

Colonoscopy preparation

The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methods are used with a MEDLINE literature search to identify pertinent clinical studies on the topic and a MAUDE (Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported complications of a given technology. Both searches were supplemented by accessing the "related articles" feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but, in many cases, data from randomized controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors.

Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the committee as a whole, and approved by the governing board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through September 2008 for articles and references related to colonoscopy preparation by using the key words "preparation," "randomized clinical trial," "colonic cleansing," "lavage," "pediatric," and "colonoscopy." Practitioners should continue to monitor the medical literature for subsequent data about the efficacy, safety, and socioeconomic aspects of these preparations.

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BACKGROUND

Colonoscopy and other methods of colonic imaging require thorough large-bowel cleansing for safe and effective completion of the procedure. For colonoscopy, inadequate preparation is responsible for up to a third of all incomplete procedures¹ and precludes up to 10% of examinations.² This outcome negatively impacts the rate of polyp^{3,4} and adenoma detection.⁵ The ideal colon preparation would rapidly and reliably clean the colon of fecal material while having no effect on the gross or microscopic appearance of the colon.^{6,7} It would require a short period for ingestion and evacuation, cause no discomfort, and produce no significant fluid or electrolyte shifts.⁸ At the same time, it would be palatable, simple, and inexpensive. Currently, the available preparation regimens fulfill some but not all of these criteria.

TECHNOLOGY UNDER REVIEW

In general, compounds used for bowel cleansing can be divided into 3 categories according to their mechanism of action: isosmotic, hyperosmotic, and stimulant preparations. Their distinct physiologic mechanisms impact the choice of preparation, especially in patients with comorbidities, elderly patients, and children. Early regimens evolved from preparations for radiologic tests and included diet restrictions for 2 to 3 days, enemas, laxatives, and large-volume (7-12 L) oral bowel lavage.^{9,10} These regimens were time consuming, uncomfortable, and inconvenient for the patient, and resulted in fluid and electrolyte disturbances. In addition, early preparations contained mannitol, which, when fermented by colonic bacteria, led to combustible amounts of luminal methane and hydrogen and created a risk for intracolonic gas explosion when using electrocautery.¹¹ This led to the development of osmotically balanced solutions formulated to provide minimal water absorption or secretion into the bowel lumen. A polyethylene glycol (PEG) electrolyte lavage solution (PEG-ELS) was originally developed in 1980,¹² and, since then, several preparations have been introduced to improve palatability and compliance (sulfate-free PEG¹³). Some more recent preparations allow for a reduced volume that needs to be ingested (PEG, also called PEG-3350 based on its molecular weight, combined with bisacodyl delayed release or magnesium citrate^{14,15}). Presently, the most commonly used adult colonoscopy preparations in the United States are PEG and oral sodium phosphate (NaP) regimens.

Isosmotic preparations

Isosmotic preparations that contain PEG are osmotically balanced, high-volume, nonabsorbable, and nonfermentable electrolyte solutions (Table 1). These solutions cleanse the bowel with minimal water and electrolyte shifts and provide evacuation, primarily by the mechanical effect of large-volume lavage. With sodium sulfate preparations, sodium absorption in the small intestine is largely reduced because of the absence of chloride, the accompanying anion necessary for active absorption against electrochemical gradient.¹⁰ The conventional total adult dose is 4 L, given orally as 240 mL every 10 minutes until rectal effluent is clear, or it is administered by a nasogastric (NG) tube at a rate of 20 to 30 mL/min.⁷ Alternatively, split dosing has also been advocated, with a portion taken the evening before and the residual taken the morning of the procedure.^{16,17} Low-volume PEG preparations are used in combination with stimulant laxatives or ascorbic acid. For one of these regimens, 10 mg of bisacodyl tablets are followed after the first bowel movement by 240 mL of preparation every 10 minutes until effluent is clear or until a total of 2 L is ingested. In another regimen, the ascorbic acid is included in the 2-L PEG solution, which is also dosed at 240 mL every 10 minutes.^{18,19} For this latter regimen, it is recommended that the patient ingest at least an additional 1 L of fluid, which makes the total volume of ingestion 3 L. Another formulation of PEG-3350, which does not contain electrolytes, has been approved and marketed as an agent to treat constipation (Table 1). This formulation has been used for colonic cleansing.²⁰ However, these PEG agents without electrolytes are not approved for bowel preparation, and the volume required and safety for use as a bowel preparation has not been adequately defined.

Hyperosmotic preparations

Hyperosmotic preparations draw water into the bowel lumen, which stimulates peristalsis and evacuation. These are small-volume preparations but, because of their hyperosmotic nature, can cause fluid shifts, accompanied by transient electrolyte-level alterations. Oral NaP is available as an aqueous solution and a tablet form.²¹⁻²³ An aqueous NaP preparation contains monobasic and dibasic NaP. It has a mean onset of bowel activity in 1.7 hours with the first dose and 0.7 hours with the second dose, a mean duration of activity of 4.6 and 2.9 hours, respectively, and end of bowel activity within 4 to 5 hours.²⁴ Each 45-mL dose contains 29.7 g NaP. Two doses of 30 to 45 mL aqueous solution are given at least 10 to 12 hours apart, with the second dose given within 5 hours of the procedure. The tablet preparations contain 1.5 g NaP and 0.5 g of inactive ingredients. One of the inactive tablet ingredients, microcrystalline cellulose (MCC), was thought to reduce visibility at colonoscopy, and a new MCC-free preparation is now available.²⁵ The dose is 40 tablets (60 g) for the MCC-

containing preparation and 32 tablets (48 g) for the MCC-free preparation, both divided into 2 doses separated by 10 to 12 hours. All NaP regimens should be taken with a minimum of 2 L of clear liquids.

Sodium picosulfate acts similarly to NaP, producing a cathartic effect by osmotic action in the bowel. This preparation is commonly used outside of the United States and in combination with magnesium citrate. Magnesium citrate is a hyperosmotic agent, with additional effects through release of cholecystokinin, and results in fluid secretion and stimulation of peristalsis. Magnesium citrate has been used in combination with other agents but, as a sole agent, has typically been less effective. A magnesium citrate-based preparation that includes a 240-mL dose of balanced magnesium solution and 20 mg bisacodyl (oral) the evening before the procedure and a 10-mg bisacodyl suppository the morning of the procedure has been developed. As a means to improving the limited preparation achieved with magnesium citrate alone, another method involves adding pulsed rectal irrigation; however, this requires skilled nursing for administration and is associated with a high cost.²⁶

Stimulant preparations

Senna, an anthracene derivative, is processed by colonic bacteria, and its active ingredients, anthraquinones and their glucosides, stimulate colonic peristalsis. A bowel response can be expected approximately 6 hours after the dose ingestion. It has been used as the primary cleansing agent, with a liquid diet, particularly in children.²⁷

Adjunctive agents

Bisacodyl is a diphenylmethane derivative that is poorly absorbed in the small intestine and that is hydrolyzed by endogenous esterases. Its active metabolites stimulate colonic motility, with an onset of action between 6 and 10 hours. Metoclopramide is a dopamine receptor antagonist that sensitizes tissue to acetylcholine, which results in improved gastric contraction and small-bowel peristalsis. It has a half-life of 5 to 6 hours. Various dietary regimens, hydration electrolyte solutions, enemas, and antigas agents are also used as adjuncts for colonoscopy preparation.⁷

EASE OF USE

The main impediments to successful colon preparation are preparation volume and taste. Isotonic PEG preparations are better tolerated and favored by 90% of patients who previously tried older cleansing methods used before the availability of PEG regimens.²⁸ The preparations still require ingestion of 2 to 4 L of fluid, which is a volume difficult to tolerate for some adults and for the majority of children, who often require NG tube administration.²⁹ When comparing 2-L to 4-L PEG preparations, patients

prefer the smaller-volume regimen.¹ Because of the salty taste and smell of PEG-ELS, sulfate-free PEG preparations were developed¹³; however, studies have not shown a clear tolerability advantage.¹ To improve taste, flavored preparations, as well as flavoring packages, can be used. Flavoring packages may increase the osmotic load, and some contain carbohydrates that, with bacterial fermentation, may lead to production of combustible gases.³⁰ Aqueous NaP preparations are of small volume but require dilution and, because of their salty taste, present difficulties to some patients. A tablet NaP preparation was developed to improve taste and tolerance, although tolerability comparison results are conflicting.^{31,32} Split-dose regimens may improve preparation efficacy but could add to patient inconvenience because of the need to take the second dose very early in the morning on the day of the procedure.

In a systematic review of 82 studies on colonoscopy preparation, statistical pooling of tolerability data was not possible because of inconsistent data collection, although it was reported that NaP was superior to PEG in a majority of studies.¹ An earlier meta-analysis reported rates of failure to complete the preparation between 0% and 12% for NaP and 3% and 32% for PEG.³³ A recent meta-analysis reviewed randomized controlled clinical trials from 1990 to 2005 and compared the tolerability, efficacy, and safety of various preparations.³⁴ Pooled data from 15 trials with 3293 patients that compared PEG and NaP preparations showed that 94.4% of patients completed taking NaP compared with 70.9% of patients taking PEG solution. The only 2 randomized pediatric trials that compared PEG with NaP involved a total of 63 children. In one study, NaP was better tolerated, but PEG was administered via an NG tube.³⁵ In the other study, 53% of the patients in the PEG group could not complete oral administration, whereas only 7% of patients required NG-tube placement for completion of the NaP regimen. Patients who received NaP found it to be more tolerable than PEG ($P < .02$).³⁶

In 2 small studies, use of adjunctive agents metoclopramide and simethicone was shown to improve tolerability of PEG preparation,^{37,38} whereas the addition of bisacodyl and magnesium citrate¹⁴ or of senna³³ decreased the amount of preparation necessary for effective cleansing. The PEG preparation with ascorbic acid was shown to be better tolerated than NaP¹⁹ and a full-volume PEG preparation.¹⁸ Carbohydrate-electrolyte solutions were used with aqueous NaP to improve palatability and hydration.³⁹

OUTCOMES DATA AND COMPARATIVE STUDIES

There is significant heterogeneity among colonoscopy preparation studies, which makes comparisons difficult. Overall, the best studied and most commonly used preparations, PEG and NaP, provide satisfactory colon cleansing

in a majority of patients. A systematic review of these 2 regimens shows similar adequate preparation rates, 75% for NaP and 71% for PEG.¹

PEG-ELS preparations are more effective than traditional cleaning preparations, including dietary restrictions, laxatives, mannitol, and large-volume bowel lavage.²⁸ Efficacy of the standard 4-L preparation can be improved by administration of split doses,^{17,40} even with minimal dietary restriction before the first dose.⁴⁰ Ingestion of the entire preparation on the day of the procedure about 5 hours before the colonoscopy improved the clean-out quality when compared with patients who received PEG-ELS the previous day, approximately 19 hours before the procedure.⁴¹ Sulfate-free PEG preparations appear to be equally as effective as regular PEG-ELS.¹⁰ Adjunctive therapies, such as bisacodyl, metoclopramide, and enemas, do not seem to improve the efficacy of full-volume PEG preparations, although the addition of simethicone improves colon visibility.⁴² Low-volume PEG preparations combined with a stimulant agent showed similar efficacy to full-volume PEG preparations.^{14,43} In a multicenter trial, a 2-L sulfate-free PEG preparation with a 10-mg bisacodyl dose was as effective as the same preparation with the initially marketed 20-mg dose bisacodyl regimen.⁴⁴ Most recently, a low-volume PEG preparation with ascorbic acid showed similar efficacy when compared with full-volume PEG¹⁸ and NaP¹⁹ preparations. In most randomized controlled trials, NaP preparations are reported to be equally or more effective compared with PEG preparations.^{22,23,45-65} The NaP tablets appear to be equally as effective as an aqueous NaP solution³¹ and a PEG preparation.²² A split-dose NaP schedule, with one dose taken the day before and one on the day of the procedure separated by 12 hours, was superior relative to a single dose.^{66,67}

In pediatrics, there is a lack of randomized controlled trials, and a wide variety of preparations are used.⁶⁸ PEG solutions were used in a few small randomized trials. Two studies compared PEG with NaP; one showed similar success rates (73% vs 71% for PEG and NaP, respectively),³⁵ and one showed that NaP was superior (40% vs 95%).³⁶ A third study found that PEG was superior to magnesium citrate with senna, and bisacodyl with an enema.⁶⁹ PEG-3350 without electrolytes was shown to be efficacious in more than 90% of pediatric patients when used over a 4-day period.²⁰ An NaP solution was found to be less effective when compared with magnesium citrate used with a low-residue diet in one study,⁷⁰ although equally effective and more acceptable when compared with the same medication in addition to an enema.⁷¹ Various other regimens, including senna or magnesium citrate with enema²⁷ and bisacodyl with enema,^{72,73} were found to be efficacious in open-label prospective trials.

In elderly patients, 2 studies with a total of 188 subjects 75 years old and older compared PEG with NaP and found them to be equally effective.^{51,58}

TABLE 1. Agents used for bowel preparation*

Product (manufacturer)	Active agent	FDA approved for bowel preparation		Quantity	Average wholesale price (\$)
		Children	Adults		
Isosmotic					
Full volume					
Colyte (SchwarzPharm, Mequon, Wis)	PEG	No	Yes		
Flavored				4000 mL	25.63
Nonflavored				4000 mL	24.44
GoLYTELY (Braintree, Braintree, Mass)	PEG	No	Yes		
Flavored				4000 mL	19.70
Nonflavored				4000 mL	18.45
NuLYTELY (Braintree)	PEG (sulfate free)	> 6 mo	Yes		
Flavored				4000 mL	26.89
Nonflavored				4000 mL	26.89
TriLyte (SchwarzPharm)	PEG (sulfate free)	> 6 mo	Yes		
Flavored				4000 mL	26.86
Low volume					
Halflytely (Braintree)	PEG and bisacodyl	No	Yes	2000 mL	52.31
MoviPrep (Salix Pharmaceuticals, Inc, Morrisville, NC)	PEG and ascorbic acid	No	Yes	2000 mL	46.80
Not approved for bowel preparation†					
MiraLax (Braintree)	PEG-3350 no electrolytes	No	No	255 g	21.73
GlycoLax (Kremers Urban Co, Wilmington, Del)	PEG-3350 no electrolytes	No	No	255 g	19.54
Hyperosmotic					
Fleet Phospho-Soda EZ-Prep (C.B. Fleet Co, Lynchburg, Va)	NaP (oral)	No	‡	75 mL (30 & 45)§	
Visicol (tablet, NaP; Salix Pharm)	NaP (oral)	No	Yes	40 Tablets	105.83
Osmoprep, (MCC-free tablet; Salix Pharm)	NaP (oral)	No	Yes	32 Tablets	52.99
Fleet, enema children (C.B. Fleet)	NaP enema	> 2 y	No	67.5 mL	1.09
Fleet Enema (C.B. Fleet)	NaP enema	> 12 y	Yes	135 mL	0.80
LoSoPrep Kit (E-Z-EM Inc, Lake Success, NY)	Magnesium citrate plus	No	Yes	1 Package	5.40
	Bisacodyl oral and suppository				
Magnesium Citrate (AmerisourceBergen, Chesterbrook, Pa)	Magnesium citrate	> 6 y	Yes	300 mL	1.43
Adjunctive agents					
Fleet Bisacodyl Enema 10 mg (C.B. Fleet)	Bisacodyl topical	No	Yes	37.5 mL	1.19

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TABLE 1 (continued)

Product (manufacturer)	Active agent	FDA approved for bowel preparation		Quantity	Average wholesale price (\$)
		Children	Adults		
Fleet Bisacodyl (C.B. Fleet)	Bisacodyl	No	No		
5-mg tablet				25 Tablets	2.90
10-mg suppository				4 Suppositories	1.95
Dulcolax (Bisacodyl 5 mg; Boehringer, Petersburg, Va)	Bisacodyl	No	No	100 Tablets	8.30
Senna (8.6 mg; AmerisourceBergen)	Senna	No	No	100 Tablets	8.99
Senna syrup (8.8 mg per 5 mL; Altaire, Aquebogue, NY)	Senna	No	No	237 mL	7.92
Sennokot (8.6 mg; Purdue Products LP, Stamford, Conn)	Senna	No	No	20 Tablets	5.56
SennaPlus (50 mg; American Health Packaging, Columbus, Ohio)	Senna and docusate sodium	No	No	100 Tablets	11.13
Metoclopramide (5 mg; Teva, Philadelphia, Pa)	Metoclopramide	No	No	100 Tablets	33.25
Gas-X (80 mg; Novartis, East Hanover, NJ)	Simethicone	No	No	12 Tablets	1.88
				36 Tablets	4.67
Mylicon Infant Drops (40 mg per 0.6 mL; J & J/Merck, Fort Washington, Pa)	Simethicone	No	No	15 mL	6.22
				30 mL	10.68
Simethicone (80 mg; Advance, Ronkonkoma, NY)	Simethicone	No	No	100 Tablets	2.99
Simethicone (125 mg; Rugby, Corona, Calif)	Simethicone			60 Tablets	5.02/ea
Mylanta (J & J/Merck)		No	No	150 mL	2.94

PEG, Polyethylene glycol; NaP, sodium phosphate.

*Adapted from Ref. 7.

†Approved only for small-volume treatment of constipation. The safety of the volume and dose for bowel preparation is not established, and the osmolarity may vary based on the volume of the solvent.

‡The FDA recommends against use of over-the-counter oral NaP for bowel preparation.

§C.B. Fleet ceased distribution and initiated a recall on December 11, 2008.

||A black box warning was added in December 2008.

SAFETY

All colonoscopy preparations may cause adverse events. The most common are electrolyte and fluid imbalance, as well as abdominal discomfort, bloating, dizziness, nausea and vomiting, adverse effects on colonic mucosa, and colonic-gas explosion. The choice of preparation is guided by comorbidities, concomitant medications, age concerns, patient preference, and cost to achieve safe and successful preparation. All oral bowel-preparation agents are contraindicated in the setting of obstruction, perforation, and severe ileus. Magnesium and phosphate preparations should be avoided in patients with renal failure.

Isosmotic preparations do not cause significant physiologic change in vital signs, serum electrolytes, weight, and blood counts, which makes them suitable for patients with liver disease and ascites, renal failure, and congestive heart disease.⁷ However, an asymptomatic increase in plasma volume and exacerbation of congestive heart failure were reported.^{74,75} Other rare adverse events reported include pulmonary aspiration, Mallory-Weiss tear, esophageal perforation, pancreatitis, colitis, cardiac dysrhythmia, hyponatremia in patients with renal failure, and a syndrome of inappropriate antidiuretic hormone secretion.^{9,76} Rates of adverse events in a meta-analysis that compared PEG with NaP showed a statistically significant increase in pain reporting among patients who were taking a PEG

preparation and in dizziness and biochemical disturbances with NaP, whereas there were no differences in nausea, vomiting, sleep disturbances, and perianal pain.³⁴

Hyperosmotic preparations have the potential to cause fluid shifts by drawing fluid from the intravascular space, potentially resulting in hypovolemia and electrolyte disturbances. Most common with NaP are hyperphosphatemia, hypernatremia, hypocalcemia, and hypokalemia.¹⁰ In a meta-analysis of 9 trials, these biochemical disturbances were reported more frequently with NaP than with PEG preparations, although no clinical symptoms were associated with these laboratory abnormalities.³⁴ Because of the potential for electrolyte abnormalities, NaP is not recommended in patients with renal disease, megacolon, bowel obstruction, ascites, and congestive heart disease.⁷⁷ A review study examined the rates of adverse events with NaP in 28 trials: 26 with aqueous, and 2 with tablet NaP preparations that involved a total of 3022 patients.⁷⁸ None of the patients in these trials had a major adverse event; however, patients with predisposing factors that could have led to adverse events were excluded. The study included reports of 6 fatalities, all associated with inappropriate dosing, and commented on 8 fatalities reported to the U.S. Food and Drug Administration (FDA) during a 6-year period, from 1997 to 2002. In comparison, during the same period, the FDA received reports on 6 fatalities with PEG preparations. In elderly patients, NaP was found to be associated with a decline in the glomerular filtration rate,⁷⁹ whereas, in children, hyperphosphatemia was present to a higher degree than previously reported in adults.³⁶ In addition, a recent series of reports describes acute phosphate nephropathy followed by chronic renal insufficiency after taking NaP for bowel preparation in patients with predominately normal renal function who were found to have calcium phosphate crystal deposition in renal tubules on kidney biopsy.⁸⁰⁻⁸² In a series of 21 patients who developed acute phosphate nephropathy, potential etiologic factors included dehydration, increased age, hypertension, and concurrent use of an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker.⁸³ These findings prompted the FDA to issue an alert in 2006 regarding the use of oral NaP for bowel preparation, particularly in individuals who were taking angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or nonsteroidal anti-inflammatory drugs,⁸⁴ and prompted some to advocate alternative colon-cleansing preparations for children and adolescents under 18 years of age.⁸⁵ In December 2008, as a result of accumulating reports of renal injury, including patients without predisposing factors, the FDA recommended that over-the-counter NaP preparations not be used for bowel preparation. This prompted the manufacturer of over-the-counter NaP to undertake a voluntary recall of its product. Furthermore, a black box warning was added to prescription NaP products, and manufacturers were required to implement a risk evaluation and mitigation strategy, including a post-

marketing trial, to further assess the incidence of renal injury.⁸⁶ Other recent reports raise further concerns about the safety of this agent across a population and indicate the potential for significant long-term reduction in the glomerular filtration rate, particularly after 2 sequential doses of NaP.^{79,87} To reduce the risk of volume depletion and electrolyte imbalance, appropriate patient selection and preprocedure, intraprocedure, and postprocedure hydration is necessary.⁷⁶ In addition to hydration with specific volume instructions for patients, use of minimally effective doses and a 10- to 12-hour interval between doses may improve safety.²⁵

In general, the PEG preparation has been shown to preserve normal colon histology.⁸⁸ However, a single randomized trial that compared PEG with no preparation described microscopic alterations, including inflammatory changes, loss of epithelial cells and mucus, and edema of the colonic mucosa, with PEG.⁸⁹ NaP can alter the microscopic and macroscopic appearance of colonic mucosa, which may mimic inflammatory diseases.⁹⁰⁻⁹² This has prompted some clinicians to avoid this preparation in patients with suspected inflammatory bowel disease or microscopic colitis.⁷

The nonabsorbable carbohydrates used for colon preparations, when fermented by colonic bacteria, can lead to production of the combustible gases hydrogen and methane. This can lead to colonic-gas explosion during electrocautery use.¹¹ This complication was previously described with mannitol preparations and also more recently with sorbitol.⁹³ In a 2007 review, a total of 10 cases of colonic-gas explosion during colonoscopy were reported, 6 with argon plasma coagulation and 4 with polypectomy, which resulted in 6 colon perforations and 1 death.¹¹ In addition to ingestion of nonabsorbable carbohydrates, incomplete colon preparation, as is typically prescribed for flexible sigmoidoscopy,⁹⁴ or inadequate preparation for colonoscopy can lead to production of a combustible level of gases.

FINANCIAL CONSIDERATIONS

Procedure cost is affected by inadequate preparation secondary to poor compliance or intolerance, which then increases the chance for an aborted procedure and the need for repeated colonoscopy.^{95,96} Product pricing for the list of products was obtained from the Red Book Pharmacy's Fundamental Reference⁹⁷ and expressed as average wholesale price (Table 1). The most expensive product is the NaP tablet preparation followed by PEG preparations, and the least expensive is aqueous NaP.

AREAS FOR FUTURE RESEARCH

There is a need for development of new preparations for bowel cleansing that would achieve uniform and

complete cleansing with improved tolerability and reduced adverse effects. The existing regimens and their combinations need to be studied in large, prospective, randomized trials to establish equivalence and to determine minimally effective doses. In addition, further studies on patient preferences associated with alternative timing of dosing are needed. The efficacy and safety of newer PEG regimens, including PEG-3350 without electrolytes, prescribed with adjunctive carbohydrate liquids (eg, sports drinks) relative to existing preparations should be assessed. Bowel preparations have not been adequately studied for special populations (eg, extremes of age, pregnant women, and patients with comorbidities).

SUMMARY

The choice of bowel preparation for colonoscopy is influenced by cleansing effectiveness, safety, ease of administration and completion, adverse effects, patient tolerance, and cost. Currently, PEG-ELS and NaP are the most frequently used preparations in the United States. Recent action by the FDA highlights emerging safety concerns for NaP preparations. The selection of a bowel-cleansing regimen should be tailored to the individual patient based on clinical comorbidities and informed patient preference.

Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; FDA, U.S. Food and Drug Administration; MCC, microcrystalline cellulose; NaP, sodium phosphate; NG, nasogastric; PEG, polyethylene glycol; PEG-ELS, polyethylene glycol electrolyte lavage solution.

REFERENCES

- Belsey J, Epstein O, Heresbach D. Systematic review: oral bowel preparation for colonoscopy. *Aliment Pharmacol Ther* 2007;25:373-84.
- Kazarian ES, Carreira FS, Toribara NW, et al. Colonoscopy completion in a large safety net health care system. *Clin Gastroenterol Hepatol* 2008;6:438-42.
- Froehlich F, Wietlisbach V, Gonvers JJ, et al. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. *Gastrointest Endosc* 2005;61:378-84.
- Harewood GC, Sharma VK, de Garmo P. Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia. *Gastrointest Endosc* 2003;58:76-9.
- Thomas-Gibson S, Rogers P, Cooper S, et al. Judgement of the quality of bowel preparation at screening flexible sigmoidoscopy is associated with variability in adenoma detection rates. *Endoscopy* 2006;38:456-60.
- Barkun A, Chiba N, Enns R, et al. Commonly used preparations for colonoscopy: efficacy, tolerability, and safety: a Canadian Association of Gastroenterology position paper. *Can J Gastroenterol* 2006;20:699-710.
- Wexner SD, Beck DE, Baron TH, et al. A consensus document on bowel preparation before colonoscopy: prepared by a task force from the American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). *Surg Endosc* 2006;20:1147-60.
- Toledo TK, DiPalma JA. Review article: colon cleansing preparation for gastrointestinal procedures. *Aliment Pharmacol Ther* 2001;15:605-11.
- Nelson DB, Barkun AN, Block KP, et al. Technology Status Evaluation report. Colonoscopy preparations. May 2001. *Gastrointest Endosc* 2001;54:829-32.
- Shawki S, Wexner SD. Oral colorectal cleansing preparations in adults. *Drugs* 2008;68:417-37.
- Ladas SD, Karamanolis G, Ben-Soussan E. Colonic gas explosion during therapeutic colonoscopy with electrocautery. *World J Gastroenterol* 2007;13:5295-8.
- Davis GR, Santa Ana CA, Morawski SG, et al. Development of a lavage solution associated with minimal water and electrolyte absorption or secretion. *Gastroenterology* 1980;78:991-5.
- Fordtran JS, Santa Ana CA, Cleveland MvB. A low-sodium solution for gastrointestinal lavage. *Gastroenterology* 1990;98:11-6.
- Adams WJ, Meagher AP, Lubowski DZ, et al. Bisacodyl reduces the volume of polyethylene glycol solution required for bowel preparation. *Dis Colon Rectum* 1994;37:229-33; discussion 33-4.
- Sharma VK, Steinberg EN, Vasudeva R, et al. Randomized, controlled study of pretreatment with magnesium citrate on the quality of colonoscopy preparation with polyethylene glycol electrolyte lavage solution. *Gastrointest Endosc* 1997;46:541-3.
- Rösch T, Classen M. Fractional cleansing of the large bowel with "Golytely" for colonoscopic preparation: a controlled trial. *Endoscopy* 1987;19:198-200.
- Aoun E, Abdul-Baki H, Azar C, et al. A randomized single-blind trial of split-dose PEG-electrolyte solution without dietary restriction compared with whole dose PEG-electrolyte solution with dietary restriction for colonoscopy preparation. *Gastrointest Endosc* 2005;62:213-8.
- Ell C, Fischbach W, Bronisch HJ, et al. Randomized trial of low-volume PEG solution versus standard PEG + electrolytes for bowel cleansing before colonoscopy. *Am J Gastroenterol* 2008;103:883-93.
- Bitoun A, Ponchon T, Barthet M, et al. Results of a prospective randomized 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;24:1631-42.
- Pashankar DS, Uc A, Bishop WP. Polyethylene glycol 3350 without electrolytes: a new safe, effective, and palatable bowel preparation for colonoscopy in children. *J Pediatr* 2004;144:358-62.
- 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.
- Kastenberg D, Chasen R, Choudhary C, et al. Efficacy and safety of sodium phosphate tablets compared with PEG solution in colon cleansing: two identically designed, randomized, controlled, parallel group, multicenter phase III trials. *Gastrointest Endosc* 2001;54:705-13.
- Vanner SJ, MacDonald PH, Paterson WG, et al. A randomized prospective trial comparing oral sodium phosphate with standard polyethylene glycol-based lavage solution (Golytely) in the preparation of patients for colonoscopy. *Am J Gastroenterol* 1990;85:422-7.
- Linden TB, Wayne JD. Sodium phosphate preparation for colonoscopy: onset and duration of bowel activity. *Gastrointest Endosc* 1999;50:811-3.
- Rex DK. Dosing considerations in the use of sodium phosphate bowel preparations for colonoscopy. *Ann Pharmacother* 2007;41:1466-75.
- Chang KJ, Erickson RA, Schandler S, et al. Per-rectal pulsed irrigation versus per-oral colonic lavage for colonoscopy preparation: a randomized, controlled trial. *Gastrointest Endosc* 1991;37:444-8.
- Trautwein AL, Vinitzki LA, Peck SN. Bowel preparation before colonoscopy in the pediatric patient: a randomized study. *Gastroenterol Nurs* 1996;19:137-9.
- Shawki S, Wexner SD. How safe is bowel preparation with oral sodium phosphate solution? *Nat Clin Pract Gastroenterol Hepatol* 2008;5:482-3.

29. Sondheimer JM, Sokol RJ, Taylor SF, et al. Safety, efficacy, and tolerance of intestinal lavage in pediatric patients undergoing diagnostic colonoscopy. *J Pediatr* 1991;119:148-52.
30. Wexner SD. Preoperative preparation prior to colorectal surgery. *Gastrointest Endosc* 1996;43:530-1.
31. Aronchick CA, Lipshutz WH, Wright SH, et al. A novel tableted purgative for colonoscopic preparation: efficacy and safety comparisons with Colyte and Fleet Phospho-Soda. *Gastrointest Endosc* 2000;52:346-52.
32. Balaban DH, Leavell BS Jr, Oblinger MJ, et al. Low volume bowel preparation for colonoscopy: randomized, endoscopist-blinded trial of liquid sodium phosphate versus tablet sodium phosphate. *Am J Gastroenterol* 2003;98:827-32.
33. Hsu CW, Imperiale TF. Meta-analysis and cost comparison of polyethylene glycol lavage versus sodium phosphate for colonoscopy preparation. *Gastrointest Endosc* 1998;48:276-82.
34. Tan JJ, Tjandra JJ. Which is the optimal bowel preparation for colonoscopy: a meta-analysis. *Colorectal Dis* 2006;8:247-58.
35. da Silva MM, Briars GL, Patrick MK, et al. Colonoscopy preparation in children: safety, efficacy, and tolerance of high- versus low-volume cleansing methods. *J Pediatr Gastroenterol Nutr* 1997;24:33-7.
36. Gremse DA, Sacks AI, Raines S. Comparison of oral sodium phosphate to polyethylene glycol-based solution for bowel preparation for colonoscopy in children. *J Pediatr Gastroenterol Nutr* 1996;23:586-90.
37. Lazzaroni M, Petrillo M, Desideri S, et al. Efficacy and tolerability of polyethylene glycol-electrolyte lavage solution with and without simethicone in the preparation of patients with inflammatory bowel disease for colonoscopy. *Aliment Pharmacol Ther* 1993;7:655-9.
38. Rhodes JB, Engstrom J, Stone KF. Metoclopramide reduces the distress associated with colon cleansing by an oral electrolyte overload. *Gastrointest Endosc* 1978;24:162-3.
39. Tjandra JJ, Tagkalidis P. Carbohydrate-electrolyte (E-Lyte) solution enhances bowel preparation with oral Fleet Phospho-soda. *Dis Colon Rectum* 2004;47:1181-6.
40. El Sayed AM, Kanafani ZA, Mourad FH, et al. A randomized single-blind trial of whole versus split-dose polyethylene glycol-electrolyte solution for colonoscopy preparation. *Gastrointest Endosc* 2003;58:36-40.
41. Church JM. Effectiveness of polyethylene glycol antegrade gut lavage bowel preparation for colonoscopy. timing is the key! *Dis Colon Rectum* 1998;41:1223-5.
42. McNally PR, Maydonovitch CL, Wong RK. The effectiveness of simethicone in improving visibility during colonoscopy: a double-blind randomized study. *Gastrointest Endosc* 1988;34:255-8.
43. Sharma VK, Chockalingham S, Clark V, et al. Randomized, controlled comparison of two forms of preparation for screening flexible sigmoidoscopy. *Am J Gastroenterol* 1997;92:809-11.
44. DiPalma JA, McGowan J, Cleveland MV. Clinical trial: an efficacy evaluation of reduced bisacodyl given as part of a polyethylene glycol electrolyte solution preparation prior to colonoscopy. *Aliment Pharmacol Ther* 2007;26:1113-9.
45. Kolts BE, Lyles WE, Achem SR, et al. A comparison of the effectiveness and patient tolerance of oral sodium phosphate, castor oil, and standard electrolyte lavage for colonoscopy or sigmoidoscopy preparation. *Am J Gastroenterol* 1993;88:1218-23.
46. Reddy DN, Rao GV, Sriram PV. Efficacy and safety of oral sodium phosphate versus polyethylene glycol solution for bowel preparation for colonoscopy. *Indian J Gastroenterol* 2002;21:219-21.
47. Chan CH, Diner WC, Fontenot E, et al. Randomized single-blind clinical trial of a rapid colonic lavage solution (Golytely) vs. standard preparation for barium enema and colonoscopy. *Gastrointest Radiol* 1985;10:378-82.
48. Felt-Bersma RJ, Kooyman G, Kuipers EJ. Colonic lavage prior to colonoscopy: comparable outcomes of two polyethylene-glycol preparations and a sodium-phosphate solution [Dutch with English abstract]. *Ned Tijdschr Geneesk* 2004;148:181-5.
49. Lapalus MG, Gaudin JL, Lemkecher T, et al. Prospective randomized single-blind trial comparing oral sodium phosphate with polyethylene glycol for colonoscopy preparation [French with English abstract]. *Gastroenterol Clin Biol* 2001;25:29-34.
50. Marshall JB, Pineda JJ, Barthel JS, et al. Prospective, randomized trial comparing sodium phosphate solution with polyethylene glycol-electrolyte lavage for colonoscopy preparation. *Gastrointest Endosc* 1993;39:631-4.
51. Seinela L, Pehkonen E, Laasanen T, et al. Bowel preparation for colonoscopy in very old patients: a randomized prospective trial comparing oral sodium phosphate and polyethylene glycol electrolyte lavage solution. *Scand J Gastroenterol* 2003;38:216-20.
52. Pontone P, Bogliolo G, Pietropaolo V, et al. Polyethylene glycol versus sodium phosphate: comparison of 2 preparations for colonoscopy [Italian with English abstract]. *G Chir* 1996;17:128-31.
53. Chia YW, Cheng LC, Goh PM, et al. Role of oral sodium phosphate and its effectiveness in large bowel preparation for out-patient colonoscopy. *J R Coll Surg Edinb* 1995;40:374-6.
54. Clarkston WK, Tsen TN, Dies DF, et al. Oral sodium phosphate versus sulfate-free polyethylene glycol electrolyte lavage solution in outpatient preparation for colonoscopy: a prospective comparison. *Gastrointest Endosc* 1996;43:42-8.
55. Martinez JL, Calleja JL. A new variable stiffness colonoscope makes colonoscopy easier: a randomized controlled trial. *Gastrointest Endosc* 2001;53:694-5.
56. Huppertz-Hauss G, Bretthauer M, Sauar J, et al. Polyethylene glycol versus sodium phosphate in bowel cleansing for colonoscopy: a randomized trial. *Endoscopy* 2005;37:537-41.
57. Henderson JM, Barnett JL, Turgeon DK, et al. Single-day, divided-dose oral sodium phosphate laxative versus intestinal lavage as preparation for colonoscopy: efficacy and patient tolerance. *Gastrointest Endosc* 1995;42:238-43.
58. Thomson A, Naidoo P, Crotty B. Bowel preparation for colonoscopy: a randomized prospective trial comparing sodium phosphate and polyethylene glycol in a predominantly elderly population. *J Gastroenterol Hepatol* 1996;11:103-7.
59. Eil C, Fischbach W, Keller R, et al. A randomized, blinded, prospective trial to compare the safety and efficacy of three bowel-cleansing solutions for colonoscopy (HSG-01*). *Endoscopy* 2003;35:300-4.
60. Lee J, McCallion K, Acheson AG, et al. A prospective randomised study comparing polyethylene glycol and sodium phosphate bowel cleansing solutions for colonoscopy. *Ulster Med J* 1999;68:68-72.
61. Young CJ, Simpson RR, King DW, et al. Oral sodium phosphate solution is a superior colonoscopy preparation to polyethylene glycol with bisacodyl. *Dis Colon Rectum* 2000;43:1568-71.
62. 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;27:120-4.
63. Cohen SM, Wexner SD, Binderow SR, et al. Prospective, randomized, endoscopic-blinded trial comparing precolonoscopy bowel cleansing methods. *Dis Colon Rectum* 1994;37:689-96.
64. Arezzo A. Prospective randomized trial comparing bowel cleaning preparations for colonoscopy. *Surg Laparosc Endosc Percutan Tech* 2000;10:215-7.
65. Golub RW, Kerner BA, Wise WE Jr, et al. Colonoscopic bowel preparations: which one? A blinded, prospective, randomized trial. *Dis Colon Rectum* 1995;38:594-9.
66. Frommer D. Cleansing ability and tolerance of three bowel preparations for colonoscopy. *Dis Colon Rectum* 1997;40:100-4.
67. Afridi SA, Barthel JS, King PD, et al. Prospective, randomized trial comparing a new sodium phosphate-bisacodyl regimen with conventional PEG-ES lavage for outpatient colonoscopy preparation. *Gastrointest Endosc* 1995;41:485-9.
68. Barrish JO, Gilger MA. Colon cleanout preparations in children and adolescents. *Gastroenterol Nurs* 1993;16:106-9.
69. Dahshan A, Lin CH, Peters J, et al. A randomized, prospective study to evaluate the efficacy and acceptance of three bowel preparations for colonoscopy in children. *Am J Gastroenterol* 1999;94:3497-501.
70. El-Baba MF, Padilla M, Houston C, et al. A prospective study comparing oral sodium phosphate solution to a bowel cleansing preparation

- with nutrition food package in children. *J Pediatr Gastroenterol Nutr* 2006;42:174-7.
71. Sabri M, Di Lorenzo C, Henderson W, et al. Colon cleansing with oral sodium phosphate in adolescents: dose, efficacy, acceptability, and safety. *Am J Gastroenterol* 2008;103:1533-9; quiz 40.
 72. Abubakar K, Goggin N, Gormally S, et al. Preparing the bowel for colonoscopy. *Arch Dis Child* 1995;73:459-61.
 73. Shaoul R, Haloon L. An assessment of bisacodyl-based bowel preparation for colonoscopy in children. *J Gastroenterol* 2007;42:26-8.
 74. Granberry MC, White LM, Gardner SF. Exacerbation of congestive heart failure after administration of polyethylene glycol-electrolyte lavage solution. *Ann Pharmacother* 1995;29:1232-5.
 75. Turnage RH, Guice KS, Gannon P, et al. The effect of polyethylene glycol gavage on plasma volume. *J Surg Res* 1994;57:284-8.
 76. Lichtenstein GR, Cohen LB, Uribarri J. Review article: bowel preparation for colonoscopy—the importance of adequate hydration. *Aliment Pharmacol Ther* 2007;26:633-41.
 77. Curran MP, Plosker GL. Oral sodium phosphate solution: a review of its use as a colorectal cleanser. *Drugs* 2004;64:1697-714.
 78. Hookey LC, Depew WT, Vanner S. The safety profile of oral sodium phosphate for colonic cleansing before colonoscopy in adults. *Gastrointest Endosc* 2002;56:895-902.
 79. Khurana A, McLean L, Atkinson S, et al. The effect of oral sodium phosphate drug products on renal function in adults undergoing bowel endoscopy. *Arch Intern Med* 2008;168:593-7.
 80. Aasebo W, Scott H, Ganss R. Kidney biopsies taken before and after oral sodium phosphate bowel cleansing. *Nephrol Dial Transplant* 2007;22:920-2.
 81. Desmeules S, Bergeron MJ, Isenring P. Acute phosphate nephropathy and renal failure. *N Engl J Med* 2003;349:1006-7.
 82. Gonlusen G, Akgun H, Ertan A, et al. Renal failure and nephrocalcinosis associated with oral sodium phosphate bowel cleansing: clinical patterns and renal biopsy findings. *Arch Pathol Lab Med* 2006;130:101-6.
 83. Markowitz GS, Stokes MB, Radhakrishnan J, et al. Acute phosphate nephropathy following oral sodium phosphate bowel purgative: an underrecognized cause of chronic renal failure. *J Am Soc Nephrol* 2005;16:3389-96.
 84. Lowry A, Hawes R, Deziel D. Addendum to a consensus document on bowel preparation before colonoscopy: prepared by a task force from the American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). *Gastrointest Endosc* 2006;64:154.
 85. Hassall E, Lobe TE. Risks of oral sodium phosphate for precolonoscopy bowel preparation in children. *Gastrointest Endosc* 2007;65:1102-4; author reply 4–5.
 86. Oral sodium phosphate (OSP) products for bowel cleansing (marketed as Visicol and OsmoPrep, and oral sodium phosphate products available without a prescription). Available at: <http://www.fda.gov/medwatch/safety/2008/safety08.htm#OSP>. Accessed December 11, 2008.
 87. Lien YH. Are oral sodium phosphate products for bowel cleansing safe for the general population? *Am J Med* 2008;121:931-2.
 88. Pockros PJ, Foroosan P. Golytely lavage versus a standard colonoscopy preparation. Effect on normal colonic mucosal histology. *Gastroenterology* 1985;88:545-8.
 89. Bucher P, Gervaz P, Egger JF, et al. Morphologic alterations associated with mechanical bowel preparation before elective colorectal surgery: a randomized trial. *Dis Colon Rectum* 2006;49:109-12.
 90. Driman DK, Preiksaitis HG. Colorectal inflammation and increased cell proliferation associated with oral sodium phosphate bowel preparation solution. *Hum Pathol* 1998;29:972-8.
 91. Rejchrt 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;59:651-4.
 92. Zwas FR, Cirillo NW, el-Serag HB, et al. Colonic mucosal abnormalities associated with oral sodium phosphate solution. *Gastrointest Endosc* 1996;43:463-6.
 93. Josemanders DF, Spillenaar Bilgen EJ, van Sorge AA, et al. Colonic explosion during endoscopic polypectomy: avoidable complication or bad luck? *Endoscopy* 2006;38:943-4.
 94. Monahan DW, Peluso FE, Goldner F. Combustible colonic gas levels during flexible sigmoidoscopy and colonoscopy. *Gastrointest Endosc* 1992;38:40-3.
 95. Chilton AP, O'Sullivan M, Cox MA, et al. A blinded, randomized comparison of a novel, low-dose, triple regimen with fleet phosphosoda: a study of colon cleanliness, speed and success of colonoscopy. *Endoscopy* 2000;32:37-41.
 96. Rex DK, Imperiale TF, Latinovich DR, et al. Impact of bowel preparation on efficiency and cost of colonoscopy. *Am J Gastroenterol* 2002;97:1696-700.
 97. Red Book Pharmacy's Fundamental Reference. Montvale (NJ): Thomson Healthcare Inc; 2007.

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