

# High-dose Bisacodyl Plus Water Lavage Compared With Oral Sodium Phosphate as Bowel Preparation for Outpatient Colonoscopy

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**Background:** The aim of this prospective study was to compare the efficacy and patient compliance of an oral high dose of bisacodyl plus water lavage and oral sodium phosphate in adults undergoing elective colonoscopy.

**Methods:** A total of 276 patients were randomized to receive an oral high-dose bisacodyl preparation (6 tablets of 5 mg bisacodyl) plus water lavage (2 L of water) or an oral sodium phosphate (NaP) preparation (90 mL in divided doses). All endoscopic procedures were conducted in the afternoon. The endoscopist was blinded to the preparation the patient had received and graded the quality of colon cleansing as excellent, good, fair, poor, or failed. Patients' demographic data, indications for the procedure, and colonoscopic findings were recorded and compared.

**Results:** Significantly improved ( $p < 0.001$ ) bowel preparation after NaP compared with bisacodyl plus water lavage was reported. The completion rate of colonoscopy was significantly lower ( $p < 0.001$ ) in the bisacodyl group (70.6%) than in the NaP group (92.9%). The detection of polyps was significantly increased ( $p = 0.017$ ) in the NaP group (43.1%) compared with the bisacodyl group (27.1%). A procedural indication of constipation was an independent predictor of failed preparation in the bisacodyl group (odds ratio, 4.8; 95% confidence interval, 1.9–12.0;  $p < 0.001$ ).

**Conclusion:** The quality of bowel preparation with oral NaP was better than that with bisacodyl plus water lavage. [*J Chin Med Assoc* 2009;72(8):402–407]

**Key Words:** bisacodyl, bowel preparation, colonoscopy, sodium phosphate

## Introduction

Inadequate colon cleansing and preparation before colonoscopy may lead to low diagnostic accuracy. The ideal preparation for colonoscopy is one that would make the colon empty out all fecal material with no alteration of the colonic mucosa. The preparation would be cheap and would not cause any patient discomfort, shifts in fluids or electrolytes. Unfortunately, all currently available preparations are still far from this ideal.<sup>1</sup>

Aqueous sodium phosphate (NaP) and polyethylene glycol–electrolyte solutions (PEG-ES) are the most popular regimens for colon cleansing worldwide. NaP

draws plasma fluid into the bowel lumen to cause osmotic diarrhea; it must be diluted before drinking to prevent emesis and accompanied by a significant amount of oral fluid to prevent dehydration. The unpleasant taste of NaP and safety concerns about its lower therapeutic index in subsets of patients with comorbid conditions such as renal insufficiency, congestive heart failure or cirrhosis, limit its use in an open-access system.<sup>1</sup> PEG-ES, because of its safety and high efficacy in colon cleansing, was introduced for bowel preparation before colon procedures. However, in a meta-analysis of randomized, controlled trials comparing PEG to NaP bowel preparations for colonoscopy, PEG was less tolerated than NaP.<sup>2</sup> Problems of safety



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and compliance with the standard NaP and PEG regimens have prompted continued investigation into alternative forms of cleansing.

Bisacodyl is a poorly absorbed diphenylmethane which stimulates colonic peristalsis; it has been used as an adjunct, like NaP and PEG-ES, for bowel cleansing.<sup>3,4</sup> Although it is commonly used for the treatment of constipation, there is little information on its use as a preparation for colonoscopy. The aim of this study was to compare the efficacy between oral high-dose bisacodyl and NaP for bowel preparation in adult outpatient colonoscopy.

## Methods

This study was a prospective, randomized, endoscopist-blinded trial. Patients presenting to our outpatient gastroenterology clinics scheduled for elective colonoscopy were eligible to participate in the study. Exclusion criteria were: (1) age < 18 years; (2) previous colon resection; (3) congestive heart failure; (4) renal insufficiency (serum creatinine level > 1.2 mg/dL); (5) preexisting electrolyte abnormalities; (6) clinically evident ascites; and (7) refusal to give consent. Our institutional review board did not require an additional consent form for this study because the study was performed as part of a performance improvement project and both preparations were accepted bowel cleansing regimens already being used in our medical center.

Patients randomized to receive oral NaP were instructed to take 90 mL, divided into 2 doses—45 mL at 8 p.m. on the day before the procedure and 45 mL at 8 a.m. on the day of the procedure. They were also instructed to take at least 250 mL of liquid with each dose, followed by an additional minimum of at least 500 mL of liquid. Those randomized to receive 6 tablets of bisacodyl (30 mg) were instructed to start preparation at 8 p.m. on the day before the procedure; they were also instructed to drink at least an extra 2 L of water within 1–2 hours after taking bisacodyl.

Study subjects received both verbal and written detailed instructions about the dietary measures and how to administer the investigational treatment. Regardless of which laxative was used, all patients were advised to ingest a low-fiber diet and encouraged to increase their water intake on the 3<sup>rd</sup> and 2<sup>nd</sup> pre-procedural days. On the day before the procedure, they were advised to take a normal lunch and a light liquid dinner, and to drink plenty of clear liquids on the day of the procedure.

On arrival at the endoscopic suite, the patients were orally interviewed with questions about their

tolerance of the preparation and any side effects. With regard to compliance to the study schedule, patients were asked if they had completed the dosing regimen as prescribed.

All endoscopic procedures were conducted between 2 p.m. and 5 p.m. using standard adult video colonoscopes (CF-Q260AL; Olympus Co. Ltd., Tokyo, Japan) by the same endoscopist (who has 9 years of practice experience, performing more than 200 colonoscopies/year), who was blinded to the preparation regimen. All the colonoscopies were performed with one-man method, and no conscious sedation was used during the procedure. At the end of the procedure, the endoscopist rated the quality of colon cleansing as: (1) “Excellent”: having a small volume of clear liquid; (2) “Good”: having a large volume of clear liquid; (3) “Fair”: having some semi-solid stools that could be washed or removed by suction; (4) “Poor”: having semi-solid stools that could not be washed or removed by suction; or (5) “Failed”: having solid stools and requiring re-preparation.

To prevent the endoscopist from becoming unblinded, patients were instructed not to discuss their colon cleansing preparation with the endoscopist, either before or during the procedure. The investigators recorded demographic and clinical data, as well as indications for colonoscopy, procedure starting time, depth of colonoscope insertion, insertion time to the cecum (from insertion in the anus to identification of cecal landmarks), total procedure time (insertion to removal of colonoscope), and reasons for failures of cecal intubation, endoscopic diagnosis and any therapeutic procedure (i.e. polypectomy).

An independent *t* test was used to compare quantitative data. The  $\chi^2$  test was used for other statistical analyses of the results for qualitative variables. Fisher's exact test was used for correction if necessary. To identify independent factors, variables that achieved statistical significance ( $p < 0.05$ ) in the univariate analysis were subsequently included in a multivariate analysis using a logistic regression procedure. For quantitative variables, the cut-off level chosen was according to clinical significance. A *p* value < 0.05 was considered significant. All *p* values were 2-tailed. Data are presented as mean  $\pm$  standard deviation.

## Results

A total of 298 patients were enrolled in this study during a 14-month period from January 2007 to February 2008. After randomization, there was a dropout of 22 patients: 17 did not show up for their colonoscopy

**Table 1.** Characteristics of the 276 patients who underwent elective colonoscopy\*

	Bisacodyl (n = 136)	NaP (n = 140)	p
Age (yr)	61.6 ± 18.5	58.9 ± 14.9	0.181
Range	20–91	19–90	
Sex			0.529
Male	91 (66.9)	88 (62.9)	
Female	45 (33.1)	52 (37.1)	
Indication			
Anemia	0	2 (1.4)	0.498
Bleeding	19 (13.9)	20 (14.3)	1.000
Constipation	38 (27.9)	34 (24.3)	0.497
Change in bowel habits	44 (32.3)	41 (29.3)	0.604
History of polyps	11 (8.1)	16 (11.4)	0.420
Cancer screening	3 (2.2)	7 (5)	0.335
Abdominal pain	17 (12.5)	16 (11.4)	0.854
Body weight loss	4 (2.9)	4 (2.9)	1.000

\*Data presented as mean ± standard deviation or n (%).

**Table 2.** Colonoscopy completion rates and reasons for failure\*

	Bisacodyl (n = 136)	NaP (n = 140)	p
Completed	96 (70.6)	130 (92.9)	<0.001
Reason for failure			
Failed preparation	32 (23.5)	1 (0.7)	<0.001
Obstructing tumor	2 (1.5)	3 (2.1)	1.000
Intolerance	6 (4.4)	6 (4.3)	1.000

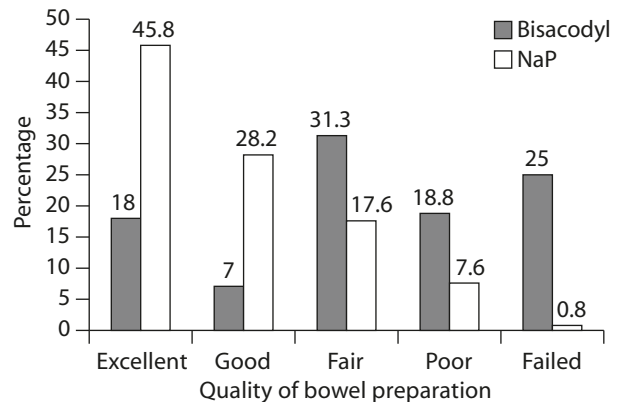
\*Data presented as n (%).

appointment or cancelled their colonoscopy appointment and 5 did not complete the dosing regimen as prescribed or follow the preparation instructions. Of the 276 patients who completed the study, 136 were randomized to the bisacodyl regimen and 140 to the NaP regimen (Table 1). There were no differences between the 2 groups with respect to age, sex distribution, and procedural indications.

Nausea was experienced to a significantly higher degree in the NaP group than in the bisacodyl group (28% vs. 7%;  $p < 0.001$ ). There were no significant differences in patient tolerance (95% vs. 96%), vomiting (4% vs. 2%), and abdominal cramps (31% vs. 34%) between the 2 groups; also, no complications were noted during colonoscopy in any of the study participants.

The completion rate of colonoscopy was significantly lower in the bisacodyl group (70.6%) than in the NaP group (92.9%). The main reason for failure to complete colonoscopy in the bisacodyl group was failed preparation (23.5%). Only 1 (0.7%) patient in the NaP group failed to complete colonoscopy due to failed preparation (Table 2).

Failed colonoscopies, due to obstructive tumor or patient's intolerance, were excluded when rating the



**Figure 1.** Quality of bowel preparation as graded by the endoscopist in the bisacodyl and sodium phosphate (NaP) groups ( $p < 0.001$ ).

quality of colon cleansing. Quality of colon preparation was therefore rated in 128 subjects in the bisacodyl group and 131 subjects in the NaP group; the quality was significantly better ( $p < 0.001$ ) in the NaP group than in the bisacodyl group (Figure 1).

Cecal intubation time was similar for both groups, as shown in Table 3. The detection of polyps was

**Table 3.** Cecal intubation time and colonoscopic findings\*

	Bisacodyl (n = 96)	NaP (n = 130)	p
Cecal intubation time (min)	10.6 ± 5.3	9.9 ± 5.7	0.365
Findings			
Polyp and tumor	26 (27.1)	56 (43.1)	0.017
Diverticulosis	8 (8.3)	14 (10.8)	0.652

\*Data presented as mean ± standard deviation or n (%).

**Table 4.** Predictors of failed preparation in the bisacodyl group (univariate analysis)\*

	Bisacodyl		p
	Failed (n = 32)	Others (n = 96)	
Age (yr)	70.8 ± 16.0	58.4 ± 18.7	< 0.001
Range	28–91	20–87	
Sex			0.385
Male	24 (75)	62 (65)	
Female	8 (25)	34 (35)	
Indications			
Bleeding	3 (9.4)	14 (14.6)	0.559
Constipation	18 (56.3)	19 (19.8)	< 0.001
Diarrhea	6 (18.8)	33 (34.4)	0.122
History of polyps	2 (6.3)	10 (10.4)	0.729
Cancer screening	1 (3.1)	2 (2.1)	1.000
Abdominal pain	2 (6.3)	14 (14.6)	0.355
Body weight loss	0	4 (4.2)	0.571

\*Data presented as mean ± standard deviation or n (%).

**Table 5.** Predictors of failed preparation in the bisacodyl group (logistic regression model)

Predictors	Odds ratio	95% CI	p
Age	2.5	0.512–12.1	0.258
Indication: constipation	4.8	1.9–12.0	< 0.001

CI = confidence interval.

significantly increased in the NaP group compared with the bisacodyl group (43.1% vs. 27.1%;  $p = 0.017$ ). The detection of diverticulosis was similar for both groups (8.3% vs. 10.8%;  $p = 0.652$ ).

In the bisacodyl group, further analysis to evaluate the predictors of failed preparation was conducted. Age was a significant univariate predictor of failed preparation in this group. In listed procedural indications, constipation was strongly associated with failed preparation (Table 4). In a multivariate logistic regression model (Table 5), a procedural indication of constipation remained the only significant predictor of failed preparation (odds ratio, 4.8; 95% confidence interval, 1.9–12.0;  $p < 0.001$ ).

## Discussion

This study examined whether high-dose bisacodyl plus water lavage provides a better-tolerated colonic cleansing preparation and superior efficacy compared to a standard oral NaP solution. The results show that oral NaP solution had similar tolerability but was more efficacious than high-dose bisacodyl plus water lavage.

Rasmussen et al found that only 1.27% of patients in their study prepared with bisacodyl and water enema had incomplete colonoscopy due to poor bowel preparation.<sup>5</sup> In this study, 23.5% of patients prepared with bisacodyl and water enema had incomplete colonoscopy due to failed preparation. Water enema is administered by a nurse in the unit; therefore, the procedure is more resource-demanding. Both of the preparations in this study were taken by patients at home without discomfort from enema. However, it seems that water lavage on colon cleansing is well tolerated but less efficacious than water enema. Some of our patients may be reluctant to comply with the request to drink 2 liters of fluid. The timing and amount of water lavage may

be important variables in obtaining good results in bowel preparation.

Poor bowel preparation has been associated with patient characteristics, such as inpatient status, being elderly, and having a history of constipation, use of antidepressants and noncompliance with cleansing instructions.<sup>6</sup> Being elderly is associated with a decline in the elasticity of the bowel wall and the autonomic innervations of the bowel both in quantity and function. These factors, combined with the frequent presence of diseases affecting the autonomic nervous system, such as Parkinsonism and diabetes mellitus, may contribute to difficulties in preparation for colonoscopy.<sup>7</sup>

The findings of this study suggest that failed preparation in the bisacodyl group cannot be attributed to age alone; a procedural indication of constipation was an independent predictor of failed preparation. Patients who have constipation may use laxatives concurrently, and therefore may not benefit from preparation with high-dose bisacodyl alone. The quality of bowel preparation may be improved by identifying groups of patients having a poor preparation by bisacodyl and using a longer or more rigorous bowel preparation regimen.

There is no published information on the management of patients who received failed colonoscopy preparation. If the patient did not consume the preparation as prescribed, it would be reasonable to repeat the same preparation, although NaP cannot be used again within 24 hours because of the risk of acute renal failure by phosphate nephropathy.<sup>1</sup> If the patient has properly consumed the preparation, rational options include repeating the preparation with a longer interval of dietary restriction to clear liquids, increasing the vigor of preparation regimens, adding another cathartic to the previous regimen, or double administration of the preparation during a 2-day period (with the exception of NaP).<sup>1</sup>

In this study, we found that better bowel preparation led to a higher rate of colon polyp detection as well as completeness of colonoscopy. Froehlich et al reported a similar result.<sup>8</sup> Several factors impact the colonoscopist's ability to see a polyp—the quality of bowel preparation being the most obvious. Therefore, the quality of colon cleansing not only influences the completeness of colonoscopy but also affects the diagnostic yield of the examination. Inadequate colon cleansing can result in missed lesions, and it is costly in terms of the need for repeat colonoscopy. Church found that it was easy for poor preparation to obscure a small polyp, and this sort of preparation was commonly found on the right side of the colon when there was a delay of more than 14 hours between ingesting the bowel-cleansing preparation and the examination

itself.<sup>9,10</sup> The timing of taking the preparation regimen is important in obtaining good results in bowel preparation;<sup>10,11</sup> the best result was when the last dose was given early in the morning a few hours prior to colonoscopy.<sup>12</sup>

Another potential explanation for the higher rate of failed preparation in the bisacodyl group is that the procedures were performed in the afternoon. Sanaka et al found that colonoscopies scheduled in the afternoon had a significantly higher incompleteness rate compared to colonoscopies scheduled in the morning. Inadequate bowel preparation resulting in suboptimal colonoscopic visualization was also significantly higher in the afternoon procedures in their study.<sup>13</sup> Timing of colonoscopy is a modifiable factor. A strategy of scheduling all colonoscopies preferably in the morning might lead to a higher completion rate. But this strategy may not be feasible in all endoscopy settings due to various practical reasons. The quality of bowel preparation in the afternoon procedures may be improved by using bowel preparation regimens such as the split dose of oral NaP used in this study, which was given not only on the day before the procedure but also on the day of the procedure itself.

There were several limitations in our study. First, we did not record the timing of bowel movements during the preparation period; there may have been wide differences in the time to onset of bowel action after ingestion of bisacodyl, because the timing of taking bisacodyl may be important in obtaining good results in bowel preparation. Second, we did not record the current medication history of patients. Third, serum electrolytes were not systematically measured, therefore, there was no information on treatment-induced electrolyte changes.

In conclusion, the quality of bowel preparation was better after oral NaP than after bisacodyl plus water lavage. The quality of bowel preparation in the afternoon colonoscopies was also better in this study by using a split dose of oral NaP, which was given not only on the day before the procedure but also on the procedural day.

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