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Clinical Review

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# High Quality Bowel Preparation - A Cornerstone to the Effectiveness of Colonoscopy as a Cancer Prevention Tool

One of the most important developments in the field of gastroenterology over the past decade has been improving the quality of screening and surveillance colonoscopy to enhance the detection and removal of premalignant polyps, thus reducing the likelihood of developing interval colon cancer. Factors which have contributed to improving colonoscopy quality have included a much greater awareness of flat and subtle polyps (especially in the right colon), the practice of careful withdrawal technique, monitoring withdrawal times and adenoma detection rates, and various technological advances, particularly related to imaging. A key component that impacts each of these factors is the quality of colon cleansing. An inadequate bowel prep dooms even the most skilled endoscopist and the best equipment. High quality bowel preparation is a necessity and serves several critical purposes, namely improving polyp detection (including the more difficult to see flat lesions, generally in the right colon),



helping to prevent right-sided cancers, and reducing the need for early repeat exams, which is costly to the health care system. A good bowel prep also makes colonoscopy much easier and quicker.

Recently, split-dose bowel preps, where part of the prep is given on the day of the exam, have become the standard of practice in many centers. However, there are a multitude of bowel prep formulations to choose from, with much uncertainty and debate regarding the optimal prep, which is often influenced by a patient's clinical status. This review will provide a brief and practical guide to help the clinician select the optimal prep and address commonly encountered problems.

# **Grading the Bowel Preparation**

The U.S. Multi-Society Task Force on Colorectal Cancer has defined an adequate colon prep as one capable of detecting polyps >5-mm.¹ Also, a bowel prep should be considered inadequate when the colonoscopy has to be repeated at an earlier date than would otherwise be indicated based on prep quality.² Endoscopists should routinely grade and report the quality of the patient's colon prep after (not before) cleaning has taken place. Bowel prep grading is important in individual patients to enable the endoscopist to make proper colonoscopy follow-up recommendations after screening and polypectomy. In addition, physicians can use this information to determine if adjustments in colon prep orders or patient counseling are needed in their practice.

The bowel prep should be graded as either "adequate" or "inadequate" (or "satisfactory" versus "unsatisfactory"). While terms such as "excellent," "good," and "poor" are appropriate to use in this setting, it is important to avoid other terms such as "fair." In our practice, endoscopists provide two descriptors of the prep. The first is the general descriptor as discussed above. This is followed by the validated Boston Bowel Preparation Score (BBPS), where each of the three colon segments is graded on a 0 to 3 scale after the segment has been cleaned. If any segment is graded as a 0 or 1, the overall bowel prep is considered inadequate. For instance, the colonoscopy report might read: "The bowel prep was adequate (BBPS = 2/3/3)," or "the bowel prep was inadequate (BBPS = 1/2/2)." A recent study showed that a total BBPS score  $\geq$ 6 and/or all segment scores >2 provides a standardized definition of adequate for 10-year follow-up colonoscopies.

## **Predictors of Inadequate Bowel Preparation**

Before discussing the options for bowel preparation, we will first consider predictors of inadequate bowel preparation. The presence of these predictors must be considered when selecting the prep and for determining whether the patient needs special help with his/her situation. Medical conditions associated with inadequate bowel preparation include chronic constipation, use of constipating meds, polypharmacy, diabetes mellitus, obesity, cirrhosis, Parkinson's disease, dementia, stroke, prior colon resection, and a prior history of inadequate colon prep.<sup>2,5-7</sup> The presence of any of these factors should alert the endoscopist as to the potential need for a more thorough prep. In addition, various socioeconomic and health literacy factors increase the risk of poor preparation resulting from the patient either not understanding and/or following instructions. Examples in this regard include Medicaid insurance and interpreter requirement.<sup>8</sup> A recent report found that low "patient activation" was an important independent risk factor predicting suboptimal bowel preparation. Patient activation refers to how engaged individuals are in their own health care. Special interventions are needed in these individuals to increase the likelihood of their following the prep instructions.

# **Selecting a Bowel Prep**

Bowel preps are evaluated and selected based on their efficacy (quality of the colon cleansing), patient tolerability, safety, and cost to the patient. The traditional 4-L PEG-electrolyte solution (PEG-ES) prep given the evening before colonoscopy was the most often used prep regimen for many years. Unfortunately, many patients could not consume the entire prep and often developed side effects, thereby commonly resulting in inadequate preparations.

Split-dose bowel preparation, in which at least part of the prep is given on the day of the colonoscopy, has been a major advance in colonoscopy bowel preparation. Regardless of the specific prep used, split-dose preps result in higher quality colon cleansing, increased patient compliance, and fewer side effects compared to full-dose preparations given entirely on the day or evening before the exam. <sup>10</sup> Split-dosing the preparation has become the standard of practice in many centers. <sup>2</sup>

Which prep should be used for patients without predictors of inadequate preparation remains a matter of much debate and confusion. A recent systematic review and meta-analysis found 4-L split-dose PEG-ES preps to be superior to other bowel preparation methods for colonoscopy. It should therefore be considered the "standard" by which new colon prep methods are compared. For patients who must pay for their colon prep, the 4-L split-dose generic PEG-ES prep represents a low-cost option. It is the "standard" prep that we use in our practice, both in our University Hospital endoscopy center and ambulatory endoscopy center.

Ingesting large volumes of fluid has been an impediment to the PEG-ES colon lavage preps. Splitting the dose (67.6 oz on the evening before the exam and 67.6 oz on the morning of the exam) has helped, but this volume can still be difficult for some patients. There have been efforts for many years to find acceptable low-volume prep options. One of the first, which came into use in the early 1990s, employed hyperosmolar oral sodium phosphate solution (Fleet Phospho-Soda). It was in widespread use until 2008 when the FDA issued a warning and required new safety measures for oral sodium phosphate products, relating to reports of acute kidney injury. Oral sodium phosphate solution is no longer available, though one sodium phosphate pill preparation is still an option. This pill form of sodium phosphate, which comes with a "Boxed Warning" will be mentioned later.

Table 1 lists the most commonly used bowel prep options. Most should be considered "lower volume" options rather than "low volume" options. The table lists the volume of fluid that must be ingested, as well as a typical retail cost of the various preparations. It is difficult to compare the efficacy of the various preps. There have been dozens of trials of varying quality, many of which have not included a 4-L split-dose PEG-ES control. Some compare a non-split prep to a split prep. Others are designed as noninferiority trials and compare two "lower volume" products.

Table 1: Colonoscopy prep options, including costs and the volume of fluid which must be ingested

Colon Prep	Ingredients	Cost**	Evening Volume	Morning Volume	Total Volume
Generic PEG-electrolyte	PEG-ES	\$20.33	2 L solution	2 L solution	
solution (PEG-ES)			67.6 oz	67.6 oz	135 oz
HalfLytely & bisacodyl	PEG, NaCl,	\$91.67	Bisacodyl with sip of water	None	
(Braintree Laboratories)	Na bicarbonate, KCl		2 L solution		1
			67.6 oz		67.6 oz
Suprep	Na sulfate, K sulfate,	\$104.87	16 oz (6oz Suprep + 10 oz water)	16 oz (6oz Suprep + 10 oz water)	
(Braintree Laboratories)	Mg sulfate		32 oz water	32 oz water	1
			48 oz	48 oz	96 oz
MoviPrep	PEG, Na sulfate, NaCl,	\$91.72	33.8 oz (MoviPrep powder + 1 L water)	33.8 oz (MoviPrep powder + 1 L water)	
(Salix Pharmaceuticals)	KCI, sodium ascorbate,		16 oz water	16 oz water	1
	ascorbic acid		49.8 oz	49.8 oz	99.6 oz
Prepopik	Na picosulfate, Mg oxide,	\$103.40	5 oz Prepopik solution	5 oz Prepopik solution	
(Ferring Pharmaceuticals)	citric acid		40 oz water	24 oz water	1
			45 oz	29 oz	74 oz
Magnesium citrate	Mg citrate solution	\$6.32	15 oz Mg citrate solution (1.5 bottle)	15 oz Mg citrate solution (1.5 bottle)	
Solution (OTC)			24 oz water	24 oz water	1
			39 oz	39 oz	78 oz
PEG 3350 powder (without	PEG	\$15.30	119 g PEG 3350 powder	119 g PEG 3350 powder	Ì
electrolytes) with Gatorade			32 oz Gatorade	32 oz Gatorade	64 oz
OsmoPrep*	Na phosphate tablets	\$141.31	20 tabs	12 tabs	Ī
(Salix Pharmaceuticals)			40 oz water	24 oz water	
			40 oz water	24 oz water	64 oz

<sup>\* =</sup> contains a "Boxed Warning"

While the 4-L split-dose PEG-ES prep remains the "gold standard" among standard preps, <sup>2,11</sup> preps using PEG-ascorbic acid (MoviPrep, Salix Pharmaceuticals) and sodium sulfate (eg, Suprep, Braintree Laboratories) represent lower volume alternatives, though they are considerably more expensive than preps using generic PEG-ES. We do not recommend the 2-L HalfLytely with 5-mg of bisacodyl prep because it is designed to be taken the evening before colonoscopy. Also, most of the trials evaluating HalfLytely employed higher doses of bisacodyl. Because of concerns raised in case reports of 10-20 mg of bisacodyl causing ischemic colitis, the dosage has been reduced to 5-mg. Sodium picosulfate, a stimulant laxative, combined with magnesium citrate, an osmotic laxative (Prepopik, Ferring Pharmaceuticals), is another recently introduced lower volume option. It should be avoided in patients with renal insufficiency and heart failure. <sup>13</sup> Preparation with magnesium citrate, an osmotic laxative, is another option. There is no standardized method for administration and only limited published data to determine its efficacy and safety profile. However, a dosing option is shown in Table 1. <sup>13</sup>

Preps have also been devised involving PEG 3350 powder without electrolytes (MiraLAX, Merck), combined with 64 oz of a sports drink, with or without bisacodyl. PEG 3350/Gatorade preps have been popular among patients because of the reduced amount of fluid patients drink (64 oz split into two doses). PEG 3350 powder is FDA approved for constipation at 17 g per day. It is not approved for use as a bowel preparation. PEG 3350 is available as a 14-day dose pack, so patients typically mix 7 doses of PEG 3350 powder (119 g) into each 32 oz of sports drink. Studies comparing the efficacy of split-dose PEG 3350/Gatorade preps with 4-L split-dose PEG-ES preps have shown mixed results, 14-16 though a recent meta-analysis showed that the former was

<sup>\*\* =</sup> cost to patient if paid out of pocket (mean price from 3 different pharmacies)

inferior in terms of bowel prep quality, while demonstrating no difference in terms of adverse effects. <sup>17</sup> Adding bisacodyl to PEG 3350/Gatorade preps may cause more side effects and may not be more efficacious. <sup>18</sup> PEG 3350/Gatorade preps should not be used in patients with predictors of inadequate bowel preparation or significant co-morbidities. In our practice, we only consider their use when patients are unable to tolerate or are unwilling to take a 4-L split-dose PEG-ES prep. Regardless of which preps a practice chooses to employ as its standard prep(s), it should monitor prep quality to make sure that the vast majority of patients have high quality colon cleansing.

Tied with PEG 3350/Gatorade as the lowest fluid volume option in Table 1 (64 oz split into two doses), is preparation using sodium phosphate tablets (OsmoPrep, Salix Pharmaceuticals). This prep contains a "Boxed Warning" and should not be considered a first-line prep due to the risk of renal injury. Its use should be reserved for healthy individuals without risk factors for acute kidney injury (eg, renal insufficiency, kidney disease, being elderly or patients on medications that affect renal perfusion/function), who have not tolerated a split-dose PEG prep or who refuse other fluid-based preps. Patients need to be given explicit instructions of the need to maintain good hydration before and during the prep, and after the procedure. If the patient has to assume the cost, it should be noted that sodium phosphate pills are also very expensive.

It is important to re-emphasize that regardless of which prep a practice uses as its standard prep that ongoing monitoring of the prep quality and safety is necessary to optimize patient care.

#### Other Considerations

## **Patient Instructions**

All patients should be given simple and easy to follow written instructions in a language they understand. They should be instructed to read them within a week before the exam. This will allow time for patients to obtain their preparation products, to stop any use of iron, and to be prepared for any advised dietary modifications. One may also consider having a nurse phone the patient to reiterate the instructions and to discuss problems that arise. Other educational material may prove valuable including the use of instructional videos and cartoon visual aids. Special measures may be needed for patients with low patient activation.<sup>9</sup>

#### Diet

The most common practice is for patients to be on a clear liquid diet the day before their colonoscopy. However, there are data to indicate that patients who undergo split-dose preps have greater satisfaction without impairing their prep quality if they consume a low-residue diet for breakfast and lunch, followed by a clear liquid diet on the day before their procedure, followed by clear liquids later. <sup>19</sup> Some recommend a low-residue diet for two to five days before colonoscopy, which we do not advocate since it is often difficult or disruptive for many patients. In our practice, we briefly tried using a low-residue diet, but stopped doing so due to frequent patient confusion and instead have resumed use of the more conventional liquid diet. We suggest that when using a low-residue diet that particular care be given to patient instruction.

#### Afternoon Colonoscopy

For patients undergoing afternoon colonoscopy, early morning same-day preparation appears to be an effective alternative to split-dose preps. <sup>20-21</sup> Same-day dosing allows patients to participate in their normal activities on the day prior to their colonoscopy.

## Risk of Aspiration with Split-Dose and Same-Day Preparations

American Society of Anesthesiologists guidelines recommend that endoscopic procedures be preceded by a fasting period of two hours for clear liquids and six hours for light meals.<sup>22</sup> Endoscopists can also be reassured in this regard by two studies which showed no increase in residual gastric volumes with split-dose preparations.<sup>23-24</sup>

# Patients with Prior Poor Preparation or Patients at High Risk for a Poor Preparation

In patients who have previously had an inadequate prep, an attempt should be made to look for reasons to account for the poor prep such as failure to follow prep instructions, taking the entire preparation on the evening before the exam, inability to tolerate the prep because of side effects, or the presence of predictors of inadequate bowel preparation. For patients who failed to respond to the original prep or who experienced side effects, an alternative or modified prep should be selected. Options include two days of clear liquid diets, giving 10-oz of magnesium citrate on day one, and then using a 4-L split-dose PEG-ES prep starting on the day preceding the exam. Other options include giving two full PEG-ES preps, or if the patient did not tolerate PEG-ES, to use an alternative preparation. Sodium phosphate tablet preparation (OsmoPrep) is an option in healthy patients who do not tolerate or refuse PEG-ES and other high-fluid volume preps. Other issues regarding sodium phosphate tablet preps are discussed above.

## **Final Comments**

Much more attention has been given in recent years to achieving high quality colon cleansing to improve the effectiveness of colonoscopy as a cancer prevention tool. Split-dose preparations have been an important advancement in this regard. Though the 4-L split-dose PEG-ES prep is still the gold standard by which other preps are measured, endoscopists and patients now have a wider choice of preparation options. Prep modifications are necessary in patients with prior poor preparations and in those who have predictors of poor preparation. Practices should monitor their colonoscopy prep quality and provide educational programs to help ensure quality colonoscopy.

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