

Bowel cleansing before colonoscopy: Balancing efficacy, safety, cost and patient tolerance

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Abstract

Effective colorectal cancer screening relies on reliable colonoscopy findings which are themselves dependent on adequate bowel cleansing. Research has consistently demonstrated that inadequate bowel preparation adversely affects the adenoma detection rate and leads gastroenterologists to recommend earlier follow up than is consistent with published guidelines. Poor preparation affects as many as 30% of colonoscopies and contributes to an increased cost of colonoscopies. Patient tolerability is strongly affected by the preparation chosen and manner in which it is administered. Poor tolerability is, in turn, associated with lower quality bowel preparations. Recently, several new developments in both agents being used for bowel preparation and in the timing of administration have brought endoscopists closer to achieving the goal of effective, reliable, safe, and tolerable regimens. Historically, large volume preparations given in a single dose were administered to patients in order to achieve adequate bowel cleansing. These were poorly tolerated, and the unpleasant taste of and significant side effects produced by these large volume regimens contributed significantly to patients' inability to reliably complete the preparation and to a reluctance to repeat the procedure. Smaller volumes, including preparations that are administered as tablets to be consumed with water, given as split doses have significantly improved both the patient experience and efficacy, and an appreciation of the importance of the preparation to colonoscopy interval have produced additional cleansing.

Key words: Bowel preparation; Colonoscopy; Adenoma detection rate; MiraLAX; Polyethylene glycol; Sodium picosulfate; Oral sulfate solution

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Core tip: Improvements in efficacy and tolerability of

bowel preparation include new formulations that are more tolerable to patients without sacrificing efficacy or safety, and a better understanding of the ideal timing of bowel preparation administration.

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INTRODUCTION

Many patients describe the bowel preparation prior to colonoscopy as the most unpleasant part of the whole procedure and the biggest deterrent to repeating it. Unfortunately, in addition to being the most loathed aspect, the bowel preparation is one of the most critical components of effective screening for colon cancer. The ideal bowel preparation, though this has not yet been developed, is one that is safe, highly effective and reliable, convenient, and tolerable enough that patients are not deterred from repeating the procedure.

Inadequate bowel preparations lead to lower adenoma detection rates and more frequent follow up intervals than would otherwise be recommended by guidelines based on colonoscopy findings. The European Panel of Appropriateness of Gastrointestinal Endoscopy found that polyp detection was related to the quality of bowel cleansing^[1]. Relative to a low quality preparation, a high quality or intermediate quality preparation produced a 1.46 and 1.73 odds ratio (OR) of polyp detection^[1]. Sherer *et al.*^[2] found a lower detection rate of advanced histology in the setting of poor preparation, though the number of polyps 6-9 mm detected was not different. In studies that have looked at early repeat colonoscopy following a suboptimal preparation, the quality of preparation is strongly associated with incidence of missed polyps and adenomas^[3-5]. Leibold *et al.*^[3] found a 42% overall miss rate after inadequate bowel prep with a 47% miss rate for adenomas less than 10 mm and 27% miss rate for adenomas greater or equal to 10 mm. Hong *et al.*^[4] found that the adenoma detection rate decreased as the quality of bowel prep decreased with a precipitous drop off seen as the quality decreased from fair to poor. Ultimately, the adenoma detection rate was associated with patient tolerability with an OR of 0.39 in the setting of poorly tolerated preparations^[6].

The evidence for the benefit of bowel preparation prior to colorectal surgery is less convincing. While it remains the overwhelming practice of surgeons to prescribe a mechanical bowel preparation, studies have not convincingly showed that it reduces the incidence of mortality, skin and soft tissue infections, or peritonitis as compared to no preparation^[7]. Recent studies have supported the use of oral and parenteral antibiotics prior

to procedure. As with the preparation for endoscopy, there is no clear superiority of one regimen over another.

Poor preparation is not an uncommon occurrence. Rates of inadequate bowel preparation are estimated to be as high as 30.2% with as many as 10% being so poor as to preclude any further evaluation^[8]. Due to the increased risk of missed polyps and decreased efficacy of screening in the face of a poor bowel prep, research has found that, in patients with a poor bowel prep, gastroenterologists are less likely to adhere to recommended screening intervals and more frequently recommend closer follow up than would otherwise be appropriate based on intra-procedure findings^[9-11]. Shortened follow up intervals translate into increased screening costs, estimated to be as much as a 12% to 22% increase, and greater inconvenience to patients^[12].

A 4 L preparation of polyethylene glycol (PEG) has been considered the gold standard in terms of prep efficacy but is reviled by patients due to its poor taste and discomfort associated with the larger volumes. Alternate formulations have been developed, but these have had other drawbacks in terms of safety, tolerability, or efficacy. Recently, new options have received Food and Drug Administration (FDA) approval and these may offer improved tolerability without sacrificing efficacy (Table 1).

POLYETHELENE GLYCOL

Four liters PEG-ELS (electrolyte lavage solution) administered in split doses is considered by most to be the standard against which all other bowel preparations are judged^[13]. A systemic review and meta-analysis by Enestvedt *et al.*^[13] found an OR of 3.46 that a split dose 4 L PEG-ELS preparation would produce a good or excellent bowel preparation compared with other methods. The pooled analysis did not reveal any other significant differences in performance measures such as overall experience or willingness of patients to repeat the procedure, or in side effects such as nausea.

Nonetheless, many studies conclude that patients prefer lower volume preparations to the full 4 L PEG. Often preceded by a stimulant laxative such as bisacodyl or magnesium citrate, 2 L PEG preparations have been found to achieve equivalent levels of bowel cleansing with enhanced patient experience^[14-19]. A 1994 study comparing single dose preparations of 4 L PEG-ELS with 2 L PEG-ELS preceded by bisacodyl found comparable cleansing^[14]. The subjects in the 2 L PEG-ELS group rated the preparation more tolerable and more patients were able to complete the preparation than in the 4 L group (93% vs 66%). Sharma *et al.*^[15] found similar results in a trial comparing 4 L PEG-ELS with 2 L PEG-ELS with bisacodyl or magnesium citrate. The quality of preparation was rated better with 2 L PEG-ELS with bisacodyl or magnesium citrate than with 4 L PEG-ELS (8.1 vs 7.8 vs 7.3). This was coupled with lower procedure times and higher patient

Table 1 Relative effectiveness and cost of available bowel preparations

Prep		% Adequate	Lesion detection rate	Cost ¹
4 L PEG	Single	51%-88% ^[16,64]	PDR 50.5%-51% ^[26,51]	PEG 3350 with electrolytes 4 L \$26.59
	Split	71.3%-92.1% ^[23,51]	ADR 27.8-34.3% ^[51,70]	
2 L PEG	Single	83.5%-91% ^[45,64]	ADR 18.8% ^[70]	Moviprep 100 g/1 kit \$91.55
	Split	74.4%-93.5% ^[45,48]		
MiraLAX	Single	67.8%-81.8% ^[29,31]	PDR 47% ^[26]	MiraLAX 8.3oz/238 g \$13.99
	Split			
Sodium Phosphate		84.3%-90% ^[35,37]	Not Available	OsmoPrep 32 tabs \$163.05
Sodium Picosulfate	Single	61.5%-82.6% ^[49,51]	PDR 38.5%-42.9% ^[51,53]	Prepopik, 2 pkts \$121.31
	Split	81.6%-87.9% ^[49,50]	ADR 23.8%-31.3% ^[51,53]	
Oral Sulfate Solution	SuPrep	94.7%-98.4% ^[44,53]	PDR 50.9% ^[53]	SuPrep 1 kit \$49.09
	Suclear	93.5% ^[45]	ADR 26% ^[53]	Suclear \$76.38

¹Prices from RxPriceQuotes.com as listed for CVS w/exception of MiraLAX which was priced at local CVS. PEG: Polyethylene glycol; PDR: Polyp detection rate; ADR: Adenoma detection rate.

satisfaction scores. Of 24 subjects who had a previous bowel prep with 4 L PEG-ELS, 88% of those in the 2 L PEG-ELS plus magnesium citrate and 56% of those in the 2 L PEG-ELS plus bisacodyl preferred the low volume preparation. A follow up study by the same group found small, likely clinically insignificant serum electrolyte changes following low dose PEG-ELS with stimulant laxatives^[20]. A low volume PEG plus ascorbic acid in comparison with 4 L PEG-ELS produced an equivalent number of adequate bowel preps (94.6% vs 90%), was better tolerated and produced fewer adverse events (80.2% vs 89.9%)^[21]. Similar results have been obtained in other studies though some have shown that cleansing in the right colon was superior with the 4 L PEG preparation^[22,23].

The relative efficacy of the 2 L PEG preparations is undiminished when it is administered as a split dose^[24,25]. A 2013 study of 2 L PEG-citrate plus bisacodyl and simethicone found that successful preps were achieved in 92.8% vs 92.1% of patients using the 2 L PEG and 4 L PEG respectively^[24]. A higher percentage of excellent right colon preps were observed in the 4 L PEG group. The 2 L PEG prep was better tolerated (31.6% reporting symptoms vs 45.2%) and more patients expressed willingness to repeat the same procedure in the future (90.6% vs 77%). Similar results were obtained using split dose 2 L PEG-ascorbic acid alone^[25]. There was no significant difference in the quality of bowel prep or number of patients achieving an adequate bowel prep in 2 L vs 4 L groups (7.0 ± 2.1 vs 7.1 ± 2.0 and 73.2% vs 76.3%)^[25]. The low volume preparation was rated significantly more tolerable with 14.3% of subjects reporting difficulty in taking the preparation vs 30.7% with the 4 L PEG preparation^[25].

MIRALAX

Though it has not been FDA approved for the purpose, MiraLAX (Bayer Healthcare, Leverkusen, Germany)

has come into widespread use as a bowel prep agent in spite of equivocal evidence supporting its efficacy as compared to FDA approved alternatives due to the convenience of using an over the counter product and superior palatability. A recent survey of practicing gastroenterologists found that one third regularly recommend some sort of MiraLAX based bowel prep to their patients with rates as high as 50% in suburban practices and a positive correlation between the number of colonoscopies performed and the likelihood of recommending a MiraLAX based bowel prep^[26]. MiraLAX based bowel preps, typically 238 mg of MiraLAX in 64oz of Gatorade, has generally, though not universally, been found to be more tolerable to patients^[27-30].

The data regarding the cleansing achieved with MiraLAX is more mixed. McKenna *et al.*^[30] found that single dose MiraLAX was non-inferior compared to 4 L of PEG-ELS, both taken the night before procedure. Both MiraLAX and PEG-ELS produced equivalent BBPS (7.0 vs 7.2) and had similar percentages of patients achieving adequate bowl preps (BBPS ≥ 6, 81.3% vs 84.3%). The authors found no difference in time to cecal intubation or withdrawal time. MiraLAX was preferred by study subjects. Similar results were obtained in a study by Samarasena *et al.*^[28] comparing split dose MiraLAX with split dose PEG-ELS. Again, no significant difference in BBPS (8.01 vs 8.33) was observed and the MiraLAX based prep was given significantly better ratings in terms of taste and tolerability with 96.8% vs 75% of subjects willing to repeat the prep in the future. A comparison of MiraLAX in Gatorade plus bisacodyl with 4 L PEG-ELS found superior results overall (93.3% vs 89.3% with excellent/good cleansing) and equivalent results when the analysis was limited to only ASA class 1 patients of which there were more in the 4 L PEG-ELS group^[31]. The authors noted that the increased rate of adequate preparations derived primarily from more frequent good and less frequent fair preparations.

Other researchers have found inferior bowel prep

with MiraLAX based regimens compared with PEG-ELS. Hjelkrem *et al.*^[27] compared split doses of 4 L PEG-ELS with MiraLAX (alone and with either bisacodyl or lubiprostone) and demonstrated inferior preps with all of the MiraLAX based preps (Ottawa score of 5.1 vs 6.9, 6.3, and 6.8). Cleansing was adequate with all preps, but there was a higher incidence of excellent preps in the Golytely arm (49% vs 15%, 20%, and 19%). No difference in adenoma detection rates was observed. A lower rate of excellent prep and overall inferior BBPS was also observed by Enesvedt *et al.*^[29] when comparing MiraLAX with 4 L PEG-ELS. PEG-ELS produced a mean BBPS of 9% and 70% of preps were rated excellent which was superior to a mean BBPS of 8% and 55% of preps rated excellent for MiraLAX. A follow up study by Enesvedt *et al.*^[32] comparing MiraLAX with PEG-ELS showed that, in addition to less frequently achieving a BBPS greater than or equal to 7, MiraLAX was associated with a lower adenoma detection rate (16.1% vs 26.2% with PEG-ELS).

There have been concerns about the safety of MiraLAX for bowel preparation after reports of severe hyponatremia^[33]. Unlike the electrolyte solutions used for prescription bowel preps, the sports drink (typically Gatorade) is not osmotically balanced and is relatively hypotonic. Two randomized controlled trials have since demonstrated comparable safety with standard 4 L PEG preparations^[28,30]. Neither trial detected a clinically or statistically significant difference in serum electrolytes. Though, the study populations were relatively small and may not detect very infrequent adverse events, it is reassuring that not even a trend toward greater electrolyte abnormalities was observed.

SODIUM PHOSPHATE

Sodium phosphate (NaP) is an osmotic laxative that was initially prescribed as a more tolerable alternative to whole gut lavage with PEG preparations. It was widely used and well tolerated by patients as a much smaller volume of fluid was required for successful prep; however, concerns about safety and confounding mucosal changes have limited the use of this agent more recently. Because of concerns of significant electrolyte disturbances and even acute renal failure, the use of sodium phosphate preps is not recommended in multiple populations including patients over the age of 55, patients taking certain medications such as angiotensin converting enzyme inhibitors (ACEi), and those with pre-existing renal disease, heart failure, and liver disease. Sodium phosphate carries a black box warning regarding the risk of acute phosphate nephropathy.

In comparison to single dose 4 L PEG-ELS, NaP produced equivalent to superior bowel cleansing with improved patient tolerability^[34-38]. The greater tolerability of NaP as compared to PEG preparation has been nearly universal^[35-38]. Subjects, including 37 who had been prepped with PEG for prior colonoscopy, rated NaP easier

to complete and less uncomfortable^[35].

Unfortunately, in spite of its superior tolerability, NaP is not without significant adverse side effects^[39]. Hyperphosphatemia following NaP has been well documented in patients with both normal and impaired renal function and has been associated with hypocalcemia. Cases of acute phosphate nephropathy have largely occurred in patients with pre-existing renal disease, but have also occurred in setting of dehydration in patients with otherwise normal renal function^[40]. NaP is thought to cause renal injury by precipitating nephrocalcinosis^[39,40]. The risk of adverse events is increased patients taking ACEi or angiotensin receptor blockers and who are of advanced age^[39]. Additional suspected risk factors include existing renal disease, female gender, volume depletion, and abnormal bowel motility^[39].

NaP has also been reported to cause mucosal inflammation and ulcerations that give the appearance of inflammatory bowel disease. A randomized control trial compared patients receiving PEG-ELS with NaP and found an association between NaP use and the presence of nonspecific aphthoid like mucosal lesions^[41]. Lesions were present in 24.5% of subjects receiving NaP vs 2.3% of those receiving PEG. Though pathological evaluation of the lesions was not consistent with IBD, the authors reported that they were endoscopically similar to those seen in Crohn's disease. This association was substantiated in a larger observational trial of 730 patients who were administered a NaP bowel prep and followed for 3 years after the procedure^[42]. In this study, only 3.3% of patients exposed to NaP demonstrated mucosal lesions on endoscopy, but these lesions were of the type seen in anti-inflammatory drug induced injury and in IBD. As a result of these observations, NaP is not recommended in patients undergoing colonoscopy to evaluate for suspected IBD^[41,42].

ORAL SULFATE SOLUTION

Sulfate is a poorly absorbed anion that does not cause significant fluid or electrolyte shifts^[43,44]. In comparison with sodium phosphate, sodium sulfate produced more liquid stool and, unlike phosphate, did not increase the propensity for calcium to precipitate in renal tubules^[43]. Oral sulfate solution (OSS) is available in two formulations: SuPrep (two doses of sodium, phosphate, and magnesium sulfate; Braintree Laboratories, Braintree, MA) and Suclear (one dose of sodium, phosphate, and magnesium sulfate followed by a second dose of PEG 3350 in 2 L of water; Braintree Laboratories, Braintree, MA).

A 2009 study by Di Palma *et al.*^[44] demonstrated equivalent bowel cleansing with OSS and 2 L PEG-ELS given as single and split doses. Split dosing was superior to single dose for both preparations (82.4% and 80.3% vs 97.2% and 95.6% for OSS and PEG-ELS respectively). OSS was associated with a higher frequency of excellent preparations in the split dose arm

(63.3% vs 52.5%). A subsequent study by this group comparing split dose OSS (SuPrep) with single dose 4 L sulfate free PEG-ELS found a significantly higher rate of adequate and excellent preparations in the OSS group (98.4% vs 89.6% and 71.4% vs 34.4%)^[45]. OSS also resulted in less residual stool in the right colon. There were small changes in serum electrolytes with OSS which the authors reported as clinically insignificant. A third study by this group compared split dose OSS plus PEG-ELS (Suclear) with split dose 2 L PEG-ELS and OSS plus PEG-ELS given the night before procedure with 10 mg bisacodyl followed by 2 L PEG-ELS^[46]. The split dose administration produced equivalent rates of successful prep (93.5% in both arms). Single dose OSS with PEG-ELS was non-inferior to PEG-ELS given with bisacodyl (89.8% vs 83.5%) and associated with significantly more excellent preparations (47.7% vs 35.6%). In both arms of the study, OSS plus PEG-ELS was associated with a higher incidence of side effects (vomiting in the split dose arm and overall discomfort in single dose arm.) The authors looked specifically at the efficacy in the elderly (age \geq 65) and found that the split dose OSS with PEG-ELS produced more successful preparations (93% vs 86%) in this population. Patients with pre-existing comorbidities (cardiac or renal disease, diabetes, and hypertension) had similar rates of adverse events with both preps.

SODIUM PICOSULFATE

Sodium picosulfate (PMC) is a stimulant laxative given in combination with an osmotic laxative component such as magnesium citrate or magnesium oxide and citric acid which combine to form magnesium citrate. PMC has been used extensively in Canada and Europe for the past 20 years, but was only recently approved for use as a bowel preparative agent in the United States. The formulation available in the United States, Prepopik (Ferring Pharmaceuticals, Parsippany, NJ), is given as a split dose. Like sodium phosphate, this is a hyperosmolar preparation may not be suitable for patients with heart failure, renal insufficiency, end stage liver disease, or baseline electrolyte abnormalities. There have been reports of clinically significant hyponatremia following PMC bowel preparations and a retrospective cohort study by Weir *et al.*^[47] confirmed that use of PMC in patients older than 65 years was associated with an increased risk of 30 d hospitalization for hyponatremia, but not with increased risk of acute neurological symptoms or mortality.

Katz *et al.*^[48] compared PMC, given as single and split doses, with single dose 2 L PEG and bisacodyl administered the day before. Single dose PMC compared favorably with single dose PEG producing successful cleansing in 83.0% vs 79.7% or patients and comparable cleansing seen throughout all segments of the colon. Adverse events were similar between the two groups, and patient acceptability was significantly greater in the PMC arm. With split dose administration,

PMC performed significantly better than single dose 2 L PEG with bisacodyl^[49]. Good or excellent Aronchick scores were more frequent in the PMC arm in both the overall colon (84.2% vs 74.4%) and in the individual segments. Again, PMC was rated more tolerable than 2 L PEG. Similar results were observed by Kojecky *et al.*^[50] in a comparison of PMC and 4 L PEG in single and split doses. Split dose regimens were preferable regardless of the agent. Single dose PMC produced a higher percentage of acceptable preps compared to PEG (82.6% vs 73%). There was no significant difference in the number of subjects with adequate prep among the remaining study arms; split dose PMC (81.6%), single dose PMC (82.6%), and split dose PEG (87.3%). Both PMC based regimens were rated more tolerable than either PEG based prep. Single dose PEG was most associated with nausea and bloating. Single dose PMC had the least abdominal pain reported, but split dose PMC had the highest association with incontinence. There was a slight preference for the single dose PMC preparation among older subjects and for the split preparation in younger subjects. These findings have been replicated in other studies with PMC achieving similar percentages of adequate bowel cleansing compared with PEG while being significantly preferred by study subjects^[51,52]. Another study evaluated PMC alone versus in combination with PEG found little additional benefit with PEG^[53]. Only in the right colon was there a significant difference in Ottawa bowel prep scores between the PMC alone and PMC plus 2 L PEG groups (1.34 \pm 1.022 vs 1.11 \pm 0.97). As in other studies, the PMC alone regimen was preferred by patients (89% vs 72.3%) and had less associated nausea.

There has been only one study directly comparing PMC with OSS^[54]. Rex *et al.*^[54] found a higher rate of successful and excellent preparations with OSS in comparison with PMC (94.7% vs 85.7% and 54% vs 26%). Unlike the OSS arm, there were 4 patients in the PMC arm who required additional preparation before the procedure could be attempted and 9 patients in whom the cecum was not reached. There was no significant difference in the polyp detection rate (50.9% vs 42.9%), adenoma detection rate (26.0% vs 23.8%), or flat lesion detection rate (9.5% vs 4.8%), and no difference in the procedure duration (mean 16.5 min vs 16.6 min). There was no difference in adverse events in the two arms and, though nausea was generally mild in both arms, subjects taking PMC reported better scores for nausea (Table 2).

TIMING OF PREP

Regardless of the preparation used, the quality of preparation has proven higher with split dose vs day before administration. This has been demonstrated most clearly with PEG based preparations. A 2005 study compared 4 L PEG preparations given as a single dose with dietary restrictions on the evening before the procedure or as a split dose without dietary restrictions

Table 2 Advantages and disadvantages of available bowel preparations

Prep	Advantages	Disadvantages
4 L PEG	Effective Safe in most populations	Poor taste Very high volumes Poorly tolerated by patients
2 L PEG	Effective Safe in most populations	Poor taste High volumes High cost
MiraLAX	Well tolerated by patients Available over the counter Existing studies indicate it is safe	Not as effective as prescription PEG preparations Rare reports of hyponatremia
Sodium phosphate	Available as oral tab	Inappropriate for use in patients with renal disease, volume depletion, heart or liver failure, or who are taking ACEi or NSAIDs Risk of acute phosphate nephropathy and subsequent chronic kidney disease
Sodium picosulfate	Well tolerated by patients	Cost
OSS	Well tolerated by patients Small volumes to be ingested	Not as effective as PEG or OSS Inappropriate for patients with heart failure, renal insufficiency, end stage liver disease, or baseline electrolyte abnormalities
	Pleasant taste Well tolerated by patients Highly effective Available as oral tab	High cost High cost Not as well studied

PEG: Preparation of polyethylene glycol; ACEi: Angiotensin converting enzyme inhibitors; NSAIDs: Nonsteroidal anti-inflammatory drugs; OSS: Oral sulfate solution.

and found that, even without dietary restrictions, the split dose preparation produced significantly better preps^[55]. A randomized control trial of evening before vs split dose PEG preparations that included both high and low volume preparations found that, regardless of the volume of preparation, split dose administration produced significantly more successful preps (75.2% vs 43.0%) and a lower rate of aborted procedures (6.9% vs 21.2%)^[56]. A pre-post study by the Veteran's Health Administration assessed efficacy and acceptance of split dose bowel preps in an elderly populations with multiple co-morbidities and found that the split dose preparations were better tolerated by patients and produced superior results^[57]. Both right and left colon preparations were improved with split dose administration (excellent/good preps achieved in 81.4% vs 63% and 85.9% vs 71.6% respectively)^[57].

These results were validated in 2 meta-analyses^[58,59]. Kilgore *et al*^[58] included 5 trials in an analysis which found split dose PEG produced an OR of 3.7 of a satisfactory bowel preparation as well as improved patient tolerability. Martel *et al*^[59] obtained similar results in an analysis of 47 trials. In this study which included split dose preparations of PEG, NaP, and PMC, the OR of a successful prep with split vs evening before preparation was 2.51. Subjects reported greater willingness to repeat the split dose preparation.

Concerns have been raised about the risk of peri-procedural aspiration with split dose regimens. In 2010, Huffman *et al*^[60] examined 712 patients with EGD of which 254 had received split dose bowel preps for concurrent colonoscopy. While the residual gastric volume was higher in patients who received the split dose preparation as compared with patients scheduled

for EGD only (19.7 mL vs 14.6 mL), there was no difference between when compared with patients who received day before preparation (20.2 mL) and the 5 mL difference is unlikely to be clinically significant^[60].

Recent studies have shed light on the reason for the improved cleansing seen with split dose preparations and highlighted the importance of a short duration between the completion of a bowel prep and the start of the colonoscopy^[61-64]. A prospective analysis of colonoscopy start times and the time of the last dose of bowel prep showed an inverse relationship between the degree of cleansing and the length of this interval^[64]. Subsequent studies have reinforced this finding and clarified the ideal time interval between bowel prep and colonoscopy. Eun *et al*^[62] compared intervals of more and less than 7 h and of more and less than 4 h and found that, in each case, superior cleansing was seen with the shorter interval. A 3 to 5 h interval produced the best cleansing throughout the colon in a prospective study by Seo *et al*^[61], though the association was not as high as with the amount of PEG ingested (OR 1.85 for prep to colonoscopy time vs 4.34 for quantity of PEG ingested).

Following from these findings, researchers have looked at the feasibility of preparations completed entirely on the morning of the planned procedure^[65-67]. Varughese *et al*^[65] compared morning only preparation with preparation completed entirely the evening prior and, consistent with the finding that the interval between preparation and procedure is a determinant of the quality of preparation, found that morning only preparation is superior to evening before preparation. Matro *et al*^[66] compared morning only to split dose administration of PEG-ELS and found equivalent cleansing and adenoma detection with improved tolerability in the morning only

group. Similar findings were obtained by Longcroft-Wheaton *et al*^[67] in comparing morning only to split dose sodium picosulfate.

CONCLUSION

Effective, safe, and reliable options for bowel preparation are becoming increasingly available though the most tolerable options remain the most costly. Improved efficacy has also been achieved with alterations in the dosing schedule, namely split dose administration and a better understanding of the optimal interval between preparation and the colonoscopy. These adjustments have proven more tolerable as well as more effective. The consensus of the major Gastrointestinal Societies is that the choice of agent should be tailored to the individual patient, but that a split dose regimen can be recommended in all cases^[68,69]. Additional research is needed to develop tools to assist providers in choosing an optimal regimen for their patients as factors such as age and comorbid conditions may affect the efficacy and safety of a particular agent. The optimal choice of bowel preparation must be guided by the circumstances of the individual patient undergoing procedure; however, low volume PEG preparations would appear to come closest to being the ideal preparatory agent in that it is effective, generally well tolerated, has an excellent safety record in a population of patients with a range of comorbid conditions, and is relatively inexpensive. Ongoing studies are evaluating the impact of interventions such as improved pre-procedure patient education and smart phone based applications that remind patients of when to take their prep are showing promise with regard to improved patient tolerability and adherence and may offer a path toward both patient and endoscopist satisfaction.

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