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Preparing for Colonoscopy

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1. Introduction

Colorectal cancer screening for average risk individuals beginning at the age of fifty has been recommended by the American Cancer Society, the American College of Gastroenterology, the American Society for Gastrointestinal Endoscopy, the American Gastroenterological Association and the American College of Radiology (Levin et al., 2008). Colorectal cancer screening has been shown to reduce the incidence and mortality of cancer of the colon and rectum due to early detection and removal of precancerous lesions and adenomas. Colonoscopy is generally considered to be the preferred method of screening despite the emergence of computed tomographic (CT) colonography and the use of other recommended screening modalities (Rex et al., 2009). Other indications for colonoscopy (ASGE, 2000) include evaluation and treatment of gastrointestinal bleeding, unexplained iron deficiency anemia, clinically significant chronic diarrhea of unexplained origin, foreign body removal, decompression of acute nontoxic megacolon or sigmoid volvulus, balloon dilation of stenotic lesions and in palliative procedures for colonic obstructive or bleeding neoplasms.

Colonoscopy requires thorough cleansing of the large intestine for full visualization as well as the safe and effective completion of the procedure. This chapter describes the rationale for bowel preparation, the types of preparations currently available, complications associated with bowel preparations and special considerations for bowel preparation in specific segments of the population. The consequences of inadequate bowel preparation, use of antibiotic prophylaxis for the procedure and management of anticoagulants and antiplatelet agents before and after colonoscopy will also be reviewed. Literature was accessed using MEDLINE (through March, 2011) for all relevant articles published in the English language.

2. Preparing for colonoscopy

2.1 Why prepare?

Inadequate bowel preparation is responsible for up to one third of all incomplete colonoscopy procedures (Belsey et al., 2007). Poor preparation precludes up to 10% of examinations (Kazarian et al., 2008), negatively impacts the rate of overall polyp (Froehlich et al., 2005; Harewood et al., 2003) and adenomatous polyp detection (Thomas-Gibson et al., 2006). In addition, poor bowel preparation raises costs due to aborted examinations

followed by repeated procedures. In a study of 200 consecutive outpatient colonoscopies, imperfect bowel preparation resulted in a 12% increase in costs at a university hospital and 22% increase in costs at a public hospital (Rex et al., 2002).

2.2 Types of bowel preparations

The ideal colon preparation should rapidly and reliably cleanse the colon of fecal material while having no effect on the gross or microscopic appearance of the colon (Wexner et al., 2006). It should require a short period for ingestion and evacuation, cause no discomfort, and produce no significant fluid or electrolyte shifts while also being palatable, simple, and inexpensive.

Agents used for bowel preparation can be divided into three main categories according to their mechanism of action, these being isosmotic, hyperosmotic, and adjunctive preparations. Polyethylene glycol-electrolyte lavage solutions (PEG-ELSs) and sodium phosphate (NaP) formulations are among the most commonly used.

2.2.1 Isosmotic bowel preparations

Isosmotic preparations that contain polyethylene glycol (PEG) are osmotically balanced, high-volume, nonfermentable electrolyte solutions (**Table 1**). These preparations cleanse the bowel with minimal water and electrolyte absorption or secretion in the bowel lumen and provide evacuation, primarily by the mechanical effects of a large-volume lavage. Standard dosing of the 4 liter PEG-ELS is 240 ml(8 oz.) every 10 minutes or a rate of 20 to 30 mL/min if administered by nasogastric tube. This intake rate is generally continued until the rectal output is clear or the entire volume of the preparation is ingested (Wexner et al., 2006). Because of the salty taste of PEG-ELS, sulfate-free PEG preparations were developed; patients by a 3:1 ratio preferred the sulfate free 4 liter PEG-ELS compared to the original formulation (76% versus 24%, $p \leq 0.0001$) with no difference in the efficacy of colonic cleansing (Di Palma and Marshall, 1990). To improve taste, flavored preparations have also been introduced. Unfortunately, flavorings may increase the osmotic load, and some contain carbohydrates that, with bacterial fermentation, could lead to production of combustible gases (Wexner, 1996).

A further development for the advancement PEG-ELSs came with reduced volume preparations. Good or excellent cleansing was reported in 87% of the patients receiving 2-liter PEG-ELSs combined with bisacodyl (irritant laxative tablets) ($n=93$) compared to 92% of patients receiving a 4-liter sulfate free PEG-ELSs ($p=0.16$). The lower volume preparation was associated with decreased abdominal fullness ($p < 0.01$), nausea ($p < 0.01$), vomiting ($p = 0.01$), and overall discomfort ($p < 0.01$) (Di Palma et al., 2003). For this regimen, dosing on the evening prior to the procedure consists of two 5 mg bisacodyl delayed release tablets followed after the first bowel movement by 240 mL of PEG-ELS preparation every 10 minutes until the excreted effluent is clear or until a total of 2 L is ingested. Only clear liquids are permitted on the day of the preparation. Another low volume PEG-ELS consists of the addition of ascorbic acid in the 2-L PEG solution, that is also dosed 240 mL every 10 minutes split into two one 1 liter doses, each accompanied by 16 oz. of clear fluid for hydration.. This regimen permits a normal breakfast and lunch followed by a light dinner (clear soup or yogurt or both) on the day prior to the procedure, followed by bowel prep starting 1 hour after the evening meal. The second liter dose can be consumed 1.5 hours after the initial 1 liter or on the morning of the colonoscopy (Wexner et al., 2006).The 2 liter PEG

with ascorbic acid was compared to 4-liter PEG-ELS in a trial where successful gut cleansing was achieved in 136 of 153 (88.9%) cases of the 2 liter PEG with ascorbic acid group and 147 of 155 (94.8%) cases of the 4 L PEG-ELS group. The 2 liter regimen was also associated with lower frequency of nausea (14% versus 23%; 95% confidence interval [CI], -17 to -1) and abdominal pain (3% versus 8%; 95% CI, -10 to -0.2). Patient ratings of acceptability and taste were better for the 2-liter PEG with ascorbic acid group than for the PEG-ELS group ($P < 0.025$) with a higher completion rate of entire preparation ($p=0.035$) (Ell et al, 2008). Collectively, these studies suggest that the 2 liter preparations of PEG-ELS are as effective as and better tolerated than the 4 liter PEG-ELS preparations.

Efficacy of the standard 4-L PEG-ELS preparation can be improved by administration of split doses, even with minimal dietary restriction before the first dose (El Sayed et al., 2003). Ingestion of the entire preparation on the day of the procedure about 5 hours before the colonoscopy has also been shown to improve the clean-out quality when compared with patients who received PEG-ELS the previous day (approximately 19 hours before the procedure) (Church, 1998).

2.2.2 Hyperosmotic bowel preparations

Hyperosmotic bowel preparations have a mechanism of action of drawing water and electrolytes into the bowel lumen, stimulating fluid loss, peristalsis and evacuation. These small-volume preparations cause fluid shifts, accompanied by electrolyte alterations (Ehrenpreis et al., 1998; Lichtenstein, 2009). Of these, the most commonly used include oral NaP available in as tablets and an aqueous solution (now withdrawn from the US market). The aqueous NaP preparation contains monobasic and dibasic NaP. The solution form of NaP contains 90 ml of solution with each 45-mL dose containing contains 29.7 g NaP. Two doses of 45 mL aqueous solution are given at least 10 to 12 hours apart, with the second dose given within 5 hours of the procedure. Each of these solutions should be diluted in 8 oz of clear liquid with a minimum of 16 oz of clear liquids to be consumed after each dose (Wexner et al., 2006). The first study (Vanner et al., 1990) compared the 4 L PEG-ELS with the 90 ml NaP solution included 102 patients randomized to receive either oral NaP solution ($n=54$) or standard PEG-ELSs ($n=48$) prior to colonoscopy. Overall, good to excellent bowel cleansing was reported in a significantly higher number of patients who received sodium phosphate (80%) compared to the patients who received PEG-ELS (33%), ($p < 0.001$). Completion of bowel preparation was also significantly higher in the NaP group (85%) compared to the PEG-ELS group (31%), ($p < 0.001$). A recent meta-analysis reviewed randomized controlled clinical trials from 1990 to 2005 and compared the tolerability, efficacy, and safety of various preparations. 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. Using a random effects model, the odds ratio of completion of preparation was 0.16 (95% CI: 0.09–0.29; $P < 0.00001$) in favor of NaP (Tan and Tjandra, 2006).

Two NaP tablet preparations are FDA approved for cleansing prior to colonoscopy. The original formulation (Visicol™) contained microcrystalline cellulose (MCC), an excipient and was thought to reduce mucosal visibility during colonoscopy, with a new MCC-free preparation now available (Osmoprep™). 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. 20 tablets are taken the night before the colonoscopy, 4

tablets every 15 minutes followed by 8 oz clear liquids and the remaining 12-20 tablets on the morning of the colonoscopy within 3-5 hours of the procedure. 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 also found to be superior relative to a single dose (Frommer, 1997). All NaP regimens should be taken with a minimum of 2 L of clear liquids. In the event that the bowel preparation is inadequate after the full dose of the NaP formulation, the reparation should be completed using a non-NaP formulation such as PEG-ELS (Wexner et al., 2006)

Clinical studies have shown the original MCC containing NaP tablet formulation to be as efficacious and better tolerated than 4 liter PEG-ELS formulation and be equally as effective as an aqueous NaP solution. (Aronchick et al., 2000). The 32 tablet MCC free NaP tablet formulation has been shown to be at least as efficacious and better tolerated than the MCC containing formulation (Wruble et al., 2007) and also with better colon cleansing and tolerability compared to the 2 liter PEG-ELS formulation (Johanson JF et al., 2007). A prospective trial (Rex et al., 2006(B)) reported that patients receiving the 32 tablet NaP formulation (n=239) compared with the 40 tablet formulation (n=236) had significantly smaller increase in serum phosphate levels from baseline (3.5 mg/dl versus 4.4 mg/dl, $p \leq 0.0002$). This improvement must be tempered by the common occurrence of electrolyte and fluid imbalances as well as serious side effects from NaP containing preparations (see below).

Recently a new sulfate based osmotic laxative (SUPREP) was approved by the FDA in August, 2010 for bowel preparation before colonoscopy containing sodium sulfate 17.5 g, potassium sulfate 3.13 g, magnesium sulfate 1.6 g in each 6 oz bottle. Sodium absorption in the small intestine with sodium sulfate preparations is largely reduced because of the absence of chloride, the accompanying anion necessary for active absorption against electrochemical gradient. Unlike oral sodium phosphate, sulfate salts do not produce renal tubular injury in animal models (Pelham, et al, 2009).

A split dose (2-Day) regimen is advocated. The efficacy of the oral sulfate solution (OSS) was compared with 4 liter sulfate free PEG-ELS in a multicenter, single-blind, randomized, non-inferiority study involving one hundred thirty-six outpatients undergoing colonoscopy. Successful or excellent bowel preparation was more frequent with OSS than with sulfate free PEG-ELS (98.4% versus 89.6%; $P = .04$ and 71.4% versus 34.3%; $P < .001$ respectively). Gastrointestinal side effects and adverse events were not significantly different between the 2 groups (Rex et al., 2010).

Other hyperosmolar bowel preparations include sodium picosulfate, a salt that has similar action as NaP, producing a cathartic effect by osmotic effect in the bowel. This preparation is commonly used alone and in combination with magnesium citrate outside of the United States, especially in the United Kingdom for bowel preparation for colonoscopy. A pooled analysis of 381 patients receiving sodium picosulfate and 369 patients receiving sodium phosphate demonstrated a significantly higher efficacy in bowel cleansing (described as good or excellent cleansing), with the NaP formulation (90%) compared with sodium picosulfate (82%) ($p = 0.004$). A similar adverse event profile was seen with the two preparations (Tan and Tjandra, 2006). The pooled analysis also demonstrated a similar efficacy of sodium picosulfate when compared to 4 liter PEG-ELSS with an additional reduction in the number of adverse events (48% versus 71% respectively, $p = 0.003$).

Product (manufacturer)	Active agent	FDA approved (adults)	Quantity
Isosmotic			
Full volume			
Colyte (Scwarz Pharm, Mequon, Wis)	PEG-3350	Yes	
Flavored			4000 ml
Nonflavored			4000 ml
GoLYTELY (Braintree, Braintree, Mass)	PEG-3350	Yes	
Flavored			4000 ml
Unflavored			4000 ml
NuLYTELY (Braintree)	PEG-3350(sulfate free)	Yes	
Flavored			4000 ml
Nonflavored			4000 ml
TriLyte (Scwarz Pharm)	PEG-3350(sulfate free)	Yes	
Flavored			4000 ml
Low volume			
Halflytely (Braintree)	PEG-3350 and bisacodyl	Yes	2000 ml
MoviPrep (Salix , Morrisville, NC)	PEG-3350 and ascorbic acid	Yes	2000 ml
Hyperosmotic			
Fleet Phospho-Soda EZ-Prep(oral)	NaP 29.7 grams/45 ml	‡	75 ml§
Visicol (tablet, NaP; Salix)	NaP (oral) 1.5 grams/tablet	Yes	40 tablets
Osmoprep (MCC-free tablet, NaP; Salix)	NaP (oral) 1.5 grams/tablet	Yes	32 tablets
Fleet enema (C.B. Fleet)	Monobasic NaP Monohydrate-19 g Dibasic NaP Heptahydrate-7 g	Yes	118 ml
SUPREP kit(Braintree, Braintree, Mass)	In 6 oz-Na sulfate-17.5g, K sulfate-3.13 g, Mg sulfate 1.6 g	Yes	360 ml

LoSoPrep kit (E-Z-EM Inc, Lake Success, NY)	Mg citrate -18 g plus 20 mg bisacodyl oral and 10 mg suppository	Yes	38.5 ml
Magnesium citrate	Mg citrate-17.45 g	Yes	300 ml
Adjunctive medications			
Senna (AmerisourceBergen, Chesterbrook,PA)	Sennosides 8.6 mg	Yes	Tablets
Bisacodyl (Amkas)	Bisacodyl 5 mg	Yes	Tablets

‡ 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.

Table 1. Agents used for bowel preparation

Magnesium citrate is another hyperosmotic agent that also promotes release of cholecystokinin, resulting in fluid and electrolyte secretion as well as stimulation of peristalsis. It is typically not effective as a sole agent for colonic cleansing; hence it is used mainly in combination with other agents. Magnesium is renally excreted and should be used in extreme caution in patients with renal insufficiency or renal failure.. Sodium picosulfate in combination with magnesium citrate has been compared to 2 liter PEG-ELS with ascorbic acid with similar efficacy (73 % versus 84% respectively, $p=0.367$) and adverse event profile. Improved preparation was seen in the ascending colon ($p=0.024$) and cecum ($p=0.003$) (Worthington et al., 2008). Magnesium citrate in combination with 2 liter PEG-ELS solution has also been shown to improve preparation quality and improve patient satisfaction compared to 4 liter PEG-ELs (Sharma et al., 1998). Combination preparations containing magnesium citrate also include 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 (Delegge and Kaplan, 2005).A pulsed rectal irrigation with magnesium citrate as also been suggested to enhance preparation for colonoscopy; however, this requires skilled nursing for administration and is associated with a high cost (Chang et al, 1991).

2.3 Additional medications/methods used in bowel cleansing

2.3.1 Bisacodyl

Bisacodyl is a poorly absorbed diphenylmethane which acts locally on the colon as a peristaltic stimulant. Its active metabolites stimulate colonic motility with an onset of action between 6 and 10 hours. It is often used as an adjunct with PEG-ELS although this combination has not demonstrated a significant difference in the quality of the preparation or amount of residual colonic fluid during colonoscopy (Ziegenhagen et al., 1992).Use of bisacodyl as an adjunct to PEG-ELS may allow patients to consume a smaller volume of PEG necessary for colonic cleansing (Sharma et al., 1998).

2.3.2 Senna

Senna is an anthraquinone derivative that is activated by colonic bacteria. These activated derivates have a direct effect on intestinal mucosa increasing the rate of colonic motility,

enhancing colonic transit and inhibiting water and electrolyte secretion. Like bisacodyl, senna can also be used as an adjunct to PEG-ELS. It has also been shown to reduce the amount of PEG-ELS required for effective bowel preparation (Iida et al., 1992).

2.3.3 Flavoring

Several methods to improve the palatability of both PEG-ELS and NaP solutions have been attempted. PEG-ELs are now available in multiple flavors including cherry, citrus-berry, lemon-lime, orange and pineapple. Carbohydrate-electrolyte solutions such as Gatorade® and Crystal Light® have also been recommended to improve the taste in PEG and NaP solutions (Wexner et al., 2006). Other methods to improve taste that are often used in clinical practice include slowing the rate of consumption, chilling the solution and consuming lemon slices with preparations.

2.4 Assessment of bowel preparation quality

The American Society for Gastrointestinal Endoscopy (ASGE) and American College of Gastroenterology (ACG) Taskforce on Quality in Endoscopy have suggested that every colonoscopy report should include an assessment of the quality of bowel preparation. They proposed the use of terms such as “excellent,” “good,” “fair,” and “poor,” but admitted that these terms lack standardized definitions (Rex et al., 2006(A)).

One validated measurement of preparation quality is the Boston Bowel Preparation Scale (BBPS), which was developed to limit inter-observer variability in the rating of bowel preparation quality, while preserving the ability to distinguish various degrees of bowel cleanliness (Lai et al., 2009). The subjective terms previously described were replaced by a 3 point scoring system applied to each of the 3 regions of the colon: the right colon (including the cecum and ascending colon), the transverse colon (including the hepatic and splenic flexures), and the left colon (including the descending colon, sigmoid colon, and rectum). The points are defined as follows: 0 = unprepared colon segment with mucosa not seen because of solid stool that cannot be cleared; 1 = portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen because of staining, residual stool, and/or opaque liquid; 2 = minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well; 3 = entire mucosa of colon segment seen well with no residual staining, small fragments of stool or opaque liquid. Each of the 3 segment scores is then summed for a total score of 0 to 9, in which 0 is unprepared and 9 is entirely clean. If an endoscopist aborts a procedure due to an inadequate preparation, then any nonvisualized proximal segments are assigned a score of 0. An instructional video demonstrating the BBPS is available and can be accessed online at <http://bmc.org/gastroenterology/research.htm> (Lai et al., 2009). In a comprehensive validation study, the BBPS was found to be a reliable instrument for assessing bowel cleanliness during colonoscopy (Calderwood & Jacobson, 2010).

2.5 Complications of bowel preparation

2.5.1 Inadequate bowel preparation

An inadequate preparation for colonoscopy can result in many complications including missed lesions, cancelled procedures, increased procedure time, and an increased potential in complication rates. Currently, there are no specific guidelines for the management of

patients in whom an adequate examination of the colon cannot be achieved due to an inadequate preparation. The ASGE has recommended the following “reasonable” approach: the same preparation can be repeated if the patient did not consume the preparation as prescribed, except not within 24 hours when using NaP because risk of toxicity. In patients who properly consumed the preparation, options include repeating the preparation with a longer interval of consuming clear liquids only before the preparation, switching to an alternative but equally effective preparation, adding another cathartic such as magnesium citrate, bisacodyl or senna to the previous regimen, or double administration of the preparation during a two-day period (with the exception of NaP). Combining preparations (example, PEG ELS and NaP solutions) may also be successful.

2.5.2 Toxicities of bowel preparation

With the exception of NaP containing preparations, most bowel preparations have been demonstrated to be safe to use in healthy individuals without significant comorbid conditions. Caution must always be taken in selecting a bowel preparation for patients with renal, hepatic or cardiac disease and those patients at the extremes of age. New data also suggests female gender and smaller body size are risk factors for complications of NaP preparations (Parakkal & Ehrenpreis, 2010).

2.5.2.1 Oral sodium phosphate

As of December 11, 2008 the FDA issued an alert about the safe use of oral NaP products and added a black box warning for acute phosphate nephropathy (Food and Drug Administration, 2008). The FDA alert also highlighted several patients at risk of developing this complication including individuals over the age of 55; patients who are hypovolemic or have decreased intravascular volume; people who have baseline kidney disease, bowel obstruction or active colitis; and those that are using medications that affect renal perfusion (such as diuretics, angiotensin converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], and possibly nonsteroidal anti-inflammatory drugs [NSAIDs]). Females of smaller body size are an additional risk group (Ehrenpreis, 2009).

Oral NaP preparations can cause fluid and electrolyte shifts secondary to the hyperosmotic nature of the products. It is often associated with the following abnormalities: hypernatremia, hypokalemia, hypocalcemia, decreased serum bicarbonate, and hyperphosphatemia (Ehrenpreis et al., 1997). Although electrolyte shifts are typically transient, clinically significant toxicities have been reported (Vanner et al., 1990). NaP preparations can also cause colonic mucosal abnormalities such as aphthoid erosions similar to those seen in inflammatory bowel disease and histologic findings including focal active inflammation, mucosal disruption and erosion, edema of the lamia propria, mucosal hyperemia, focal hemorrhage, lymphoid nodules and ulceration (Rejchrt et al., 2004). Physicians are advised to avoid using NaP preparations when evaluating patients with inflammatory bowel disease or patients with diarrhea of unknown etiology.

2.5.2.2 PEG

The most common adverse effects with PEG ELS are abdominal fullness, nausea and bloating. Rare events include Mallory-Weiss tears, esophageal perforation, toxic colitis, pill malabsorption, pulmonary aspiration, hypothermia, cardiac arrhythmias, PEG-induced pancreatitis and inappropriate antidiuretic hormone secretion (Clark & DiPalma, 2004). The

use of PEG-based solutions is contraindicated in patients with gastric outlet obstructions, small and large intestinal obstruction, and suspected bowel perforation.

2.5.2.3 Magnesium Preparations

Magnesium citrate should be used with caution in patients with renal insufficiency or renal failure because it is eliminated by the kidney. Fatal reports and episodes of hypermagnesemia have been reported in patients with suspected or known renal failure or elderly patients (Schelling, 2000).

3. Other considerations

3.1 Antibiotic prophylaxis

Transient bacteremia can occur during colonoscopy due to bacterial translocation of normal colonic flora into the bloodstream. Translocated bacteria may potentially adhere in remote tissues such as the endocardium. Antibiotic prophylaxis was commonly used in some high risk patients before colonoscopy, primarily to prevent infective endocarditis. However, the American Heart Association (AHA) and the American Society of Gastrointestinal Endoscopy (ASGE), in 2007 and 2008 respectively, have revised their recommendations regarding antibiotic prophylaxis before procedures including colonoscopy (Banerjee et al, 2008; Wilson et al, 2007). Both societies classify cardiac patients as low, moderate, or high risk for endocarditis. New guidelines suggest that, antibiotic prophylaxis before including colonoscopy with or without biopsies or polypectomy is no longer recommended in any risk group including those considered to be high-risk. This change in practice came about mainly because of a lack of convincing evidence to demonstrate a risk of endocarditis from gastrointestinal procedures. In addition, harmless bacteremia occurs in some daily activities such as tooth brushing. For example, in a study done by Lockhart et al., routine tooth brushing was associated with bacteremia in 23% of subjects (Lockhart et al, 2008). Bhanji et al. reported a 46% bacteremia rate (Bhanji et al, 2002), and Banerjee reported a 68% rate (Banerjee et al, 2008). Bacteremia can occur after colonoscopy, with rates ranging from 0-25%, and an average mean rate of 4.4% (Banerjee et al, 2008; Nelson, 2003). In contrast, a study done by Goldman showed that blood cultures were positive in 1% of patients after sigmoidoscopy (Goldman, 1985). Microorganisms causing transient bacteremia during and after gastrointestinal procedures are generally believed to have little potential to cause infective endocarditis. Normal skin floras are the most common organisms isolated from blood cultures after colonoscopy (although these could be a contamination during blood draw), (Llach et al, 1999; Levy, 2007). Despite more than 16 million colonoscopies and sigmoidoscopies that are done in each year in the United States (Seeff et al, 2004), there have been only 15 cases of infective endocarditis having a temporal relation with these procedures. The potential side effects of prophylactic antibiotics to prevent an extremely small number of cases of infective endocarditis are felt to clearly outweigh their possible benefit (Banerjee et al, 2008; Wilson et al, 2007; Van der Meer, 1992).

In cirrhotic patients with or without ascites in the absence of gastrointestinal bleeding who undergo colonoscopy, the risk of bacteremia is low. Llach et al. prospectively studied 58 patients underwent colonoscopy. Four of these patients had positive blood cultures; none developed symptoms or signs of infections (Llach et al, 1999).

Patients on peritoneal dialysis may be at risk for infectious complications of colonoscopy. In fact, there are several case reports of peritonitis in patients on peritoneal dialysis after

colonoscopy especially following polypectomy (Bac et al, 1994; Ray et al, 1990). The 2005 International Society for Peritoneal Dialysis (ISPD) recommendations state that these patients have antibiotic prophylaxis before any procedure involving abdomen and pelvis including colonoscopy, and emptying the peritoneal fluid prior to the procedure (Piraino et al, 2005); however, these prevention strategies were not addressed in 2010 ISPD guidelines (Li et al, 2010).

Antibiotic prophylaxis is not recommended by the ASGE before colonoscopy or any other GI procedures in patients who have prosthetic vascular grafts or cardiovascular devices such as pacemakers (Banerjee et al, 2008). However, the AHA recommends antibiotic prophylaxis for procedures occurring within the first 6 months of prosthetic vascular grafts while graft epithelialization is occurring (Wilson et al, 2007).

Antibiotic prophylaxis is not recommended for patients who have prosthetic orthopedic devices undergoing colonoscopy, due to their low risk of infection (Banerjee et al, 2008). However, scattered cases of infections in prosthetic joints after colonoscopy have been reported (Vanderhooft et al, 1994; Cornelius et al, 2003).

3.2 Management of antiplatelet agents

Antiplatelet agents are used widely to treat patients with cardiovascular and cerebrovascular diseases as well as acute and chronic pain. Aspirin and other nonsteroidal anti-inflammatory drugs (NSAID) are not believed to increase the risk of significant bleeding after colonoscopy whether biopsies and/or polypectomies are performed. Use of aspirin was not a risk factor for polypectomy-associated bleeding in a study of 1657 patients (Hui et al, 2004). Recommendations regarding the management of antithrombotic agents before endoscopic procedures published by the ASGE in 2009 classify the procedures from low-risk to higher-risk (see **Table 2**). In addition, cardiovascular conditions are also classified from low-risk to higher-risk (see **Table 3**), (Anderson et al, 2009). Colonoscopy with or without biopsy is considered a low risk procedure, however if polypectomy is done, the risk is considered higher. The ASGE recommends that aspirin and NSAIDs should not be discontinued prior to colonoscopy if one of them is used alone and if their use is necessary in any of risk groups. There is some evidence that combination of aspirin and other NSAIDs increases the risk of bleeding after polypectomy (Grossman et al, 2010), thus discontinuation of NSAIDs two to three days before polypectomy is recommended in patients on combined therapy.

Dipyridamole, another antiplatelet agent, used either alone or in combination with aspirin may be continued in patients undergoing colonoscopy with no significant risk of bleeding, however its safety is unknown in high risk procedures such as polypectomy (Zuckerman et al, 2005).

Thienopyridines (Ticlopidine, clopidogrel, prasugrel) are newer antiplatelet agents. The AHA recommends their use for a minimum of one month after placement of bare metal stents and one year for drug-eluting stents (King et al, 2008). Use of clopidogrel alone is not associated with an increased risk of post-polypectomy bleeding, however when combined with other antiplatelet agents, bleeding risk is increased (Singh et al, 2010). Due to the high rate of stent thrombosis associated with early cessation of dual antiplatelet (clopidogrel with aspirin), it is recommended that discontinuation should be avoided whenever possible (Iakovou et al, 2005). The ASGE recommends not discontinuing thienopyridines in patients

undergoing low-risk procedures including colonoscopy with or without biopsy (Anderson et al, 2009). In patients undergoing high-risk procedures including polypectomy, endoscopists are advised to consider the patient’s risk for thromboembolic phenomenon. If the patient is considered to have a low-risk condition, thienopyridines can be discontinued 7-10 days before the procedure. Alternatively, procedures should be postponed until the time when thromboembolic risk is low (Anderson et al, 2009). In low-risk patients who discontinue thienopyridines, continuation of aspirin alone if they are on dual antiplatelet therapy or initiation of aspirin before procedure should be considered. This may decrease the risk of thromboembolic events without increasing the chance of developing significant bleeding. Thienopyridines should be restarted as soon as safely possible with consideration for their underlying indication and the procedure that has been performed (Anderson et al, 2009).

Glycoprotein IIb/IIIa receptor inhibitors (Eptifibatide, tirofiban, abciximab) are administered in some patients of acute coronary syndrome, however when elective colonoscopy is considered, patients are typically not taking one of these drugs. When patients require emergent colonoscopy for acute GI bleeding, these antiplatelet agents should be discontinued (Anderson et al, 2009).

In patients who develop GI bleeding while on any anti-platelet agents, the decision to continue, stop, or reverse the antiplatelet effect should be tailored case-by-case, based on the severity of bleeding, the risk of thromboembolic events. A discussion with relevant consultants in this setting is advised. Diagnostic and therapeutic colonoscopy in the setting of acute lower GI bleeding while using antiplatelet agents has been deemed to be safe and is recommended (Anderson et al, 2009).

Low risk procedure	High risk procedures
Diagnostic(EGD, colonoscopy, flexible sigmoidoscopy) including biopsy	Polypectomy
Enteroscopy and diagnostic balloon-assisted enteroscopy	Therapeutic balloon-assisted enteroscopy
ERCP without sphincterotomy	Endoscopic homeostasis
Enteral stent deployment(without dilation)	Tumor ablation by any technique
Capsule endoscopy	Pneumatic or bougie dilation
EUS without FNA	Biliary or pancreatic sphincterotomy
	PEG placement
	EUS with FNA
	Cystogastrostomy
	Treatment of varices

Table 2. Procedure risk for bleeding: adapted from ASGE guidelines (Anderson et al, 2009).

Low risk condition	High risk condition
Uncomplicated or paroxysmal non-valvular atrial fibrillation	Atrial fibrillation associated with valvular heart disease, prosthetic valves, active congestive heart failure, left ventricular ejection fraction <35%, history of a thromboembolic event, hypertension, diabetes mellitus, or age>75 year
Bio prosthetic valve	Mechanical valve in any position and previous thromboembolic event
Mechanical valve in aortic position	Mechanical valve in mitral position
Deep vein thrombosis	Recent (<1 year) placed coronary stent
	Acute coronary syndrome
	Non-stented percutaneous coronary intervention after myocardial infarction

Table 3. Condition risk for thromboembolic event: adapted from ASGE guidelines (Anderson et al, 2009).

3.3 Management of anticoagulants

The approach to the performance of colonoscopy in patients receiving anticoagulation agents (warfarin, heparin, low-molecular weight heparins) is another commonly encountered dilemma for the gastroenterologist. Using warfarin is not believed to increase the risk of significant bleeding in patients undergoing colonoscopy and other low-risk procedures (see table 2). The ASGE recommends continuation of warfarin for these procedures (Anderson et al, 2009). In high-risk procedures including polypectomy, there is an increased risk of bleeding (Hui et al, 2004). If patient is in a low thromboembolic risk group (see table 3), warfarin should be discontinued before a high-risk procedure, until the international normalized ratio (INR) is normal or nearly normal (Anderson et al, 2009). Vitamin K should be avoided since it delays the development of a therapeutic INR once warfarin is resumed. If patient is in a high thromboembolic risk group, bridging therapy (discontinue warfarin and administer heparin or LMWH) should be considered, however deferring the procedure to a time when the thromboembolic risk is low, is a better strategy whenever possible, depending on the degree of emergency of colonoscopy. The appropriate time to reinstitute warfarin and other anticoagulants after colonoscopy and other procedures is not clear. The ASGE recommends resumption of warfarin on the evening after procedure and heparin 2-6 hours after the procedure; however the risk of bleeding versus the risk of thromboembolic events should be weighed carefully and discussion with relevant consultants is suggested (Anderson et al, 2009).

4. Special considerations for colonoscopy preparations

4.1 Elderly

Age does not, by itself, increase the risk to colonoscopy. Colonoscopy can be performed in octogenarians and older patients (Lagares-Garcia et al, 2001; Lukens et al, 2002). A significant problem encountered in the performance of colonoscopy in the elderly is the achievement of adequate bowel preparation. Dementia, cerebrovascular accident, diabetes mellitus, renal failure, chronic obstructive pulmonary disease, chronic constipation, use of

narcotics and tricyclic antidepressants are conditions that are associated with poor bowel preparation (Reilly & Walker, 2004; Ness et al, 2001; Taylor & Schubert, 2001). All of these conditions are more common among elderly, however, even after eliminating all these independent predictors for inadequate bowel preparation, age still remains an independent risk factor for inadequate preparation, (Qureshi et al, 2000; Ure et al, 1995).

Colonoscopy preparations often cause fecal incontinence in elderly patients, regardless of the type of bowel preparation, due to the large volume rectal output in a short time that these preparations induce. Thomson et al. found that approximately 25% of elderly experienced at least one episode of fecal incontinence during bowel preparation for colonoscopy (Thomson et al, 1996).

The elderly are at increased risk of severe electrolyte imbalances from sodium phosphate containing colonoscopy preparations (Beloosesky et al, 2003; Gumurdulu et al, 2004). Elderly are also more likely to have comorbidities including renal failure, congestive heart failure, and cirrhosis that increase risk for electrolyte abnormalities and sudden change in intravascular volume. Additionally, the elderly are more likely to be on medications such as diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs) and angiotensin converting enzyme inhibitors that are other potential causes for electrolyte abnormalities and change in intravascular volume when NaP is used (Anderson et al 2009; Ainley et al, 2005; Desmeules et al, 2003). Of interest, studies have suggested that the efficacy of sodium phosphate is similar to nonelderly adults and comparable with PEG (Thomson et al, 1996; Seinela et al, 2003).

Magnesium citrate causes electrolyte and fluid disturbances, especially in patients with renal dysfunction. Cases of hypermagnesemia have been reported in elderly patients after magnesium citrate preparations even without known kidney disease (Kontani et al, 2005; Schelling, 2000).

Polyethylene glycol (PEG) does not, in general, cause fluid and electrolytes imbalance. However, a study done by Ho et al. showed that hypokalemia can occur after PEG preparation (Ho et al, 2010). Due to its large volume, PEG is contraindicated in patients with impaired swallowing function, (as seen in patients with stroke, dementia and Parkinson's disease) all of which are more common among the elderly. If colonoscopy is necessary in patients with these problems, a nasogastric tube can be inserted to administer the solution. However, it is possible that this approach does not decrease the risk of aspiration (Marschall et al, 1998).

4.2 Female patients

There is no data regarding the differences between men and women related to the success of bowel preparation for colonoscopy. However, there are data regarding differences in completion of colonoscopy, procedure tolerance, difficulty of the procedure rated by colonoscopist, and detection of polyps. Completion of colonoscopy is less likely in females, especially if there is a history of hysterectomy (Church, 1994). Women have longer colons comparing to men, resulting in requirement for more time to perform colonoscopy, more discomfort to the patients, and increased technical difficulties in performance of the procedure. In a study performed by Saunders et al., female colons were 10 cm longer than men's ($P=0.005$). Technically difficult examinations were reported in 31% of women comparing to 16% of men (Saunders et al, 1996). Female gender was also an independent predictor of difficult colonoscopy in a study performed by Anderson (Anderson et al 2001).

In another study, looping of the colonoscope was more frequent ($P = 0.0002$) and the procedure was more painful ($P = 0.0140$) in women than in men (Shah et al, 2002). Detection of polyps and adenomas were lower in post-hysterectomy women compared to women without a hysterectomy ($P = 0.008$). In addition, sigmoidoscopy was more painful ($p < 0.001$), more difficult ($p < 0.001$), and less extensive ($p < 0.0001$) in this group, (Adams et al, 2003). Women, especially of smaller stature are at increased risk of electrolyte abnormalities and renal injury from NaP-containing colonoscopy preparations.

4.3 Pregnancy

While the safety of colonoscopy and sigmoidoscopy has been established in the general population, colonoscopy during pregnancy has only been described in small case series and case reports. The main two concerns in performing colonoscopy during pregnancy are maternal and fetal complications including usual complications of colonoscopy, premature delivery, low birth weight, fetal anomalies, placental abruption, fetal compression, medication toxicity, and stillbirth. In a retrospective study by Cappell et al. there were no maternal complications in 48 flexible sigmoidoscopies and 8 colonoscopies performed in pregnant women done during different trimesters (Cappell et al, 1996). Effects of the procedure on vital signs, including oxygen saturation, were clinically and statistically insignificant. Four fetal demises were reported in the study, but all 4 cases occurred in high-risk pregnancies and at least 2 months after the procedure. The group who underwent colonoscopy or sigmoidoscopy had similar outcomes in term of premature delivery, low birth weight, and cesarean section compared to aged-matched pregnant women who did not undergo endoscopy (Cappell et al, 1996). In another retrospective study from the same authors, there were no major maternal complications in 20 pregnant women undergoing colonoscopy. Mild, transient hypotension occurred in 2 patients (Cappell et al, 2010). The colonic preparations in their study included PEG, sodium phosphate, magnesium citrate, and water/saline enemas. Anesthetics and sedative medications that were administered during colonoscopy included meperidine (category B drug during pregnancy), morphine (category C), fentanyl (category C), midazolam (category D), diazepam (category D), propofol (category B), and thiopental (category C). Six patients underwent the procedure without anesthesia. No fetal distress occurred during colonoscopy in the 6 patients who underwent fetal heart rate monitoring. In this study, also, there were no statistical differences between study group and the national average for pregnancy outcomes or a matched group in term of fetal outcomes including involuntary abortion, premature delivery, low birth weight, low Apgar score, cesarean section rate, congenital defects or stillbirth. Despite the estimate that 1500 colonoscopies are done annually during pregnancy in the United States, there are no prospective studies on colonoscopy in pregnancy (Cappell et al, 2010). Based on the aforementioned retrospective studies, it appears that both colonoscopy and sigmoidoscopy are safe in pregnancy. Even though PEG, NaP and magnesium citrate are category C drugs, they were administered for colonoscopy preparation without maternal or fetal complications (Cappell et al, 2010, although our group would strongly advise against the use of NaP containing preparations in these patients). The diagnostic and therapeutic yield for colonoscopy or sigmoidoscopy is highest for rectal bleeding compared to abdominal pain, constipation, or diarrhea (Cappell et al, 1996; Cappell et al, 2010). The safest timing for colonoscopy or sigmoidoscopy during pregnancy is not known, however, sigmoidoscopies were performed almost equally in all three trimesters in

the first study while colonoscopies took place primarily in the second trimester in the second study by Cappell, (Cappell et al, 1996; Cappell et al, 2010). The ASGE recommends using PEG-ESL for colonoscopy preparation during pregnancy (Anderson et al, 2009). However, there are no controlled studies on the use and safety of PEG during pregnancy. The ASGE also suggests that colonoscopy should only be performed when the potential benefit outweighs the potential risks. ASGE guidelines for endoscopy in pregnant and lactating women published in 2005 recommend the following: procedures must always have a strong indication, defer to second trimester if possible, use category A or B sedative medications with the lowest effective dose, minimize procedure time, place pregnant patients with a left pelvic tilt or left lateral position. However, these recommendations are based on expert opinions rather than solid evidence based data (Qureshi et al, 2005).

4.4 Low body weight

Lower body mass index (BMI) has been associated with more difficult colonoscopy, lower cecal intubation rate, longer insertion time and more painful colonoscopy (Anderson et al, 2001; Chung et al, 2007); however there are no data regarding if bowel preparation affects these findings. There are also no data to indicate that changes need to be made in the duration of the preparation, timing, and the amount of lavage solutions administered in the preparation for colonoscopy in patients with a low BMI. A pharmacokinetic analysis of liquid NaP colonoscopy preparation performed by our group has demonstrated that lower body weight individuals, particularly females, develop more pronounced hyperphosphatemia, acidosis, and decreased ionized calcium than normal weight or obese individuals when using these preparations (Ehrenpreis, 2009).

4.5 Possible inflammatory bowel disease, ischemic colitis, or non-steroidal anti-inflammatory drug-induced colitis

Colonic mucosal changes that mimic grossly inflammatory bowel disease (IBD) changes or non-steroidal anti-inflammatory drug-induced colitis have been described with NaP preparations. Colonoscopic findings include aphthoid lesions, erosions and ulcers (Rejchrt et al, 2004). Histologically, focal nonspecific inflammation, mucosal erosion, edema of the lamina propria, focal hemorrhage, and ulceration are seen (Rejchrt et al, 2004). In early studies, these mucosal changes were seen in more than 24% of patients who used NaP for bowel preparation (Zwas et al, 1996). More recent studies with a larger number of patients suggest that these changes occur in 3.3% of patients using these preparations (Rejchrt et al, 2004). Due to these potential mucosal changes, AGSE discourages the use of NaP as a bowel cleanser in the initial colonoscopy in patients with a suspicion of IBD (Anderson et al, 2009).

4.6 Diabetes mellitus

Bowel preparation seems to be less effective in diabetic patients. In a study done by Taylor and Schubert, there was a significant difference in the quality of the bowel preparations with PEG ELS between diabetic and non-diabetic patients ($p < 0.001$) (Taylor & Schubert, 2001). Only 62% of the diabetic group had a preparation rated as good or better compared to 97% of the non-diabetic group ($p < 0.001$) (Taylor & Schubert, 2001). In this study, 9% of diabetic patients had a preparation rated as poor or futile, necessitating repeat colonoscopy compared to none in patients without diabetes ($p < 0.01$). Among the diabetic group, there was no difference in bowel preparation between patients on insulin and not on insulin,

those with hemoglobin A1c (Hb A1c) values $>8\%$ and those with values $<8\%$, and those with and without diabetic neuropathy (Taylor & Schubert, 2001). In another study done by Oztur et al. using NaP as a bowel cleansing agent, optimal bowel cleansing was achieved in 70% diabetics compared to 94% in the non-diabetic group ($P = 0.002$). Among the diabetic patients, there was a significant correlation between the quality of bowel cleansing and HbA1c level, duration of diabetes mellitus, and presence of late complications of diabetes ($P < 0.05$) (Ozturk et al, 2010). Of note, both of the aforementioned studies were small. In a larger study of 362 patients, diabetes was independent predictor of poor bowel cleansing in patients using PEG as the agent for preparation (Chung et al, 2009).

4.7 Colonoscopy preparation in children

Colonoscopy is relatively uncommon in pediatric population. There are no uniform protocols or national guidelines for colonoscopy preparation. PEG ESL is the most common bowel cleansing agent used in pediatrics. However the large volume and potentially unpleasant taste of these solutions has been a major limitation in their use. Placement of a nasogastric tube has been used in some studies. In one study, PEG ESL was better tolerated than total gut irrigation using normal saline with added potassium. Both regimens demonstrated equivalency for side effects and efficacy (Chattopadhyay et al, 2004). PEG-3350 without electrolytes (Miralax) has been increasingly used for bowel cleansing for colonoscopy in children. PEG 3350 solution was first studied with a 4 day regimen, showing safety, efficacy, and tolerability in children (Safder et al, 2008). A subsequent study showed that even a one day regimen of PEG-3350 is effective in 93% of children (Adamiak et al, 2010).

Bisacodyl with NaP enemas has been tested in different studies with a high rate of compliance and bowel preparation. In a study of 98 children between 30 months to 12 years of age, the compliance of the bisacodyl with NaP enema group was 100%, compared to 88% in PEG group. Good to excellent bowel preparation achieved in 95% in bisacodyl with NaP enema group compared to 88% in PEG ESL group (Shaoul & Haloon L, 2007). However, another study of 70 children did not show the same results. PEG ESL was superior for bowel cleansing ($p < 0.0001$) but was inferior to NaP enema in terms of tolerance and compliance ($p < 0.003$) (Dahshan et al, 1999).

Oral NaP was studied for use as a bowel preparation for pediatric colonoscopy. One study showed that NaP was superior to PEG-based solutions in term of tolerance, compliance and bowel cleansing (Gremse et al, 1996). However, there is potential risk of electrolytes and fluid disturbance in NaP. Our group recommends avoidance of these preparations in children.

Magnesium citrate was used combined with senna (X-prep) in some pediatric patients. This combination was shown to be superior to bisacodyl combined with a NaP enema ($p < 0.0001$), but inferior to PEG ELS ($p < 0.075$) in term of quality of bowel cleansing (Dahshan et al, 1999). Overall tolerance and compliance were significantly better than PEG ELS ($p < 0.003$) (Dahshan et al, 1999). In another study, magnesium citrate was used with bisacodyl and demonstrated to be superior to NaP ($P = .013$) in term of bowel cleansing. Both regimens were equivalent for tolerance and compliance (El-Baba et al, 2006). In a third study of 48 children, magnesium citrate was used with a NaP enema for a 3 days protocol and compared to a one day regimen of oral NaP alone (Sabri et al, 2008). Bowel cleansing was similar in two groups (71% good or excellent) and side effects were similar except nausea

which was more frequent in NaP. However, patients stated that they were more willing to repeat NaP alone compared to the combination regimen (77% vs 32%, respectively, $P < 0.006$) (Sabri et al, 2008).

5. Conclusion

The choice of bowel preparation for colonoscopy should be individualized after thorough patient screening. Next generation lower volume regimens have been developed that are well tolerated and preferred by the patients over traditional larger volume bowel preparations. NaP preparations are generally more effective and better tolerated than PEG-ELs. However there is increasing concern regarding toxicity of NaP formulations, especially in light of the availability of newer, potentially better tolerated preparations.

6. Future research

There is ongoing research to develop safe bowel preparation regimens that provide good bowel cleansing along with better patient tolerability and low side effect profile. Further research is also needed for effect of bowel preparations in the elderly, pregnant women and children as well as in patients with significant morbidities. Gender based risk of adverse effects is a newly studied phenomenon that requires additional study.

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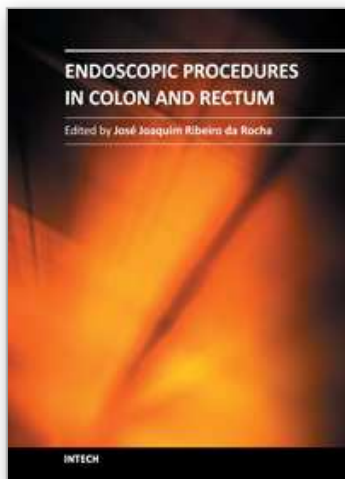
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