

RAPID COMMUNICATION

## Comparative study of two bowel preparation regimens for colonoscopy: Senna tablets vs sodium phosphate solution

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to sodium phosphate solution in bowel preparation for colonoscopy, but senna may be considered an alternative laxative.

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### Abstract

**AIM:** To compare the efficacy and acceptance of senna tablet and sodium phosphate solution for bowel preparation before colonoscopy.

**METHODS:** One hundred and thirty four patients, who needed elective colonoscopy, were randomly allocated to take 180 mg senna tablet or 95 mL sodium phosphate solution on the day before colonoscopy. The efficacies of both laxatives were compared using the mean difference of colon-cleanliness score of the rectum, sigmoid segments, descending colon, transverse colon and cecum. The scores were rated by two observers who were blinded to the laxatives administered. The higher score means that the colon is cleaner. The efficacy of both laxatives were equivalent if the 95% confidence interval of the mean difference of the score of colon lie within -1 to +1.

**RESULTS:** On intention-to-treat analysis, the mean cleanliness scores in the four segments of colon except the cecum were higher in the sodium phosphate group than those in senna group ( $7.9 \pm 1.7$  vs  $8.3 \pm 1.5$ ,  $8.0 \pm 1.8$  vs  $8.5 \pm 1.4$ ,  $7.9 \pm 2.0$  vs  $8.5 \pm 1.3$ ,  $7.9 \pm 2.0$  vs  $8.2 \pm 1.4$  and  $7.2 \pm 1.7$  vs  $6.9 \pm 1.4$ , respectively). The 95% confidence intervals (95% CI) of mean difference in each segment of colon were not found to lie within 1 point which indicated that their efficacies were not equivalent. The taste of senna was better than sodium phosphate solution. Also, senna had fewer side effects.

**CONCLUSION:** The efficacy of senna is not equivalent

### INTRODUCTION

Adequately cleansed colon is essential for colonoscopy. Inadequate bowel preparation might lead to missed diagnosis, increasing the time of colonoscopy by 7.5%-10.3% and increasing cost 12%-22%<sup>[1]</sup>. Ness *et al*<sup>[2]</sup> reported that the incidence of inadequate bowel preparation was 21.7% and 5.4% had poor preparation leading to cancellation or abortion of procedure. Currently, the laxatives of choice for bowel preparation are sodium phosphate solution (NaP) and polyethylene glycol solution (PEG). Despite its efficacy<sup>[3-5]</sup>, phosphate solution has poor taste. It may cause electrolyte imbalance, severe nausea and vomiting. The advantage of PEG is its minimal effect on intravascular volume and serum electrolyte balance, but this large-volume laxative is difficult for many patients to tolerate. Although PEG and NaP are equally effective in colonic cleansing<sup>[6]</sup>, NaP is better tolerated. However, NaP may be contraindicated in certain patient populations. The selection of a colonoscopy preparation requires clinical judgment, cost and informed patient preference<sup>[7,8]</sup>.

Senna (*Cassia angustifolia* Vahl, *Leguminosae*, Indian senna, Tinnevely senna) is a laxative that stimulates the intestinal motility and affects epithelial transport of water and electrolytes. The main advantages of senna are low cost, safety and ease of ingestion. It had been combined with other laxatives for bowel preparation, and their efficacy ranged from 70% to 85%<sup>[9-12]</sup>. There are few studies on the efficacy of high-dose senna tablet alone. The aim of

this study was to compare the efficacy and acceptance of senna tablet and sodium phosphate solution for bowel preparation before colonoscopy.

## MATERIALS AND METHODS

The study was carried out as a randomized, controlled (equivalent), single-blind trial from June to November 2003. The study population consisted of adult patients who required elective colonoscopy. The exclusion criteria were: (1) known allergy to senna or sodium phosphate solution; (2) presence of severe metabolic, renal and cardiac conditions; (3) bed-ridden or psychotic patient; (4) pregnancy; (5) patient taking laxatives within one week prior to enrollment; and (6) patients who had previous colonic resection surgery. The study was approved by the Ethical Committee Board of the hospital.

The patients were allocated into two groups and they were advised to take full liquid diet two days before colonoscopy. The control group took sodium phosphate solution (Swift® 90 mL, Berlin Pharmaceutical Industry Co. Ltd., Thailand). The experimental group took senna tablet, 180 mg (24 tablets of 7.5 mg /tab, Senokot®, Reckitt Benckiser, Thailand). The patients took the laxatives in divided doses at 14.00 pm and 16.00 pm on the day before colonoscopy. Since the duration of action of NaP is within 6 h, so the laxatives should not interfere the patient's sleeping time.

### Data collection

Shortly before colonoscopy, nurses interviewed each patient to assess compliance, acceptance and side effects of laxatives by using visual analog scale. The colonoscopist and his assistant independently rated the quality of bowel cleansing, using visual analog score (VAS) as followed: 0-2 = numerous solid feces, 3-5 = semi-solid feces, 6-7 large volume of liquid feces, 8-10 = small volume of clear liquid or no feces. In an equivalent trial<sup>[13]</sup>, it was important to pre-specified that (1) the mean score should lie above seven to assure that both laxatives were effective, and (2) the 95% confidence intervals of the mean difference lie between -1 and +1 VAS score in all segments of colon. The sample size calculation was based on testing equivalence with power 0.8 and 10% drop out<sup>[14]</sup>. The variance of VAS score from our pilot study was 2.93.

Before data analysis, the 95% limit of agreement<sup>[15]</sup> of cleansing score between two colonoscopists will be calculated to confirm the agreement on the assumption that the mean score difference between them should lie within two points. The score used for analysis were the average score from two colonoscopists. The VAS score for acceptance and side effects of the two laxatives were analyzed using Student's *t* test. The outcome variables of accepted and side effects of laxatives were also measured using VAS score. The patients were asked to grade the taste of the laxative as follows: 0-2 = hard to ingest, 3-5 = ingested with very bad feelings, 6-7 = easily ingested, and 8-10 = easily ingested with good feelings. The scores of the side effects (nausea and vomiting, abdominal pain, vertigo and sleeplessness) were rated as follows: 0-2 = no symptom, 3-5 = mild symptom, 6-7 = moderate symp-

**Table 1 Demographic and baseline colonoscopic data of the patients (n = 67)**

Characteristics of patients	Senna	NaP
Sex (M/F)	22 : 45	30 : 37
Age (yr, mean ± SD)	54.3 ± 12.7	51.6 ± 12.6
Body weight (kg, mean ± SD)	59.1 ± 10.7	61.8 ± 12.6
Constipation (Yes/No)	9:58	14:53
Laxative users (Yes/No)	6:61	12:55
Previous Obs-gyn surgery	6:61	7:60
Diabetes (Yes/No)	7:60	6:61
Colonoscopic diagnosis		
Normal study	44 (65.7%)	40 (62.5%)
Polyp	8 (12.1%)	4 (6.2%)
Diverticulosis	4 (6.0%)	8 (12.5%)
Carcinoma	4 (6.0%)	6 (9.3%)
Inflammatory bowel disease	6 (9.0%)	3 (4.6%)
Other	1 (1.5%)	3 (4.6%)
Time of colonoscopy (min, mean ± SD)	19.3 ± 14.2	18.2 ± 10.1
Incomplete colonoscopy	4 (6.0%)	5 (7.8%)
Therapeutic:Diagnostic colonoscopy	16:51	14:50

**Table 2 The cleansing score, acceptance score and side effects of laxatives (n = 67)**

Segment	Senna (mean ± SD)	NaP (mean ± SD)	95% CI of differences
Rectum	7.9 ± 1.7	8.3 ± 1.5	-1.0 to 0.1
Sigmoid colon	8.0 ± 1.8	8.5 ± 1.4	-1.0 to 0.1
Descending colon	7.9 ± 2.0	8.5 ± 1.3	-1.2 to 0.0
Transverse colon	7.9 ± 2.0	8.2 ± 1.4	-0.9 to 0.3
Ascending colon and cecum	7.2 ± 1.7	6.9 ± 1.4	-0.2 to 0.8
Acceptance score			
Taste	8.6 ± 1.9	5.1 ± 2.8	<i>P</i> < 0.001
Side effects			
Nausea & vomiting	0.9 ± 0.2	3.0 ± 3.5	<i>P</i> < 0.001
Abdominal pain	1.3 ± 2.3	1.4 ± 2.4	<i>P</i> = 0.8
Vertigo	0.7 ± 1.6	1.3 ± 2.3	<i>P</i> = 0.08
Sleeplessness	1.2 ± 2.7	1.4 ± 2.5	<i>P</i> = 0.65
Adverse event	2:67	2:64	

tom, and 8-10 = severe symptom.

## RESULTS

Patient's flow in this study is shown in Figure 1. One hundred and seventy patients were enrolled, but thirty patients did not meet eligibility criteria. One hundred and thirty-six patients were randomly allocated to take senna tablet or NaP solution. Two patients did not take laxatives due to error in packaging. Among the 134 patients who took a laxative, 3 patients did not attend colonoscopy and 10 patients did not have complete colonoscopy for various reasons.

Both groups of patients were comparable with regard to demographic data, diagnosis and other colonoscopic data (Table 1). However, the efficacy of senna tablet was not equivalent to NaP solution (Table 2). The mean

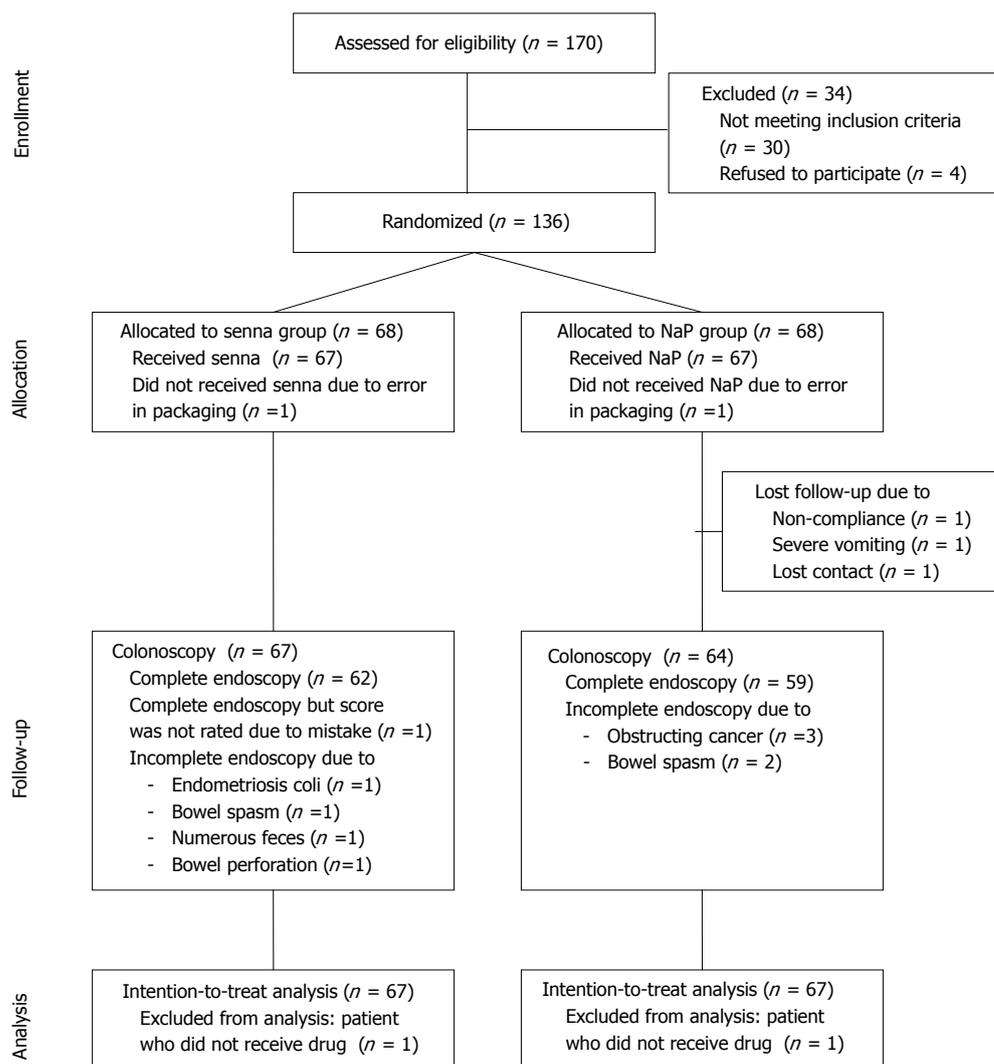


Figure 1 Flow diagram of patients progress through the phases of a randomized trial.

cleansing scores of NaP solution were higher than senna tablet in four segments of the colon except in the ascending colon and the cecum. The 95% CI of the mean difference exceeded 1 point in three segments of the colon. In the other two segments of the colon, they lied nearly over 1 point. By intention-to-treat analysis, we included all patients who had taken the laxatives whether they had complete or incomplete colonoscopy. For the missing data in both groups, we assigned the lowest score in each group (worst-case approach). For example, the lowest cleansing score in senna group was two, while that in NaP group was four.

The cleansing score, acceptance score and side effects of the two laxatives are shown in Table 2. The patients accepted senna tablets more than NaP solution and those patients who took senna tablets had less nausea and vomiting. There were four adverse events in this study. In the senna group, 1 patient had post-polypectomy bleeding which ceased spontaneously, and 1 patient had sigmoid perforation during colonoscopy due to fixation of the sigmoid colon; this patient had received long-term steroid treatment of myasthenia gravis and also had previous left hip surgery. In the NaP group, 2 patients had broncho-

spasm after colonoscopy and both recovered after 24 h.

## DISCUSSION

NaP solution and PEG had widely been used for bowel preparation because of their similar efficacy, Hwang *et al*<sup>[16]</sup> claimed that NaP group had higher completion rate than PEG group (84.2% vs 27.5%,  $P < 0.001$ ) and NaP appeared to be more cost-effective<sup>[16]</sup>. In contrast, senna was not popular for bowel preparation. Fear of adverse effects might responsible for its underuse. Serious adverse effects of senna, such as asthma, hepatitis, hypertrophic osteoarthropathy, cachexia, hypo-gammaglobulinemia, finger clubbing and tetany, had been reported<sup>[17-21]</sup>. However, these adverse effects were uncommon and resulted from long-term and large amount used. There are no epidemiologic data to support neoplastic potential of senna compound<sup>[22]</sup>. The inconsistent efficacy of senna might be another reason for its underuse. Two studies by Chilton *et al*<sup>[11]</sup> and Valverde *et al*<sup>[23]</sup> showed that senna (X-prep) solution alone or senna in combination with other laxatives were better than PEG or NaP solution. On contrary, two other studies by Dahshan *et al*<sup>[24]</sup> and Arezzo *et al*<sup>[12]</sup> showed that

those standard laxatives were better than senna. Moreover, Hangartner *et al*<sup>[9]</sup> and Borkje *et al*<sup>[10]</sup> concluded that senna has no clinical difference compared with those laxatives. Radaelli *et al*<sup>[25,26]</sup> had claimed that high-dose senna had 97.3% efficacy in bowel cleansing, and that 288 mg of senna was better than 4 L of PEG-ES (90.6% *vs* 79.7% efficacy,  $P = 0.003$ ). In contrast, our study showed that 180 mg of senna tablets did not have equivalent efficacy as NaP solution. The inconsistencies of these results were hardly explained. Bowel cleansing may be affected by other factors, such as gender, age, obesity, race, constipation, previous abdominal surgery and associated complicated diverticular disease<sup>[27]</sup>. In addition, the mean score of senna group was also above seven points and we imply that senna has some effect in bowel cleansing and it may be alternative laxative for bowel preparation.

In addition, we noticed that the mean cleansing score of cecum in the senna group was higher than that in the NaP group. This phenomenon might be related to timing of laxative intake. Church *et al*<sup>[28]</sup> suggested that the patients who took laxatives 5 h before colonoscopy had better result than patients who took laxative 1 d before colonoscopy. The VAS scores of taste, nausea and vomiting in the senna group were significantly better compared with the NaP group (Table 2). However, in term of pain symptom, senna was not found to be better than NaP. These findings confirmed our rational background knowledge that senna had more palatability and less nausea and vomiting than NaP solution. The adverse events occurred in 4 patients were not related to laxatives but were related to colonoscopy or anesthetic procedure.

In conclusion, senna does not have the same efficacy as oral NaP solution. However, senna has better compliance and fewer side effects than NaP. Senna may be prescribed as an alternative laxative for bowel preparation in patients who have contraindications to NaP solution.

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