However, the addition of stewed apricot juice improved the overall quality of the bowel cleansing to 94.1%.

The quality of bowel cleansing depends on the patient’s tolerance and compliance with the preparation regimen. If a cleansing agent is poorly tolerated and not fully consumed, adequate cleansing will not be achieved. For this reason, combination regimes are beneficial, a conclusion supported by other authors. Apricot is highly valued food which is regularly consumed and considered to have medical applications. Increased alimentary fiber due to consumption of apricot increases fecal output and improves gastrointestinal motility and emptying [25]. Thus, while it is beneficial for the treatment of constipation, apricot itself is not suitable for colonoscopy preparation owing to its high fiber content. The other effect of apricot is related to its acidity, especially its malic and citric acid contents. It has been shown that these strong acids accelerate the spontaneous contractions of rat colons [26]. Therefore, this effect may increase gastrointestinal motility and colonic emptying. As apricot juice contains malic and citric acid, it was hypothesized that drinking stewed apricot juice during colonoscopy preparation may have an additive effect on colon cleansing.

In the present study, the two groups did not significantly differ with regard to experiencing adverse effects such as nausea, vomiting, abdominal pain, bloating, weakness, anal irritation and sleep disturbance. However, abdominal pain was observed at a slightly higher rate in the stewed apricot juice plus senna group than in the senna alone group ( $p = 0.065$ ). This may have been caused by the additional effect of sorbitol in apricot juice. Colic-type abdominal pain may also be caused by senna due to the laxative’s irritation of the bowel wall [18]. Nevertheless, it did not seem to affect patient compliance and preference in the current study, as 62 of 68 patients (91.2%) expressed a willingness to repeat the procedure with the same combination ( $p < 0.037$ ). Previous studies showed severe adverse effects associated with senna, such as tetany, clubbing, cachexia, hepatitis and hypertrophic osteoarthropathy, which may have limited its use in colonoscopy preparation until today [27-30]. However, none of these adverse events were experienced in the current study.

Cleansing of the right side of the colon can be considered to be significantly important. Therefore, the evaluations of the left, transverse, and right colon segments were performed separately. Smaller polyps are more likely to be missed during colonoscopy and polyps of the right colon seem to be smaller in size than those of the left colon. Rondagh et al. also reported that

advanced right colon adenomas were likely to be non-polypoid [31]. Moreover, Gupta et al. determined that the majority of right colon polyps have a tendency to advanced histology [32]. As a result, these lesions are more likely to be missed during colonoscopy, thereby leading to subsequent progression to colorectal cancer, particularly when the cecum and ascending colon are covered with solid fecal layers. Although the difference was not significant, a slightly higher rate of polyps was found in the right colon in the stewed apricot juice group (12/19 vs. 4/13,  $p = 0.072$ ). One possible conclusion is that the addition of stewed apricot juice to senna results in a more accurate diagnosis of right colonic lesions. However, this cannot be stated with any certainty based on the results of the current study, due to the comparatively small number of patients in the sample.

This study has several limitations. First, only the Ottawa Bowel Preparation Scale was used to evaluate the quality of bowel preparation. Second, no monitoring of the laboratory values and electrolytes was performed. Third, the study was conducted on a relatively small number of outpatients without serious comorbidities. Thus, the results cannot be applied to patients with comorbidities. Although the cost-effectiveness of the regimens was not evaluated, senna is known to be an economical bowel cleansing agent and stewed apricot juice is unlikely to add a significant cost. Finally, since only the investigator was blinded to the study because the patients could not be blinded, this may have affected patient consistency and satisfaction results.

## CONCLUSIONS

Despite the limitations, the results of this study show that a precolonoscopic preparation regimen with senna alone does not seem to be effective. However, the addition of natural, stewed apricot juice, a frequently consumed food item, to senna significantly improves the cleansing outcomes without additional adverse effects. Based on these results, stewed apricot juice should be recommended to patients using senna for colonoscopy preparation, particularly those with suspected right side colonic lesions.

**List of Abbreviations:** Polyethylene glycol (PEG), Sodium phosphate (NaP), European Society of Gastrointestinal Endoscopy (ESGE)

**Competing Interests:** The authors declare that they have no financial interests or conflicts of interest.

## Authors' Contributions:

Bulent Yasar, MD, collected the data, performed the analysis and interpretation of the data, and prepared the manuscript. Evren Abut, MD, collected the data, performed the analysis and interpretation of the data, and prepared the manuscript. Huseyin Kayadibi, Assoc. Prof., contributed to the interpretation of the data and preparation of the manuscript. Fatih Akdogan, MD, contributed to the interpretation of the data and preparation of the manuscript. Can Gonen, Assoc. Prof., contributed to the interpretation of the data and preparation of the manuscript. Drafting and critical revision of the article was performed by all authors. All authors have approved the final version of the manuscript.

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