

# Bowel cleansing for colonoscopy: prospective randomized assessment of efficacy and of induced mucosal abnormality with three preparation agents

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## Bibliography

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**Background and study aims:** Bowel-cleansing studies are frequently underpowered, poorly designed, and use subjective bowel cleansing assessments. Consensus on efficacy, tolerability, and preparation-induced mucosal abnormalities is lacking. This study aimed to clarify the differences in efficacy and preparation-induced mucosal inflammation of sodium phosphate (NaP), colon-LYTLEY (PEG), and Picoprep (Pico).

**Patients and methods:** This was a prospective randomized single-blinded trial of ambulatory patients to assess the efficacy of bowel preparation and preparation-induced mucosal inflammation. Proceduralists who were blinded to the preparation taken, assessed both bowel cleansing by using the Ottawa bowel preparation assessment tool and preparation-induced mucosal inflammation.

**Results:** Of the 634 patients, 98% ingested more than 75% of the bowel preparation and data were complete for colonic preparation scoring in 99%.

The preparation used, time of procedure, and patient sex all independently impacted on bowel cleansing. NaP was less efficacious than PEG ( $P < 0.001$ ) and Pico ( $P < 0.001$ ) for morning procedures whereas all bowel preparations were equally efficacious for afternoon procedures. Preparation-induced mucosal inflammation was 10-fold greater with NaP ( $P = 0.03$ ) and Pico ( $P = 0.03$ ) compared with PEG.

**Conclusions:** This is the largest published prospective randomized blinded study on this topic and the first to evaluate the three major classes of preparation with a validated tool. The bowel preparation used, time of procedure, and patient sex all independently impacted on bowel cleansing. NaP gave the worst preparation for morning procedures whereas all preparations were equally effective for afternoon procedures. NaP and Pico induced mucosal inflammation 10-fold more frequently than PEG, a finding that requires further investigation.

## Introduction



Colonoscopy is a common procedure that requires bowel cleansing preparation for adequate colonic assessment. Poor preparation reduces the detection of colonic lesions and results in 10%–20% of colonoscopies being aborted [1]. This results in repeated examinations, which impact on waiting lists and healthcare costs while increasing the risk of complications. Bowel cleansing preparations are classified into three broad groups: osmotic, polyethylene glycol (PEG), and stimulatory laxatives. Osmotic laxatives, such as sodium phosphate (NaP), draw fluid into the colonic lumen. PEG laxatives with electrolytes are retained within the colon where they act as a bowel cleanser without significant fluid exchange. The stimulant laxatives, such as sodium picosulphate (Pico), act primarily by enhancing smooth muscle contractility but also may increase luminal water.

More than 80 published trials have investigated colon cleansing preparations; however, almost all are underpowered with poor study design and ill-defined outcome measures [2]. Only 12 prospective randomized studies have included more than 100 patients in each study arm [3–13]. Of these, nine examined colon cleansing efficacy; however, all but one relied on subjective “in-house” assessment criteria for bowel cleansing. None of these in-house assessments had been validated, and as none was an objective assessment comparison between studies is extremely difficult [2]. Meta-analyses suggest that NaP may be a better cleansing agent than PEG [14, 15], but due to the subjective assessments, consensus has not been achieved. Recently a calibrated externally validated outcome assessment tool of bowel cleansing has been developed [16], but as yet it has only been used in two studies [13, 17].

The efficacy of bowel cleansing must be balanced against any colonic mucosa effects. Colonic ulceration/inflammation has been reported in 3%–24% of patients taking NaP [18] compared with 1%–2% of patients taking PEG [19]. These studies, however, were open-labeled, nonrandomized [19], or underpowered to detect differences between the preparations [18]. Further studies are required to determine whether the preparations do induce acute mucosal inflammation. This study was designed to clear some of the confusion that surrounds the efficacy of three of the most commonly used bowel preparation agents in a community setting. It also aimed to identify whether there are any differences in the rates of preparation-induced mucosal inflammation between the preparations.

## Methods



### Inclusion and exclusion criteria

This was a prospective randomized single-blinded trial during 2008–09 comparing three commonly used colon-cleansing agents. NaP (CB Fleet Co. Pty Ltd., Braeside, Victoria, Australia), Pico (Pharmatel Fresenius Kabi Pty Ltd., Pymble, New South Wales, Australia), and colonLYTLEY (PEG, Dendy Pharmaceutical Pty Ltd., Dendy, Victoria, Australia). Ethical approval was obtained from the Southern Metropolitan Area Health Service Human Research Ethics Committee, and the study was registered as a clinical trial at ClinicalTrials.gov (Identifier: NCT00750763). All patients were community-based ambulatory patients at Kaleeya Hospital, a public hospital in Perth, Western Australia. All patients were included with the exception of those with confirmed or suspected inflammatory bowel disease (IBD), current nonsteroidal anti-inflammatory drug (NSAID) use (excluding low-dose aspirin), heart failure (New York Heart Association class > 2), renal failure (glomerular filtration rate < 30) [2], and those aged over 75 years [2].

Patients were randomized using random number generation (Generator Pro 1.69, Segobit Software) to receive PEG, NaP or Pico. Patients were randomized by the principal study investigator at the time of clerical booking for the patient's colonoscopy. As the reported incidence of colonic ulceration/inflammation is 3%–24% with NaP and 1%–2% with PEG, patients were randomized in the ratio of 2:1:1 (PEG:NaP:Pico) in order to identify statistical differences between PEG and the other preparations. Patient demographics were also recorded (► Table 1).

### Patient preparation instructions

All patients were sent written instructions and were telephoned by a trained endoscopy nurse to discuss diet and bowel preparation instructions prior to commencing the preparation. In line with the routine practice at our institution, all patients commenced a minimal-residue diet 2 days prior to colonoscopy and were restricted to clear fluids on the day before their colonoscopy. The bowel preparation agents NaP and Pico were taken as a split course separated by 12 hours.

Patients on a morning list taking NaP were instructed to:

1. 7.00 a.m. the day prior to colonoscopy, add 15 mL of NaP oral solution USP to a full glass (250 mL) of water and drink. Repeat twice within 20 minutes.
2. Drink at least three more glasses (250 mL) of clear liquid (total 750 mL).
3. 7.00 p.m. add 15 mL of NaP oral solution USP to a full glass (250 mL) of water and drink. Repeat twice within 20 minutes [17].
4. Drink at least three more glasses (250 mL) of clear liquid (total 750 mL).
5. Continue to drink clear fluids until 2 hours before the colonoscopy.

Patients on an afternoon list took their first NaP preparation at 7.00 p.m. the night before colonoscopy, and the second at 7.00 a.m. on the day of the procedure.

Patients on a morning list taking Pico were instructed to:

1. Dissolve the contents of two sachets of Picoprep (each containing 10 mg sodium picosulfate, 3.5 g magnesium oxide, and 12.0 g citric acid) into two glasses of water (250 mL) and store in the refrigerator.
2. At 3 p.m. on the day prior to the colonoscopy drink one glass of Picoprep. At 9 p.m. drink the second glass of Picoprep.
3. Drink one glass of water each hour while taking the preparation.
4. Continue to drink clear fluids until 2 hours before the examination.

Patients on an afternoon list took their first Picoprep at 9.00 p.m. the night prior to colonoscopy and the second at 7.00 a.m. on the day of the procedure.

Patients on a morning list taking PEG were instructed to:

1. Dissolve the contents of four sachets of PEG in 4 L of water and store in the refrigerator. Cordial may be added (not with red, green or blue coloring).

Patient characteristics	Bowel preparation (n = 634)		
	PEG	NaP	Pico
Patients, n (%)	284 (45)	179 (28)	171 (27)
Age, mean ± SD, years	53.2 ± 13.1	52.7 ± 12.1	55.3 ± 12.6
< 40 years, n (%)	41 (14)	22 (12)	18 (11)
40–49 years, n (%)	58 (20)	43 (24)	36 (21)
50–59 years, n (%)	85 (30)	56 (31)	50 (29)
60–69 years, n (%)	76 (27)	48 (27)	44 (26)
70–74 years, n (%)	24 (9)	10 (6)	23 (14)
Male, n (%)	127 (45)	83 (46)	82 (48)
Primary indication, n (%)			
Abdominal pain	23 (8)	15 (8)	18 (11)
Altered bowel habit	66 (23)	34 (19)	24 (14)
Bleeding/anemia	124 (44)	71 (40)	71 (42)
Screening	60 (21)	56 (31)	54 (32)
Weight loss/miscellaneous	11 (4)	3 (2)	4 (2)

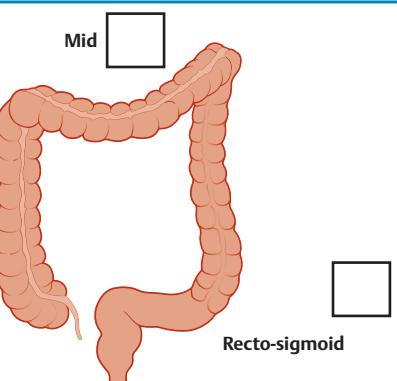
**Table 1** Demographic data. Sex, age, and primary indication for colonoscopy distributed by bowel preparation.

NaP, sodium phosphate; PEG, polyethylene glycol; Pico, sodium picosulfate.

**Ottawa Bowel Preparation Assessment Tool**  
(Rostom et al Gastrointest Endosc 59; 4: 2004)

**A regional score per segment (Zero to four):**

0 = perfect prep (excellent)  
1 = mild staining but mucosa seen (good)  
2 = suction needed to see colonic wall (fair)  
3 = wash & suction needed (poor)  
4 = unable to see colonic wall (very poor)



**A general fluid score (Zero to two):**

0 = No fluid  
1 = Moderate volume  
2 = Large volume

**Total Regional Score**  
(Range 0 to 12)

**Total Fluid Score**  
(Range 1 to 2)

**TOTAL SCORE**  
(Min. 0 to Max. 14)

**Fig. 1** Ottawa bowel preparation assessment tool.

- Commence drinking the solution at 4 p.m. If the total volume is not consumed during the evening, complete the preparation at the earliest opportunity the following morning.
- Continue to drink clear fluids until 2 hours before the examination.

Patients on an afternoon list took their PEG as for patients on the morning list and continued to drink clear fluids up until 2 hours before the examination.

### Preparation efficacy and mucosal inflammation assessments

At colonoscopy, the proceduralist, who was blinded to the agent taken, assessed colonic cleansing using the Ottawa bowel preparation assessment tool (► Fig. 1) [16].

A score between 0 (perfect preparation) and 4 (unable to see the colonic wall) was given to each of three segments of the colon (right, mid, and rectosigmoid), and this score was combined with a general score for fluid in the colon to achieve the overall Ottawa bowel preparation score. All endoscopists underwent training prior to the study to standardize their use of the assess-

ment tool. If the colonoscopy was abandoned due to poor preparation, the preparation scores for any regions proximal to intubation were rated as 4 (poor).

The presence of mucosal inflammation/ulceration detected by the expert endoscopist was photographed and biopsied. Only findings of mucosal inflammation/ulceration with photographic proof and/or histological confirmation of acute inflammatory changes were considered to have a true mucosal abnormality. Photographic images and histology review were undertaken with the reviewer blinded to the bowel preparation used. The endoscopic mucosal abnormalities were considered to be associated with the bowel preparation if no other explanations were found.

### Statistics

There is a minimum incidence rate of 3% for mucosal ulceration/inflammation observed with NaP and an estimated 1% incidence with PEG. The rate of mucosal inflammation with Pico has yet to be determined and it has been assumed that the rate will be similar to NaP at 3%. The number of patients required to detect significance with type I error of 0.05 at 80% power between the mucosal inflammation rate of PEG and both NaP and Pico is 765 patients in a ratio of 2:1:1 (PEG:NaP:Pico). This number also enabled similar or greater power to estimate differences between bowel-cleansing efficacies.

Bowel preparation scores were analyzed on a combined scale and on an individual basis. General linear mixed models examined the effects of sex, consultant, time, age group, and bowel preparation. Consultant was used as a random effect and two-way interactions were again considered. Results are presented as least square means (least square means are adjusted means, or estimated means, that have been controlled for other variables) and 95% confidence intervals (CIs). Fluid was analyzed with scores of 1 and 2 combined to create a dichotomous outcome. This outcome was analyzed with effects for the linear mixed model approach as above. Odds ratios and 95% CIs are presented. Analysis of the dichotomized bowel preparation score was undertaken using a generalized estimating equations approach with effects as mentioned for the linear mixed model approach above. Odds ratios and 95% CIs are presented. It should be noted that no corrections for multiplicity have been made in these analyses.

### Results



#### Early termination of the study

A blinded interim analysis was performed after 600 patients had been recruited due to clinical concerns that a group of patients had worse bowel preparation. This blinded analysis identified significant differences in bowel cleansing and mucosal inflammation/ulceration between the bowel preparations used, and therefore the study was terminated early. This decision was made by physicians external to the study design following assessment of the interim analysis. There were no cases of renal failure, death or need for hospitalization within 48 hours of the colonoscopic procedure in any of the patients.

#### Patient characteristics

A total of 634 patients were recruited and randomized. ► Table 1 summarizes patient sex, age, and the primary colonoscopic indication. No significant differences were detected between these parameters and the bowel preparation taken. All patients con-

	A score of 4 in right colon	A score of 4 in mid-colon	A score of 4 in rectosigmoid	At least one score of 4	Total regional score of 7 or greater
PEG, n (%)	20 (7)	8 (3)	8 (3)	20 (7)	48 (17)
NaP, n (%)	32 (18)	11 (6)	5 (3)	33 (19)	57 (32)
Pico, n (%)	7 (4)	2 (1)	1 (0.6)	8 (5)	26 (15)

NaP, sodium phosphate; PEG, polyethylene glycol; Pico, sodium picosulphate.

firmed they had followed the dietary restrictions and the instructions for the allocated bowel preparation. A total of 255 patients in the PEG group (90%) ingested the full preparation, with 277 (98%) taking 75% or more ( $> 3$  L). The remaining seven patients took 50% (2L) of the preparation. A total of 172 patients (96%) in the NaP group ingested the full preparation. The remaining seven patients took 50% of the preparation. All 171 patients (100%) in the Pico group took the full preparation.

### Colon cleaning efficacy

Data were complete in 625 patients (99%) (279 PEG, 177 NaP, 169 Pico). Of these 625 patients, intubation of the cecum or terminal ileum was achieved in 617 (99%) (cecum 80/617; ileum 537/617). Five patients had their procedure abandoned due to discomfort (two PEG, two NaP, one Pico). In three of these patients the hepatic flexure was reached and the right colon preparation could be assessed. Five patients had the procedure abandoned due to poor preparation and a preparation score of 4 was given to each segment proximal to the insertion site as per the methods (four PEG, one NaP). Overall a completed Ottawa bowel preparation score was obtained for 625 patients.

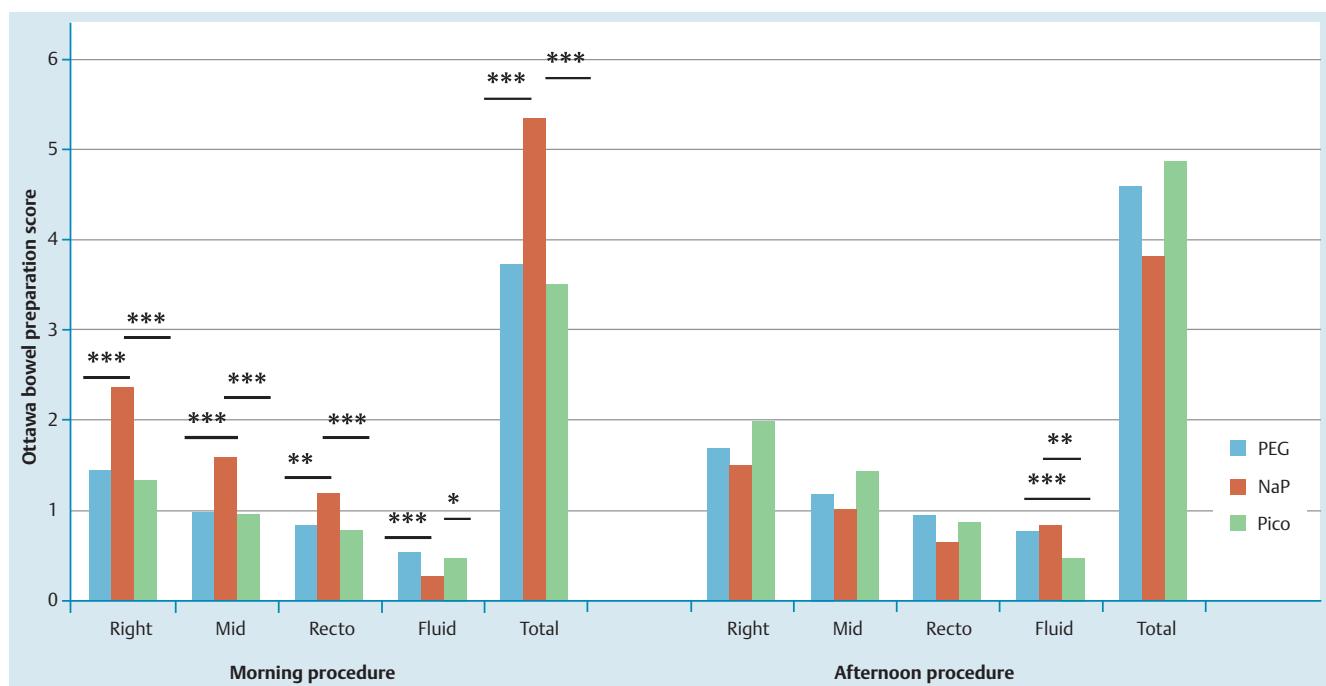
An Ottawa bowel preparation regional score of 3 indicates that washing and suction is required in order to get good views of the bowel wall and the preparation provided suboptimal cleansing of the bowel region, whereas a score of 4 indicates that the

bowel wall is unable to be cleaned sufficiently to allow appropriate mucosal examination. A total regional score (a score that adds each of the three regional scores but excludes the total fluid score) of 7 or greater indicates that at least one of the three bowel regions was assessed as a regional score of 3 and that the mucosal examination of at least one region was compromised. Overall 21% of patients had a total regional score of 7 or greater (► Table 2), and patients taking NaP were significantly more likely to fall into this category than those taking Pico (32% vs. 15%, odds ratio [OR] = 2.78, 95%CI 1.14–6.78;  $P = 0.024$ ) and those taking PEG, though this was not significant (32% vs. 17%, OR = 2.42, 95%CI 0.99–5.95;  $P = 0.053$ ).

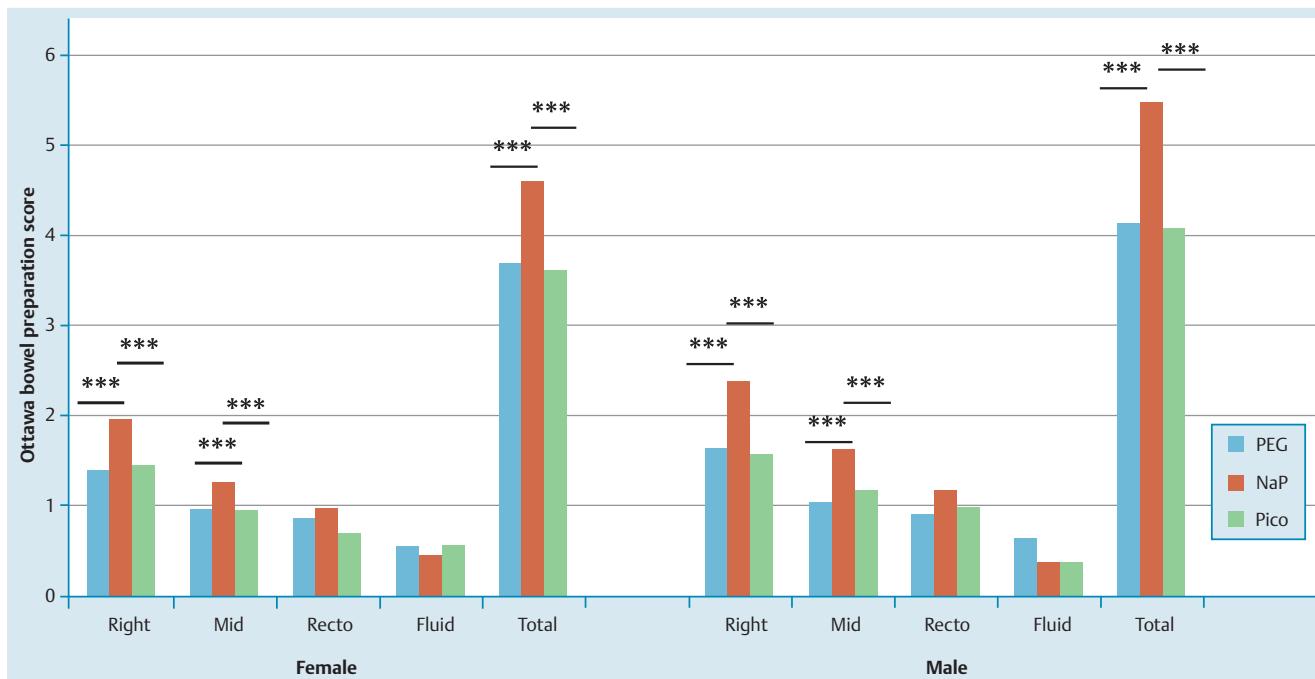
No difference was observed between PEG and Pico in the number of patients with a total regional score of 7 or greater (OR = 1.15, 95%CI 0.78–1.69;  $P = 0.48$ ). The percentage of patients with at least one regional score of 4 was also numerically greater in those patients receiving NaP (19%) compared with patients receiving PEG (7%) or Pico (5%) (► Table 2).

The level of bowel preparation was affected by the time of the procedure (► Fig. 2) and patient sex but not by patient age. In the morning procedures, NaP ( $n = 134$ ) was observed to have the highest mean total bowel preparation score, which was significantly greater than PEG ( $n = 232$ ) and Pico ( $n = 138$ ) (least square mean difference = 1.62, 95%CI 0.52–2.73,  $P < 0.001$  and 1.84, 95%CI 0.65–3.02,  $P < 0.001$ , respectively). No difference in

**Table 2** Bowel preparation and bowel cleansing assessment. A score of 4 represents very poor preparation.



**Fig. 2** Ottawa bowel preparation scores by bowel preparation and time of procedure. A significant interaction in the bowel preparation scores was observed between the time of procedure and bowel preparation used. The average score for each bowel preparation is presented by time of procedure, for the region of the bowel assessed, overall fluid score, and total bowel preparation score. For procedures undertaken in the morning, the right, mid, rectosigmoid, and total bowel preparation scores were statistically higher for NaP than for either PEG or Pico using multivariable analysis. In the afternoon there were no significant differences in the bowel preparation scores between preparations apart from for the fluid score. \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ .



**Fig. 3** Ottawa bowel preparation scores by bowel preparation and patient sex. Average score for each bowel preparation is presented by sex of the patient for the region of the bowel assessed, overall fluid score, and total bowel preparation score. In both males and females the right, mid, and total bowel preparation scores were statistically higher for NaP than for either PEG or Pico using multivariable analysis. \* $P<0.05$ ; \*\* $P<0.01$ ; \*\*\* $P<0.001$ .

the mean score was detected in patients receiving either PEG or Pico. In the afternoon procedures, however, the use of NaP ( $n=45$ ) gave the lowest overall score but this was not significantly different from that observed in patients taking PEG ( $n=52$ ) or Pico ( $n=33$ ). The overall bowel preparation scores for PEG and Pico were not significantly different between the morning and afternoon lists ( $P=0.21$  and  $P=0.11$ , respectively); however, for patients taking NaP the overall bowel preparation scores were significantly better in the afternoon ( $P=0.048$ ). Sex independently impacted on the overall bowel preparation scores with males scoring significantly worse than females regardless of the bowel preparation used, the indication for the procedure, and the time of procedure (least square mean difference = 0.59, 95%CI 0.091 – 1.09;  $P=0.020$ ). Despite the differences between the sexes, however, the associations identified between the bowel preparation used and colon cleansing scores were consistent with findings that were controlled for the time of the procedure (Fig. 3). Individual components of the preparation score demonstrated similar patterns for the right colon, mid colon, and rectosigmoid colon with all demonstrating significant effects of the bowel preparation used, the time of the procedure, and patient sex. For morning procedures ( $n=504$ ), the right, mid, and rectosigmoid colon scores for NaP were significantly worse than for PEG ( $P<0.001$ ,  $P<0.001$ ,  $P=0.002$ , respectively), and Pico ( $P<0.001$  for all), although no significant differences were observed between PEG and Pico in any of these regions. For afternoon procedures ( $n=130$ ), there were no significant differences detected between any of the bowel preparations. The scores in the right and mid colon were significantly worse for males (least square mean difference = 0.24, 95%CI 0.052 – 0.44,  $P=0.013$  and 0.18, 95%CI 0.006 – 0.35,  $P=0.043$ , respectively). No significant differences were detected between males and females for the rectosigmoid colon scores.

Bowel fluid scores were significantly affected by bowel preparation used and the time of the procedure. For morning procedures,

NaP gave lower fluid scores than Pico ( $P=0.049$ ) and PEG ( $P<0.001$ ), whereas PEG and Pico were again not significantly different. For afternoon procedures, however, NaP was more likely to provide higher fluid scores than Pico ( $P=0.004$ ), but was not significantly different from PEG. Pico also scored significantly lower fluid scores than PEG ( $P<0.001$ ).

### Mucosal abnormalities associated with the bowel preparation

Visible mucosal abnormalities were biopsied and photographed (Table 3).

Aphthous ulceration was observed in five patients, mucosal erythema in a further seven, and both abnormalities were observed in one patient. Histology of all specimens confirmed mild non-specific acute colitis not consistent with Crohn's disease (Fig. 4).

Mucosal inflammation/ulceration occurred in 0.35% (1/284) of patients taking PEG compared with 3.4% (6/179) receiving NaP (OR = 9.8, 95%CI 1.17 – 453;  $P=0.03$ ), and 3.5% (6/171) receiving Pico (OR = 10.2, 95%CI 1.23 – 474;  $P=0.026$ ).

### Discussion

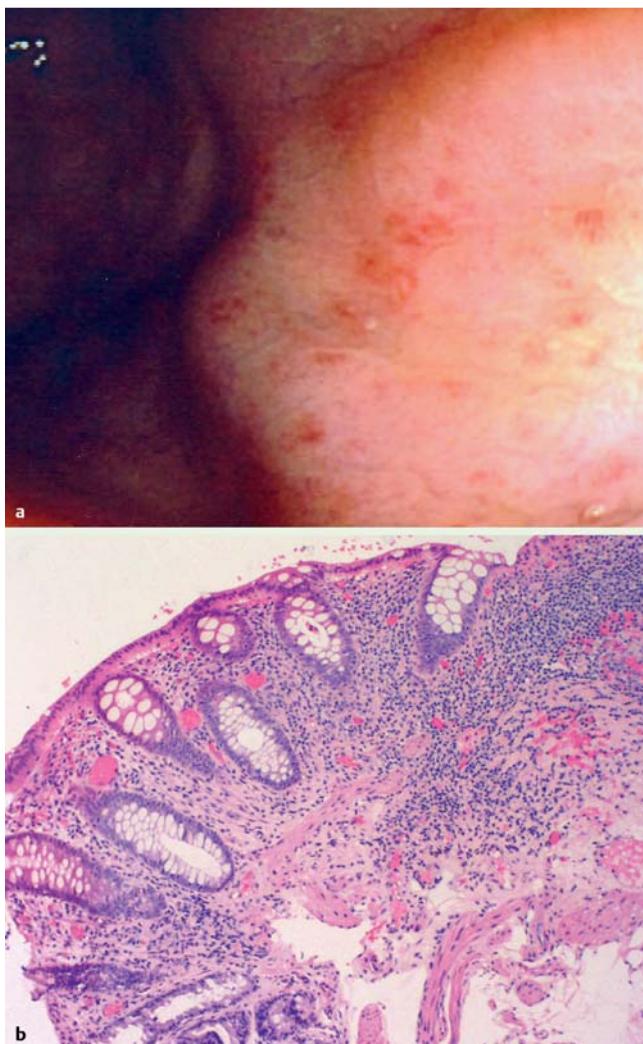
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Colonoscopy is an extremely common procedure. Unfortunately the literature contains numerous underpowered studies that utilize subjective bowel-cleansing criteria. Our study is the largest prospective randomized controlled trial on this topic, in a community setting and using an objective validated assessment tool to examine three bowel preparations spanning the three main classes of agents – osmotic, stimulant, and high molecular weight nonabsorbable polymer. All patients in this study were ambulatory and had confirmed compliance to the dietary instructions, and 98% took 75% or more of the preparation agent as directed. The collection of bowel preparation data was also extremely good

Bowel preparation	Macroscopic findings	Microscopic findings
PEG	Aphthous ulceration of ileum and erythema of cecum	Mild active ileocolitis
NaP	Aphthous ulceration of rectum	Mild nonspecific active colitis
NaP	Aphthous ulceration of rectum	Mild nonspecific active colitis
NaP	Aphthous ulceration of rectum	Mild nonspecific active colitis
NaP	Aphthous ulceration of sigmoid colon	Mild nonspecific active colitis
NaP	Erythema of sigmoid colon	Focal active colitis
NaP	Erythema of cecum	Mild active colitis
Pico	Erythema (patchy) throughout colon,	Nonspecific active colitis
Pico	Erythema of sigmoid colon	Focal active colitis
Pico	Erythema of rectum	Focal nonspecific active proctitis
Pico	Aphthous ulceration of sigmoid colon	Focal ulceration with active colitis
Pico	Erythema of sigmoid colon	Nonspecific focal active colitis
Pico	Erythema of rectum	Mild nonspecific active proctitis

NaP, sodium phosphate; PEG, polyethylene glycol; Pico, sodium picosulphate.

**Table 3** Mucosal abnormalities observed at colonoscopy and following histological analysis.



**Fig. 4** Bowel preparation associated with acute inflammatory changes. **a** Endoscopic view of the rectal mucosa. **b** Histology of the rectal biopsy demonstrating focally active inflammation involving crypts, and the surface epithelium with neutrophils and red cell extravasation.

with 99% of patients ( $n = 625$ ) having complete assessment of colonic cleansing.

All patients were sent written instructions and were telephoned to discuss diet and bowel preparation instructions. All were placed on a minimal residue diet for 2 days and restricted to clear fluids on the day prior to their colonoscopy. Although these in-

structions are not necessarily routine across institutions, they were consistent across the three preparations in our study and thus allow for comparison between the efficacies of the agents. The adherence to dietary and bowel preparation instructions, however, may potentially be greater in our study population than would be expected in the general community, as these patients were taking part in a clinical trial.

The primary goal of any bowel preparation agent is bowel cleansing. Other studies comparing the bowel preparation agents have been very inconsistent, some observing that Pico provides a superior cleansing compared with NaP [6], whereas others report the reverse [8]. In an attempt to avoid the subjective or nonvalidated assessments of colon cleansing used in earlier studies, the validated Ottawa bowel preparation assessment tool was used. Overall, the bowel preparations were fairly good across the bowel preparation groups. Due to the large patient numbers in this study, however, we were able to identify that preparation scores were significantly impacted by the bowel preparation used, the time of the procedure, and patient sex. The overall bowel preparation, right colon, and mid colon scores were identified to be significantly worse in males regardless of the preparation used and independent of patient age, indication for the procedure, and time of procedure. This could suggest that despite patients confirming that they had been compliant to instructions and had ingested the bowel preparation agents as directed, males did not in fact take the full preparation, resulting in worse colon cleansing. Despite the differences observed between the sexes the associations identified between the various bowel preparation efficacies were maintained.

In contrast to other studies and two meta-analyses that used nonvalidated methods of preparation assessment [7, 14, 15], the osmotic agent, NaP, was a less effective agent than PEG. NaP delivered the worse overall and regional Ottawa preparation scores for colonoscopies undertaken in the morning when compared with PEG and Pico. It is possible, however, that these differences could be secondary to the protocol used. Separating the two bottles of NaP by 12 or 24 hours has been demonstrated to be more effective than a separation of 6 hours [17]. This, however, requires patients having a procedure in the morning to commence the second bottle of NaP at 7.00 p.m. with the recommendation to drink at least three more glasses of clear liquid (750 mL). As patients go to bed, the amount of fluid drunk with this second bottle of NaP may be less than patients taking their second bottle at 7.00 a.m. on the day of the procedure. This may result in reduced fluid intake, dehydration, and a worse bowel preparation, particularly notable in the right colon. The timing of NaP ingestion

has also been observed in other studies to impact on the level of bowel preparation [5]. There were, however, no significant differences observed between the preparations for procedures undertaken in the afternoon, although NaP was numerically better than either Pico or PEG. Greater patient numbers may have identified significance, but our findings suggest that the osmotic agent NaP resulted in a higher Ottawa score for mean overall cleansing and for each colonic segment, which could result in greater difficulty in detecting polyps and should be borne in mind when selecting the bowel preparation regimen. Efficacy of the NaP preparation taken in the morning for afternoon procedures, however, may potentially be improved if patients can be encouraged to drink more fluids overnight.

It has been reported that ulcerative colitis may flare up following a colonoscopic examination [20]. The reasons for this are unclear, but if the bowel preparation can induce mucosal inflammation [18, 19], then the preparation may provoke reactivation of this inflammatory condition. In our study, all patients with confirmed or suspected IBD or those taking NSAIDs were excluded. Our findings identified that acute mucosal inflammation/ulceration occurred significantly more frequently with NaP and Pico compared with PEG. The bowel preparation agents are thus not always benign and can negatively impact on the intestinal mucosal integrity. Although correlation between bowel preparation-induced mucosal inflammation/ulceration and flaring up of IBD is lacking, this could still be a contributing factor to the postcolonoscopic flare-ups in patients with ulcerative colitis and requires further consideration.

In summary, this is the largest prospective randomized blinded study published on this topic, and is the first to evaluate the three major classes of bowel-cleansing preparations with a validated assessment tool of bowel-cleansing efficacy. Due to the large patient numbers we were able to identify that the bowel preparation agent used, the time of the procedure, and patient sex all independently impacted on bowel cleansing. NaP was not as efficacious for morning procedures compared with PEG or Pico. This is also the first paper to assess the level of acute mucosal inflammation in a blinded randomized study in patients receiving NaP, Pico or PEG. The findings demonstrated that acute mucosal inflammation was 10-fold greater in patients receiving NaP or Pico when compared with PEG. Although further work is required to clarify the significance of these inflammatory changes, these findings may provide some justification for the use of PEG in patients suffering from IBD.

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**Competing interests:** None

## References

- 1 Byrne MF. The curse of poor bowel preparation for colonoscopy. *Am J Gastroenterol* 2002; 97: 1587–1590
- 2 Belsey J, Epstein O, Heresbach D. Systematic review: oral bowel preparation for colonoscopy. *Aliment Pharmacol Ther* 2007; 25: 373–384
- 3 Cohen SM, Wexner SD, Binderow SR et al. Prospective, randomized, endoscopic-blinded trial comparing precolonoscopy bowel cleansing methods. *Dis Colon Rectum* 1994; 37: 689–696
- 4 Golub RW, Kerner BA, Wise WE Jr. et al. Colonoscopic bowel preparations – which one? A blinded, prospective, randomized trial. *Dis Colon Rectum* 1995; 38: 594–599
- 5 Frommer D. Cleansing ability and tolerance of three bowel preparations for colonoscopy. *Dis Colon Rectum* 1997; 40: 100–104
- 6 Schmidt LM, Williams P, King D, Perera D. Picoprep-3 is a superior colonoscopy preparation to Fleet: a randomized, controlled trial comparing the two bowel preparations. *Dis Colon Rectum* 2004; 47: 238–242
- 7 Law WL, Choi HK, Chu KW et al. Bowel preparation for colonoscopy: a randomized controlled trial comparing polyethylene glycol solution, one dose and two doses of oral sodium phosphate solution. *Asian J Surg* 2004; 27: 120–124
- 8 Tjandra JJ, Chan M, Tagkalidis PP. Oral sodium phosphate (Fleet) is a superior colonoscopy preparation to Picoprep (sodium picosulfate-based preparation). *Dis Colon Rectum* 2006; 49: 616–620
- 9 Bitoun A, Ponchon T, Barthet M et al. Results of a prospective randomised multicentre controlled trial comparing a new 2-L ascorbic acid plus polyethylene glycol and electrolyte solution vs. sodium phosphate solution in patients undergoing elective colonoscopy. *Aliment Pharmacol Ther* 2006; 24: 1631–1642
- 10 Kastenberg D, Barish C, Burack H et al. Tolerability and patient acceptance of sodium phosphate tablets compared with 4-L PEG solution in colon cleansing: combined results of 2 identically designed, randomized, controlled, parallel group, multicenter phase 3 trials. *J Clin Gastroenterol* 2007; 41: 54–61
- 11 Lichtenstein GR, Grandhi N, Schmalz M et al. Clinical trial: sodium phosphate tablets are preferred and better tolerated by patients compared to polyethylene glycol solution plus bisacodyl tablets for bowel preparation. *Aliment Pharmacol Ther* 2007; 26: 1361–1370
- 12 Schanz S, Kruis W, Mickisch O et al. Bowel preparation for colonoscopy with sodium phosphate solution versus polyethylene glycol-based lavage: a multicenter trial. *Diagn Ther Endosc* 2008; 2008: 713521
- 13 Hookey LC, Vanner SJ. Pico-salax plus two-day bisacodyl is superior to pico-salax alone or oral sodium phosphate for colon cleansing before colonoscopy. *Am J Gastroenterol* 2009; 104: 703–709
- 14 Hsu CW, Imperiale TF. Meta-analysis and cost comparison of polyethylene glycol lavage versus sodium phosphate for colonoscopy preparation. *Gastrointest Endosc* 1998; 48: 276–282
- 15 Tan JJ, Tjandra JJ. Which is the optimal bowel preparation for colonoscopy – a meta-analysis. *Colorectal Dis* 2006; 8: 247–258
- 16 Rostom A, Jolicoeur E. Validation of a new scale for the assessment of bowel preparation quality. *Gastrointest Endosc* 2004; 59: 482–486
- 17 Rostom A, Jolicoeur E, Dube C et al. A randomized prospective trial comparing different regimens of oral sodium phosphate and polyethylene glycol-based lavage solution in the preparation of patients for colonoscopy. *Gastrointest Endosc* 2006; 64: 544–552
- 18 Zwas FR, Cirillo NW, el-Serag HB, Eisen RN. Colonic mucosal abnormalities associated with oral sodium phosphate solution. *Gastrointest Endosc* 1996; 43: 463–466
- 19 Rejchart S, Bures J, Siroky M et al. A prospective, observational study of colonic mucosal abnormalities associated with orally administered sodium phosphate for colon cleansing before colonoscopy. *Gastrointest Endosc* 2004; 59: 651–654
- 20 Menees S, Higgins P, Korsnes S, Elta G. Does colonoscopy cause increased ulcerative colitis symptoms? *Inflamm Bowel Dis* 2007; 13: 12–18