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ORIGINAL ARTICLE

Randomized Study Comparing Two Regimens of Oral Sodium Phosphates Solution Versus Low-Dose Polyethylene Glycol and Bisacodyl

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Abstract *Purpose* Low-volume bowel preparation regimens for colonoscopy are reported to improve patient acceptance and compliance. We sought to compare the bowel cleansing efficacy, tolerability, and acceptability of three low-volume regimens: an oral sodium phosphates solution 45/45 ml (NaP-45/45), a reduced-dose oral sodium phosphates solution 45/30 ml (NaP-45/30), and polyethylene glycol plus bisacodyl (PEG-2L). *Results* A total of 121 patients were evaluated (mean age 55.2 ± 8.9 years). Bowel cleansings rated as excellent and good were significantly different among the groups: NaP-45/45 = 98%, NaP-45/30 = 88%, and PEG-2L = 76% ($P < 0.04$). Side effects were not significantly different except for greater thirst in the NaP-45/45 group ($P = 0.001$) and increased vomiting in females using PEG-2L (two-tailed interaction, $P < 0.10$). Willingness to retake the preparation was higher among the sodium phosphates regimens (88, 95, and 73%, respectively; $P = 0.019$). *Conclusions* Better cleansing and willingness to retake the regimen was achieved with the oral sodium phosphates solutions than with polyethylene glycol plus bisacodyl.

Keywords Bowel preparation · Colonoscopy · Polyethylene glycol · Sodium phosphates

Introduction

An estimated 49,960 people are expected to die from colorectal cancer in the USA in 2008, and approximately 148,810 new cases are expected to be diagnosed [1]. Among new cases, only 39% are estimated to be detected in Stage A, early enough to offer the best prognosis possible [2]. Colonoscopy screening has been shown to reduce the expected morbidity and mortality of colorectal carcinoma by 76–90% [3, 4].

Efforts to improve colorectal cancer screening rates have focused on making the screening more acceptable to patients. These efforts include enhanced fecal occult blood testing (FOBT) through stool-based immunological testing or DNA testing [5, 6], serologic assays for colonic neoplasia, and advances in computed tomographic colonography (CTC, or virtual colonography) [7, 8]. However, if a polyp is detected by any screening method, the patient must still undergo colonoscopy for polyp removal. One of the major deterrents to colonoscopy is patient dissatisfaction with the bowel preparation process [9–11]. In addition to improving screening rates, measures that improve patient compliance with bowel cleansing regimens might also help to reduce costs associated with repeat colonoscopies due to poor bowel preparation [12].

This study has been presented in abstract form at the 2005 ACG Annual Meeting.

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Fleet® Phospho-soda® (sodium phosphates oral solution, NaP; C.B. Fleet Co., Lynchburg, VA) is marketed as an over-the-counter laxative in the USA and as a bowel preparation worldwide. Because of the relatively small volume required, NaP has been extensively utilized and shown to be an effective cathartic for bowel cleansing prior to colonoscopy, radiographic procedures, and surgery [13–20]. The most commonly used dosage is a split regimen of two 45-ml doses separated by 6–12 h (45/45 ml). However, while this regimen is generally better tolerated and more acceptable than 4 l of polyethylene glycol (PEG) lavage, nausea, vomiting, anal irritation, and serum electrolyte shifts associated with NaP do occur [13, 15–19, 21].

Despite slight differences in formulations, most PEG regimens require a total of 4 l for adequate bowel cleansing. This bowel preparation is poorly tolerated by many patients due to the large volume and because of side effects, such as bloating, nausea, and abdominal cramping [13, 15–19]. To reduce the volume of fluid, a new regimen was developed consisting of four 5-mg bisacodyl delayed-release tablets followed by 2 l polyethylene glycol solution (HalfLytely; Braintree Laboratories, Braintree, MA). The Food and Drug Administration (FDA) approved this regimen in 2004 as a prescription preparation for bowel cleansing prior to colonoscopy [22].

This pilot study was conducted between 25 October 2004 and 01 March 2005 with the primary purpose of comparing the efficacy of three bowel cleansing regimens prior to elective colonoscopy: a commercially available and well studied product (Fleet Phospho-soda with lemonade flavoring dosed at 45 ml in the evening followed by 45 ml the next morning), a reduced dosage product not marketed at the time (Fleet EZ-Prep archetype[1] dosed at 45 ml in the evening followed by 30 ml the next morning), and a newly marketed reduced dosage product (HalfLytely). The patients' self-rating of tolerance and acceptability and the incidence of adverse experience (AEs) were secondary endpoints.

Methods

Patient Selection

Adult men and women at least 18 years of age who were scheduled to undergo screening colonoscopy at a gastroenterology clinic (Gastroenterology Associates of Tidewater, P.C, Chesapeake, VA) and met screening criteria were invited to participate in the study. All patients were required to have a documented serum creatinine <1.5 mg/dl drawn within 45 days prior to enrollment, and women of child-bearing potential were required to have a negative serum pregnancy test.

Candidates with a history or presence of congestive heart failure, myocardial infarction within the prior 6 months, uncontrolled hypertension (diastolic blood pressure >105 mmHg), evidence of dehydration, renal or hepatic insufficiency, ascites, electrolyte abnormalities, gastrointestinal obstruction, gastric retention, bowel perforation, toxic colitis, toxic megacolon, ileus, a history of prior bowel surgery within the last 2 years, or active inflammatory bowel disease were excluded. Patients with known allergies to any of the ingredients of the tested products were also excluded.

The study protocol was reviewed and approved by an institutional review board (RCRC, 4009 Banister Lane, Austin, TX), and all patients signed an approved informed consent form prior to entering the study.

Study Design and Randomization

The study employed a randomized and single-blinded design with three parallel groups. The endoscopists were blinded to the bowel preparation assignment, and patients were instructed not to discuss their bowel preparation regimen with the examining physician. A computer-generated randomization list was prepared by the study biostatistician and all study medication kits were labeled with the randomization code on the outside. Research coordinators at the site managed the study medications and randomization list in such a manner as to maintain the study blind, and patients were randomly assigned to one of three bowel preparation regimens based on the order in which they completed study screening. In addition, each arm was balanced for gender with separate randomization lists for males and females; this step was taken to assure gender balance within the regimen because published reports have demonstrated gender differences in tolerability to bowel preparations [23]. For this pilot study, the sample size of 40 patients in each group (total 120 patients) was calculated to be sufficient to detect a difference in bowel preparation response of 20% between regimens with a power of 70%.

Study Procedures

Patients were randomized to receive one of three bowel cleansing regimens: NaP-45/45, an oral sodium phosphates solution with lemonade flavoring—45 ml at 7 p.m. the evening before colonoscopy and 45 ml at 6 a.m. the following morning (or 3 h before leaving for the clinic); NaP-45/30, an oral sodium phosphates solution with

[1] Study conducted during earlier development of Fleet Phospho-soda EZ-Prep with the product not finalized or marketed until September, 2006.

lemonade flavoring—45 ml at 7 p.m. the evening before colonoscopy and 30 ml at 6 a.m. the following morning (or 3 h before leaving for the clinic); PEG-2L: 20 mg bisacodyl delayed-release tablets (four 5-mg tablets) at 12 noon the day before the colonoscopy, followed by 2 l of PEG solution with electrolytes after the first bowel movement (or at 6 p.m. if none has occurred). To preserve a minimum of 10 h between the sodium phosphates doses, the evening dose was to be taken earlier than 7 p.m., if necessary.

The outpatient study design called for patients to follow the manufacturers' instructions regarding diet and fluids as outlined in the professional labeling and as previously reported [22, 24]. Those randomized to NaP-45/45 and NaP-45/30 were to have a regular breakfast followed by a low-residue lunch and then clear liquids until after the exam the following day. Patients randomized to PEG-2L were to have clear liquids beginning the morning before colonoscopy until after the examination the following day. Rather than controlling the total amount of clear liquid to be consumed, all patients were instructed to drink a minimum of three additional large glasses (240–360 ml) of clear liquid during the evening and then were encouraged to consume additional clear liquids ad libitum. This approach was taken to assure that adequate hydration was available to individual patients without mandatory amounts or limits regardless of the bowel preparation method.

Evaluation Methods

The bowel cleansing scoring system was similar to that previously described [14, 15, 20]. Examining endoscopists recorded a global preparation assessment (GPA) based on the following definitions: excellent = small or no volume of clear liquid, good = moderate or large volume of clear to semi-clear liquid, fair = some semi-solid stool that could be suctioned or washed away, or poor = some semi-solid or solid stool that could not be suctioned or washed away. The GPA score was coded from 1 = poor to 4 = excellent for analysis. A total of six endoscopists participated in this study. Study endoscopists participated in a teaching session on the grading assessment scales at initiation of the protocol to enhance interobserver consistency of bowel preparation grading.

In addition, a residual stool score (RSS) was calculated by evaluating each of five intestinal segments (rectum, descending colon, transverse colon, ascending colon, and cecum) for the amount and consistency of residual stool and percentage of bowel wall visualized. Each segment was scored on a scale of 0 (best) to 4 (worst) as follows:

- Stool amount: 0 = none, 1 = minimal, 2 = small, 3 = moderate, 4 = large;
- Stool consistency: 0 = none, 1 = clear yellow liquid, 2 = muddy liquid, 3 = particulate stool, 4 = solid stool;
- Percentage wall visualized: 0 = >95%, 1 = 85–94%, 2 = 75–84%, 3 = 50–74%, 4 = <50%.

The scores were summed for each segment (range = 0–12), and the individual segment sums were then averaged on a per-patient basis to generate a RSS for each patient. A lower RSS indicated better colon cleansing. The RSS grading system has been demonstrated to have a high degree of statistical correlation with the GPA ($r = -0.76$, $P < 0.001$) [14].

Each patient completed a questionnaire evaluating the acceptability (ease of preparing the medication, ease of drinking the medication, and taste of the medication) of their assigned bowel preparation regimen. For patients assigned to the NaP regimens, these evaluations were made following each of the two doses, while patients assigned to the PEG-2L regimen completed their evaluation following the single preparation dose. In addition, on the morning of their procedure, each patient self-rated their overall tolerance of the bowel preparation medication and the overall bowel preparation process (entire 2 days of preparation regimen including medications, diet, and clear fluids) on a 5-point Likert scale: "very poor/difficult," "poor," "okay," "good," and "very good/easy." The responses to these questions were coded for analysis as 1 = very poor/difficult to 5 = very good/easy.

Tolerability was captured as the incidence of 12 commonly reported adverse experiences (AEs) associated with bowel preparations after each dose of medication (two doses for NaP regimens and one dose for the PEG-2L regimen). Each AE was recorded as either "none," "mild," "moderate," or "severe," and intensity was coded as 0 = none to 3 = severe. For analysis, incidence was positive if the AE was coded above 0 on any occasion.

Statistical Methods

Statistical analyses were performed on an intent-to-treat (ITT) basis with all patients who were administered at least one dose of study drug included in the efficacy analyses. If an exam was not performed due to inadequate bowel cleansing (e.g., the patient reported not having a bowel movement), then the GPA was imputed as "poor," and the bowel cleansing section scores were imputed as "4." All patients who received one or more doses of study medication were included in the safety analysis. Statistical analyses were performed using SAS (SAS Institute, Cary, NC), with significance being reached when the two-tailed test yielded a probability of 0.05 or less for main effects, or ≤ 0.1 for tests of interaction; the higher significance level for interactions was chosen because the sample sizes of the

means in the interaction are smaller, and a higher significance level provides protection from missing important interactions.

The GPA and RSS were analyzed for significant differences using analysis of variance (ANOVA) with orthogonal contrasts to partition the variability into the following components: NaP regimens by gender (i.e., NaP-45/45 vs. NaP-45/30, gender, the interaction of gender and the two NaP regimens), the mean of NaP regimens versus PEG-2L, and gender within PEG-2L. Since the comparisons were orthogonal and made within the single analysis, no corrections were necessary for multiple tests. To allow comparisons with the published literature, a positive response to the bowel preparation was defined as either an "excellent" or "good" GPA. This binary outcome was analyzed by logistic regression for statistical significance using the contrasts above. The response rate was reported as the percentage of patients and referred to as "clinical efficacy" to reflect that the colon was sufficiently cleansed to permit an adequate exam.

Responses to questions of acceptability and overall tolerance of the medication and of the bowel preparation process were analyzed by an ANOVA with regimen and gender as factors. The significance of differences in willingness to repeat the dosing method was evaluated by logistic regression.

Patients assigned to the PEG-2L regimen completed one questionnaire in the evening following ingestion of their bowel preparation dose, while patients assigned to either NaP regimen completed questionnaires after the evening dose and the morning dose. For NaP patients, the worse case response to each AE was used in the analysis. Logistic regression was used to assess the significance of regimen and gender simultaneously in the incidence reporting of each of the 12 commonly reported AEs. Intensity was analyzed with an ANOVA with factors of regimen and gender.

Results

Demographics

The study was conducted between October 2004 and March 2005. During that time, 131 patients were screened and 121 were enrolled in the study (seven withdrew consent, two were rescheduled outside the study window, and one was withdrawn for failure to comply). Study participants were balanced by regimen and gender (Table 1), and the sample included 97 (80%) Caucasians, 22 (18%) African-Americans, and two (2%) of Filipino descent. Body mass index (BMI) was not significantly different by regimen or between genders, with 23 patients (19%) classified as normal (BMI < 25); 54 (45%) as overweight (BMI 25–29.9), and 44 (36%) as obese (BMI > 30). The indications for colonoscopy were not markedly different by regimen, with the primary purpose listed as "screening" in 66% of patients.

Bowel Cleansing Efficacy

The GPA ratings for each regimen are shown in Fig. 1. Analysis of mean GPA scores by regimen and gender are shown in Fig. 2; there was a significant interaction between regimen and gender ($P = 0.07$). This Figure illustrates that higher GPA scores (better bowel cleansing) were recorded for the NaP regimens than the PEG-2L regimen ($P < 0.01$). Analysis of the GPA scores showed a significant difference in bowel preparation efficacy between the two NaP regimens, with NaP-45/45 demonstrating higher scores (cleaner colon) than NaP-45/30 (3.50 ± 0.64 vs. 3.42 ± 0.64, respectively, $P = 0.01$). Gender differences were not significant within the PEG-2L regimen ($P = 0.79$) but there was a significant interaction of gender with NaP regimens ($P = 0.05$); males in the NaP-45/30 group

Table 1 Patient demographics and indication for colonoscopy

Variables	Regimens		
	NaP-45/45 ($n = 40$)	NaP-45/30 ($n = 40$)	PEG-2L ($n = 41$)
Male:female	20:20	20:20	20:21
Mean age, years (range)	54.8 (21–75)	54.7 (29–69)	56.0 (36–82)
Screening, family history, or cancer surveillance	29	26	25
History of polyps	5	7	4
Bleeding	3	2	9
Abnormalities on computed tomography scan	1	1	0
Change bowel habits	1	2	1
Diarrhea	1	1	1
Inflammatory bowel disease	0	1	0
Left lower quadrant pain	0	0	1

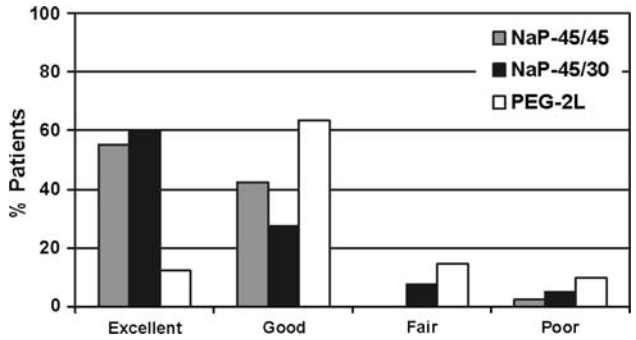

Fig. 1 Global preparation assessment by regimen. *NaP-45/45* oral sodium phosphates solution 45/45 ml, *NaP-45/30* oral sodium phosphates solution 45/30 ml, *PEG-2L* polyethylene glycol plus bisacodyl

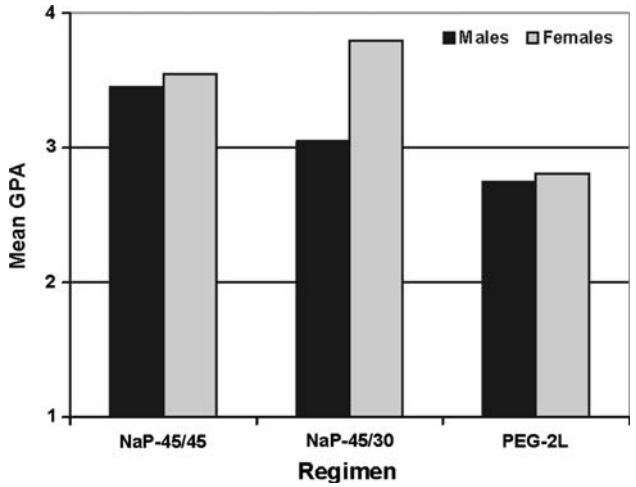

Fig. 2 Mean global preparation assessment (*GPA*) scores, by regimen and gender. A higher mean GPA score indicates a better bowel preparation

demonstrated a worse GPA mean score than females in this group.

Our analysis of bowel preparation by clinical efficacy (percentage of excellent + good scores) revealed a significant difference among regimens ($P < 0.04$), but not between genders ($P = 0.24$). Clinical efficacies were 39/40 (98%) for NaP-45/45, 35/40 (88%) for NaP-45/30, and 31/41 (76%) for PEG-2L. Orthogonal contrasts within the logistic regression model showed a significant difference in clinical efficacy for the NaP regimens versus PEG-2L ($P = 0.01$), but not between the two NaP regimens ($P = 0.12$).

Mean residual stool scores were significantly different between NaP regimens versus PEG-2L (2.65 ± 1.69 vs. 3.72 ± 1.81, respectively; $P = 0.01$). Means between the NaP regimens trended toward significance (NaP-45/45 2.34 ± 1.20 vs. NaP-45/30 2.98 ± 1.20; $P = 0.06$). The interaction of the NaP regimens and gender was significant

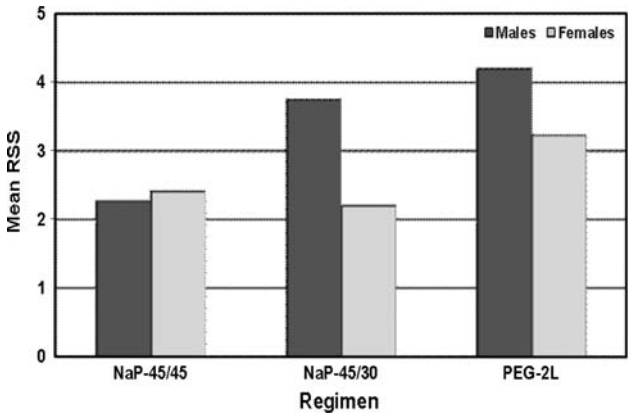

Fig. 3 Mean residual stool score (*RSS*) by regimen and gender. A lower mean RSS indicates a better bowel preparation

($P = 0.02$), while gender differences were not significant within the PEG-2L regimen ($P = 0.07$) (Fig. 3). The RSS was highest (poorer preparation) in the PEG-2L group and lowest (better preparation) in the NaP-45/45 group. Mean RSS was lower in females (2.41 ± 1.30) and males (2.27 ± 1.13) in the NaP-45/45 group compared to females (3.23 ± 1.99) and males (4.20 ± 1.51) in the PEG-2L group. In the NaP-45/30 group, females demonstrated a similar mean RSS (2.20 ± 1.68) as patients in the NaP-45/45 group, while males in the NaP-45/30 group had a higher mean RSS (3.75 ± 2.14) than females in this group. The correlation between the GPA and RSS was 0.70 ($P < 0.01$).

Acceptability

Patients in all groups combined rated the preparation of bowel cleansers as "easy" or "very easy" 88% of the time (18%, easy; 70%, very easy). However, as Fig. 4 illustrates, the mean ease of preparing the bowel cleansers was significantly different among regimens, with PEG-2L being scored as the easiest (PEG-L = 4.90 ± 0.37, NaP-45/45 = 4.45 ± 0.75, NaP-45/30 = 4.66 ± 0.60; $P < 0.01$). Mean ease of drinking the bowel preparation was not different among regimens (NaP-45/45 = 3.09 ± 0.66, NaP-45/30 = 3.52 ± 1.04, PEG-2L = 3.27 ± 0.95; $P = 0.47$). A gender difference was observed in females who rated drinking the preparation more difficult than males for all regimens ($P = 0.01$). Taste was not significantly different by regimen ($P = 0.71$) or gender ($P = 0.07$). Most patients (86%) rated taste as "okay" or better.

Patients' self-rating of mean tolerance to the medication was not significantly different among the regimens (NaP-45/45 = 4.05 ± 0.75, NaP-45/30 = 4.10 ± 0.71, PEG-2L = 3.80 ± 1.01; $P = 0.25$), or by gender ($P = 0.20$). Mean overall tolerance of the preparation process was significantly different among the three regimens, with the

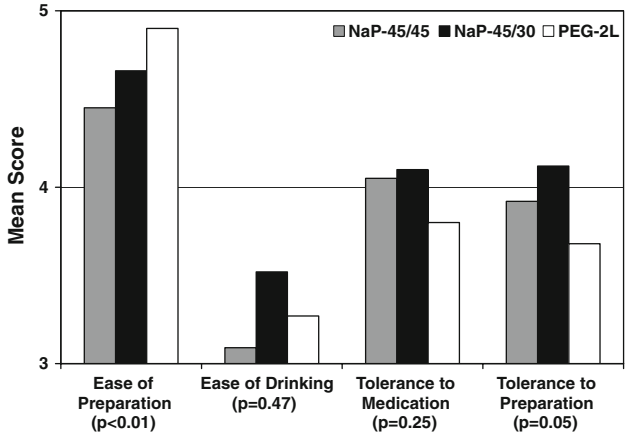

Fig. 4 Patients' self rating of acceptability and tolerance

NaP-45/30 regimen scoring the highest (NaP-45/45 = 3.92 ± 0.76, NaP-45/30 = 4.12 ± 0.82, PEG-2L = 3.66 ± 0.82, $P = 0.05$). No significant gender differences were observed for mean overall tolerance of the preparation process ($P = 0.74$).

Willingness to Repeat Preparation Process

A significant difference was observed in the percentage of patients willing to repeat their assigned regimen for future exams ($P = 0.02$). Patients in the NaP-45/30 group reported the highest willingness to retake the regimen in the future. Ten patients (24%) assigned to the PEG-2L group were unwilling to retake the regimen compared to five (13%) in the NaP-45/45 group and two (5%) in the NaP-45/30 group. Nine of the ten subjects who were unwilling to repeat the PEG-2L regimen were females, three of the five subjects who were unwilling to repeat the NaP-45/45 regimen were females, and both subjects in the NaP-45/30 group were females. A review of the unsolicited comments from the subjects in the PEG-2L group suggested that the volume and taste of the liquid were the primary reasons for their decision; reasons for unwillingness to repeat the NaP regimens had no pattern.

Tolerability

The incidence and significance values for commonly reported AEs by regimens and gender are shown in Table 2. The P values reported in Table 2 are intended to indicate the strength of the disagreement with the hypothesis that the mean incidence is the same for all three regimens and are not adjusted for multiple testing. Thirst was reported more often by NaP-45/45 patients than NaP-45/30 or PEG-2L patients ($P < 0.01$). There was a significant interaction of gender by regimen for the incidence of vomiting ($P = 0.08$), with more females in the PEG-2L regimen reporting vomiting than did females in the other two regimens and males in all regimens. Since the interaction was significant, the incidences for vomiting are reported in Table 2 separately by regimen and gender. Separate logistic regression by regimen showed that the odds ratio (OR) for vomiting was 11.7 for females versus males ($P = 0.03$) in the PEG-2L group. An equal number of patients (two males, one female) in each NaP group reported vomiting; these gender differences were not statistically significant (OR 0.474, female vs. male, $P = 0.56$). There was a significant gender difference in the incidence of nausea, weakness, anal irritation, indigestion, and overall discomfort among regimens, with females reporting these AEs more often than males regardless of regimen assignment. Analysis of the intensity scores showed results similar to the incidence results (data not shown).

Discussion

The results of this pilot study demonstrated that oral sodium phosphates solution, taken either at a dose of 45 ml the evening prior to the exam and 45 ml on the morning of the exam, or as a 45-ml dose the evening prior to the exam and 30 ml the morning of the exam, provided better bowel cleansing than 20 mg of bisacodyl tablets plus 2 l PEG. Patient acceptability and tolerance to the medication was similar across all three regimens, but willingness to repeat the process and patient overall tolerance to the prep process was better for the NaP regimens. Most of the patients who reported an unwillingness to repeat their bowel preparation were females who had been assigned to receive PEG-2L. Differences in tolerability reporting by gender have been described previously [23].

Over the years, researchers have investigated several different combinations of cathartic formulations and dosages in search of an acceptable and efficacious low-dose, low-volume bowel preparation that may lead to a better experience for the patient and a more thorough colonoscopic examination [25–27]. Di Palma et al. reported that the combination of 20 mg bisacodyl delayed-release tablets followed by 2 l of PEG (HalfLytely) produced excellent or good bowel preparation in 87.1% of patients and a significant reduction in fullness, nausea, vomiting, and overall discomfort when compared to a 4-l regimen [27]. However, 6.5% of patients in the 2-l PEG regimen were reported to have "inadequate" bowel preparation compared to 0% in the 4-l PEG regimen ($P < 0.05$), and changes in the labeling have recently been made to warn of the potential for neurologic and gastrointestinal tract effects with PEG products [28].

Table 2 Incidence of commonly reported adverse experiences by regimen and odds ratios by gender

Adverse experience	Regimen				Odds ratios	
	NaP-45/45 ($n = 40$)	NaP-45/30 ($n = 40$)	PEG-2L ($n = 41$)	Regimen *P* value	Gender (female:male)	Gender *P*-value
Nausea	21	17	20	0.64	3.87	<0.01
Vomiting[a]						
Male	2	2	1	0.082[a]		
Female	1	1	8			
Bloating	28	22	26	0.38	1.47	0.31
Cramps	19	22	20	0.77	0.61	0.17
Weakness[b]	13	14	11	0.72	2.95	0.01
Chills[b]	17	17	19	0.88	1.51	0.27
Anal irritation	28	22	24	0.35	1.95	0.08
Headache	14	8	9	0.25	0.63	0.27
Thirst	27	15	11	0.001	1.44	0.36
Hunger	24	22	25	0.84	0.68	0.30
Indigestion	11	9	8	0.66	4.03	<0.01
Overall discomfort	28	28	32	0.65	2.20	0.06

Incidence data are given as the numbers of patients

[a] Significance of the gender × regimen *P* value for this adverse experience of 0.08 required a separate tabulation of incidence. See text for odds ratios of gender within each regimen

[b] One patient on PEG-2L did not answer these questions

Poon et al. compared 2-l PEG against 45/45 ml NaP administered on the day of the exam approximately 4–6 h before the colonoscopy [29]. In the NaP group, the two doses were administered 2 h apart, an interval significantly shorter than the manufacturer's recommendation of 10–12 h. Overall bowel cleansing was not significantly different between the two regimens, although it was noted that there was significantly better cleansing in the cecum when the NaP regimen was used. No differences were observed between the two groups with regard to willingness to repeat the regimen, ease of consumption, acceptability of the regimen, or the endoscopists' overall satisfaction with the quality of the regimen as measured on a visual-analog scale.

The combination of 2 l of PEG with high doses of vitamin C was first investigated in a pilot study in 2000 and reported in 2005 [30]. In that report, a series of six combinations of PEG (2 l of either 100 or 125 g/l), together with sodium sulfate (5–7.5 g/l), sodium ascorbate, or ascorbic acid (0, 5, or 10 g/l), were compared in a double-blind, crossover design where efficacy was evaluated as stool volume output. Efficacy, acceptability, and tolerability were generally similar among the study regimens. Minor changes in serum chemistry were noted, but all values remained within normal limits with no significant differences among preparations.

Along with the advent of low-dose PEG regimens, a low-residue NaP tablet (OsmoPrep Tablets; Salix Pharmaceuticals, Morrisville, NC) has been approved recently by the FDA. Rex et al. compared the bowel cleansing efficacy of three split-dose NaP tablet regimens taken the evening before and morning of colonoscopy: 40 standard NaP tablets, 40 low-residue NaP tablets, and 32 low-residue tablets [31]. Colon cleansing was rated as "excellent" or "good" in 95% of patients assigned to the original 40-tablet formulation, 97% in the 40-tablet low-residue regimen, and 95% in the 32-tablet low-residue regimen. Less pronounced changes in serum electrolyte levels from baseline to examination were reported with the 32-tablet low-residue regimen as compared to either of the 40-tablet regimens.

A recent study by Johanson et al. compared a reduced-dose 2-l PEG regimen plus bisacodyl (HalfLytely) to a 32-tablet sodium phosphates regimen (OsmoPrep) [32]. The authors found that the mean overall and ascending colon cleansing scores for NaP were significantly better than those for PEG-2L ($P < 0.0001$). Patients treated with NaP reported significantly fewer adverse events and gastrointestinal symptoms than PEG + bisacodyl. Transient changes in laboratory parameters were observed in both treatment groups, but electrolyte changes were more common and of greater magnitude in the NaP group.

In our study, we used a reduced dose of sodium phosphates in the NaP-45/30 group that closely emulates the sodium phosphates content of the 32-tablet OsmoPrep regimen. Thirty-two tablets of OsmoPrep provide 48 g of sodium phosphates, while 75 ml of Phospho-soda provide 49.5 g of sodium phosphates. We found that superior bowel preparation was achieved with either a 45/45-ml or 45/30-ml sodium phosphates regimen compared to 20 mg of bisacodyl delayed-release tablets followed by 2 l PEG solution. Response rates to the bowel preparation were statistically similar between the 45/45-ml and 45/30-ml NaP groups.

Although an association between male gender and poorer colon preparation has been noted previously [33], this was not consistently true among our study groups. We found that males in the NaP-45/30 group demonstrated the poorest preparation when compared to females in the same group and to both males and females in the NaP-45/45 group. The bowel cleansing efficacy between male and female patients within the 45/45-ml NaP group and the PEG-2L group was not significantly different.

Each of the regimens had similar incidences of AEs reported and similar acceptability profiles. Patients in the NaP-45/30 regimen reported the best tolerance to the medication and bowel preparation process and the highest willingness to repeat the preparation for a future exam. Within each of the regimens, a significant gender difference in bowel preparation tolerability and efficacy was found; females were more likely than males to report common AEs, including nausea, vomiting, and overall discomfort.

The single-site design is a limitation of the study. Our study design also did not prospectively capture information regarding the completion of study medications, although anecdotal evidence (e.g., patient write-in responses and reports of vomiting) would suggest that females in the PEG-2L group had the most difficulty consuming the entire bowel preparation. Despite these limitations, the significant differences observed in both efficacy and acceptability suggest that sodium phosphates in either the 45/45-ml regimen or 45/30-ml regimen is a more efficacious bowel preparation for colonoscopy than 2-l PEG with bisacodyl. The cost comparison also favors oral sodium phosphates (mean retail of $US 18.99 for Fleet Phospho-soda E-Z-Prep versus $US 41.83 for HalfLytely).

It should be remembered that proper patient selection is critical whenever a bowel purgative is prescribed [21, 24, 28]. The sodium phosphates bowel preparation is not appropriate for all patients, and recent reports of acute phosphate nephropathy illustrate the critical importance of appropriate patient selection [34–38]. Patients with clinically significant impairment of renal function, congestive heart failure, and ascites should not receive sodium phosphates [24]. Our study excluded patients with contraindications to oral sodium phosphates.

Given the superior acceptability and similar tolerability and efficacy of the 45/30-ml reduced-dose sodium phosphates regimen compared to the standard 45/45-ml regimen, the lower dose regimen should be recommended as the dosing standard. Our results suggest that there may be significant gender differences in bowel preparation tolerability and efficacy, a topic that has received little study. Further investigation is needed to determine whether these differences in bowel preparation response might warrant dose modification for some patient groups.

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