Bowel Preparation: Current Status

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ABSTRACT

Despite emerging evidence from randomized controlled trials and meta-analyses questioning its use, mechanical bowel preparation (MBP) continues to hold an accepted place among surgeons. MBP has been administered to patients for over a century, and though the methods and agents used for intestinal cleansing have evolved over time, many surgeons still embrace MBP as a necessary, essential regimen. The accepted rationale for MBP includes evacuation of stool to allow visualization of the luminal surfaces as well as to reduce the fecal flora, which is believed to translate into lower risk of infectious and anastomotic complications at surgery. The authors describe the history of MBP as it relates to colorectal surgery and review the agents currently used for mechanical bowel preparation. Additionally, they summarize the recent trials, meta-analyses, and other emerging data from the medical literature that suggest MBP offers no benefit as a preoperative measure and question its place in current surgical practice.

KEYWORDS: Mechanical bowel preparation, colorectal surgery, polyethylene glycol, sodium phosphate

Objectives: On completion of this article, the reader should know the agents commonly used for mechanical bowel preparation (MBP) and understand the findings of recent randomized clinical trials and meta-analyses regarding the utility of MBP in elective colon and rectal surgery.

Mechanical bowel preparation (MBP) prior to colorectal surgery procedures has long been an accepted and ingrained practice among surgeons. Although the methods and agents used for intestinal cleansing have changed and evolved over time, mechanical bowel preparation has been administered to patients for over a century. Surgeons view it as a necessary, essential regimen. In fact, despite emerging evidence to the contrary from several randomized controlled trials and meta-analyses regarding this practice, MBP continues to hold an accepted place among surgeons. A 2003 survey of practicing colorectal surgeons revealed that 99% of respondents continue to employ MBP, though 10% did question its role in elective surgery.¹

The accepted rationale for MBP includes evacuation of stool to allow visualization of the luminal surfaces as well as to reduce the fecal flora, which is believed to translate into lower risk of infectious and anastomotic complications at surgery. Although the removal of stool permitting mucosal inspection at colonoscopy is well established and not controversial, the latter rationale—the reduction of infectious and anastomotic complications by MBP—has not been supported by evidence and has recently been challenged in the medical literature. Here we describe the history of MBP as it relates to colorectal surgery and review the agents currently used for mechanical bowel preparation. Additionally, the article summarizes the recent trials, meta-analyses, and other

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emerging data from the medical literature that suggest MBP offers no benefit as a preoperative measure and question its place in current surgical practice.

HISTORY

The support for MBP originated in the early 20th century, when the high rates of infectious complications associated with abdominal surgery prompted surgeons to employ special diets and/or laxatives to evacuate the gastrointestinal (GI) tract prior to surgery. As the practice became more widespread, advances in antibiotic therapy also developed which, in conjunction with MBP, were shown to further decrease perioperative infection and thereby reinforced the notion of MBP and its benefits.^{2,3} By the 1970s, the practice of MBP was routine and accepted among surgeons. A variety of methods was employed during this time, ranging from dietary restriction with cathartics to enemas to large-volume saline irrigation via a nasogastric tube.^{4,5} Polyethylene glycol (PEG)-based solutions, commonly used today, were introduced soon thereafter as a superior alternative to previous regimens, with improved patient tolerance, less systemic absorption and electrolyte derangement, and less time required for preparation prior to surgery.⁶

An early challenge to the dogma of MBP came from Hughes in 1972, who claimed that the risks of sepsis and anastomotic complications were no greater in unprepared bowel and argued against the practice as unnecessary.⁷ Irving and Scrimgeour supported this claim when they published in 1987 a case series of patients without bowel preparation and no anastomotic complications.⁸ Evidence accumulated in trauma patients, showing low postoperative infectious complications in emergency colon surgery cases with unprepared bowel, also prompting a reevaluation of the indications for MBP.^{9,10}

Based on this new disparate view that questioned the role for MBP, the first randomized controlled trials comparing MBP to no MBP were performed in South America and Europe and published in the 1990s.¹¹⁻¹³ Several other trials followed; however, the conclusions of these trials were limited by variable methodology and inclusion criteria. Perhaps the most well-known critical analysis of this fundamental question regarding MBP versus no MBP was addressed by a Cochrane Library systemic database review, first published in 2003 and updated in 2005.¹⁴

This historical background surrounding MBP helps frame our understanding and interpretation of contemporary studies that attempt to address the role of MBP in elective colorectal surgery. These recent clinical trials and meta-analyses will be reviewed below.

BOWEL PREPARATION AGENTS

To better understand the debate and controversy surrounding the role of MBP in colorectal surgery, it is worthwhile first to review the various regimens employed and the bowel preparation agents that are currently in use today as well as their mechanisms, effectiveness, and potential side effects. Dietary restriction, cathartics, and enemas formed the original framework of colon preparation. However, patient discomfort with enemas and laxatives, potential for inadequate caloric intake with nutrition manipulation, as well as hospitalization in cases of elemental diet administration proved cumbersome as well as costly. Transition to orthograde gut lavage with large volume ingested saline solutions was then undertaken.¹⁵ Due to the large fluid ingestion required for effectiveness, requirement for hospitalization and nasogastric tube placement, intolerable side effects, and large fluid shifts with potential for electrolyte instability, alternate regimens were sought.

Mannitol was found to be an excellent cathartic with minimal effects physiologically when compared with saline lavage. A major detriment, however, was that fermentation by colonic bacteria generated combustible gases, methane and hydrogen. With the introduction of oxygen during insufflation at colonoscopy and an electrical source such as cautery for polypectomy, the concern for combustion was soon realized. Multiple case reports in the world literature described explosions occurring during colonoscopy after mannitol preps. These case reports, as well as the fear of explosion with the addition of electrocautery during surgery, prevented universal acceptance of this method of colonic cleansing.¹⁶⁻²⁰

Polyethylene glycol (PEG) lavage solution was first introduced in 1980.⁶ PEG solutions are isoosmotic electrolyte lavage solutions that are nonabsorbable, causing little to no fluid shifts or electrolyte disturbances. ColyteTM (Schwarz Pharma, Inc., Milwaukee, WI) and GoLYTELYTM (Braintree Laboratories, Inc. Braintree, MA) are the most familiar commercial examples used in today's practice. After introduction of this solution, multiple studies proved its safety, efficacy, and tolerability when compared with traditional bowel preparative regimens.²¹ Mucosal changes have been observed to occur within the bowel wall following the use of PEG regimens. Notable histologic changes include the loss of superficial mucus and epithelial cells as well as inflammatory changes.²²

PEG solutions are large volume preps requiring the patient to ingest 4 L of solution. The salty taste as well as ardor in taking the large volume makes patient compliance an important issue. The addition of bisacodyl, senna, or magnesium citrate to traditional 4 L PEG regimens has been shown to improve colonic cleansing during colonoscopy.²³⁻²⁵ Addition of these adjuncts has also allowed for lower volume (2 L) PEG

solutions to be administered with equivalent or increased efficacy and improved patient tolerability.^{26–28} Prokinetic agents and enemas when combined with oral lavage have not been shown to improve efficacy or decrease patient symptoms.^{29,30} PEG solutions are contraindicated in patients with any sensitivity to the components of the solution, gastrointestinal obstruction, gastric retention, bowel perforation, toxic colitis, toxic megacolon, or ileus. PEG solutions are considered category C drugs in pregnancy and have not been well studied in this patient population.³¹

In 1990, sodium phosphate (NaP), a saline laxative, was introduced as a safe, more efficacious, and less costly form of bowel preparation when compared with PEG in its initial study.³² NaP solutions (Fleet Phospho-SodaTM, Fleet Laboratories, Lynchburg, VA) are concentrated, low-volume hyperosmotic solutions that exert an osmotic effect to draw fluid into the bowel lumen to assist in transit of contents.³³ These solutions are administered as two 4.5 oz dispensations that are diluted and ingested by the patient at preset times, based on surgeon preference, the day prior to elective colorectal surgery. Electrolyte alterations that may occur include hyperphosphatemia, hypocalcemia, hypernatremia, and hypokalemia, which in most patients are minimal and/or transient in nature.

Similar to PEG solutions, NaP administration has been associated with colonic mucosal changes, including multiple aphthous ulcerations that appear histologically as a focal basal neutrophilic cryptitis with crypt apoptotic bodies.^{34,35} These mucosal changes are noted more frequently in the left colon and rectum and can be confused with the aphthoid ulcerations typically seen in Crohn's disease. In distinction to Crohn's disease, however, the mucosal findings in patients who have ingested NaP are discrete, superficial, petechial lesions with a normal background mucosa that tend to regress on repeat evaluation.³⁶

A tablet form of NaP was developed in 2000 showing equal or improved efficacy and/or improved tolerance when compared with both liquid NaP, PEG, and PEG plus bisacodyl regimens.^{37–39} These tablet preparations (OsmoPrepTM and VisicolTM, both Salix Pharmaceuticals, Morrisville, NC) offer an alternative to the solution-type NaP formulation. The tablet preparation regimen consists of 28 to 40 tablets given the day prior to the elective procedure or in a split dose manner, similar to the fluid formulation.

A patient's medical history may influence the selection of preparation utilized. Patients with impaired renal function, dehydration, hypercalcemia, hyperphosphatemia, congestive heart failure, or advanced liver disease could experience severe complications with NaP administration including phosphate nephropathy.^{40,41} This is especially true in hypertensive patients taking certain medications, namely angiotensin convert-

ing enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB). It is also not recommended for the use in children < 5 years old, patients with small intestinal disorders and/or gut dysmotility disorders. Absolute contraindications include obstruction, ileus, perforation, diverticulitis, severe colitis, toxic megacolon, gastric retention, and gastric paresis. Fatal fluid and electrolyte shifts can occur and it is necessary to maintain adequate hydration while undergoing the preparation.^{22,42}

Since the introduction of NaP preparations, multiple studies have evaluated the two forms of preparation (PEG versus NaP) head-to-head. They have determined an equally if not improved efficacy, tolerability, and lower cost of NaP over PEG.^{22,43–45} The benefit of PEG solutions over NaP preparations includes their ability to avoid fluid shifts or electrolyte disturbances; thus, they are relatively safe in patients with CHF, renal failure, and advanced liver disease or ascites. The cost of PEG solutions can be two to three times as expensive as NaP preparations.

SUMMARY OF TRIALS AND META-ANALYSES

Over the past few years and as recent as mid-2008, numerous clinical trials and meta-analyses have been performed in an attempt to understand the role of MBP in elective colorectal surgery.^{11–14,46–60} Learning from earlier trials, these studies were carefully constructed to render the MBP and no MBP arms equivalent in terms of age, sex, gender, ASA class as well as indications for surgery, the type of preparation given in the MBP arm, and the level and type of anastomosis performed (ileo-colic, colocolic, colorectal). These studies are summarized in Table 1 and are discussed below.

The issue of MBP versus no MBP received a thorough treatment from the Cochrane Library in the form of a familiar Cochrane Database review published in 2005.¹⁴ This comprehensive meta-analysis included nine clinical trials and a total of 1592 patients. Most provocative in the Cochrane review was the overall finding of more frequent anastomotic leaks in the MBP group, a difference that was statistically significant (6.2% leak rate for MBP versus 3.2% for no MBP, $p = 0.003$). Upon stratification and subgroup analysis of this primary outcome measure—anastomotic leakage—by site (low anterior resection and colonic surgery), the analysis still favored no MBP over MBP, but this difference demonstrated no statistical heterogeneity. A similar stratified analysis between colonic and rectal surgery was feasible in four of the nine studies, and though the results were deemed inconclusive, they tended to favor the omission of MBP. The analysis did display a statistically significant difference favoring no MBP for decreasing the rates of peritonitis. For other outcome measures, the review also favored no MBP in

Table 1 Comparison of Randomized Controlled Trials of Mechanical Bowel Preparation versus No Mechanical Bowel Preparation

Study	# of Patients	MBP Agent	Anastomotic Leaks with MBP (%)	Anastomotic leaks without MBP (%)	P Value	Wound Infections with MBP (%)	Wound Infections without MBP (%)	P Value
Brownson et al, 1992 ¹²	179	PEG	11.9	1.5	0.03	5.8	7.5	0.77
Santos et al, 1994 ¹¹	149	Mineral oil, agar and phenolphthalein; enema; mannitol (3 day regimen)	10.4	5.3	0.34	23.6	11.7	0.08
Burke et al, 1994 ¹³	169	Sodium picosulfate	3.7	4.6	1	4.9	3.4	0.71
Fillman et al, 1995 ⁴⁸	60	Mannitol	8.7	4.3	1	3.3	6.7	1
Tabusso et al, 2002 ⁴⁹	47	Mannitol or PEG	20.8	0	0.04	8.3	0	0.49
Miettinen et al, 2003 ⁵⁰	267	PEG	3.8	2.5	0.72	3.6	2.3	0.72
Bucher et al, 2005 ⁵¹	153	PEG	6.4	1.3	0.21	12.8	4	0.07
Ram et al, 2005 ⁵⁴	329	NaP	0.6	1.3	1	9.8	6.1	0.22
Fa-Si-Oen et al, 2005 ⁵⁵	250	PEG	5.6	4.8	0.78	7.2	5.6	0.79
Zmora et al, 2006 ⁵⁶	249	PEG	4.2	2.3	0.48	6.7	10.1	0.36
Pena-Soria et al, 2007 ⁵⁷	97	PEG	8.3	4.1	0.05	12.5	12.2	1
Jung et al, 2007 ⁵⁸	1343	PEG, NaP, enema	1.9	2.6	0.46	7.9	6.4	0.34
Contant et al, 2007 ⁵⁹	1354	PEG + bisacodyl or NaP	4.8	5.4	0.69	13.4	14.0	0.75

MBP, mechanical bowel preparation; NaP, sodium phosphate; PEG, polyethylene glycol.

terms of decreased mortality, wound infection rates, noninfectious extraabdominal complications, and reoperation rates, but none of these differences were statistically significant. Although this analysis was limited by a relatively small number of studies, the Cochrane review authors concluded that “there is no convincing evidence that MBP is associated with reduced rates of anastomotic leakage after elective colorectal surgery. On the contrary, there is evidence that this intervention may be associated with an increased rate of anastomotic leakage and wound complications.”¹⁴ The authors reiterated a belief raised in other studies, that the use of MBP frequently resulted in a “semi prepared” colon full of liquid feces that was difficult to control, often leading to spillage and peritoneal contamination, thus explaining the higher rates of complications found in the MBP group.

Other large, randomized clinical trials were published following the 2005 Cochrane review. In 2007, Jung and colleagues from Sweden published a multicenter randomized trial assessing the benefits of preoperative MBP in elective colonic surgery.⁵⁸ The authors evaluated a total of 1343 patients between the MBP and no MBP groups, with each arm sharing similar demographics, indications for operation, perioperative antibiotic prophylaxis, and type/level of anastomosis. The overwhelming majority of patients in the MBP arm received either polyethylene glycol or sodium phosphate preparation. This study showed no significant differences between the two arms in terms of cardiovascular

complications, general infectious complications, surgical site infections, and overall complications. The authors concluded that complication rates are not lowered by MBP and that MBP can therefore be omitted before elective colonic resection.

Also in 2007, Contant et al⁵⁹ from the Netherlands reported their results of a multicenter randomized trial addressing MBP and elective colorectal surgery. Following random assignment of 1354 patients to either MBP or no MBP before elective colorectal surgery, the authors evaluated rates of anastomotic leakage as well as other complications between the two groups. Leak rates were observed to be similar (4.8% for MBP versus 5.4% for no MBP); however, patients who had MBP and an anastomotic leak had fewer abscesses than patients who had a leak and no preoperative MBP. The authors found no other differences between the two arms for the outcome measures of septic complications, fascia dehiscence, and mortality.

One shortcoming of the previous clinical trials and meta-analyses was the relatively low numbers of patients having distal colon and/or rectal surgery. In 2005, Bucher and colleagues reported a randomized trial comparing MBP versus no MBP in elective left-sided colorectal surgery.⁵¹ In 153 patients randomized to either arm, this study demonstrated a leak rate of 6% in the MBP group compared with 1% in the no MBP group ($p = 0.021$). This study also showed higher overall rates of abdominal infectious complications, extraabdominal morbidity, and hospital stays in the MBP group,

differences that were all statistically significant. These findings prompted the authors to opine that elective left-sided colorectal surgery without MBP is safe and is associated with reduced postoperative morbidity. To address the issue of rectal surgery without MBP, an initial retrospective review of rectal cancer patients undergoing surgery without MBP or a protective diverting ostomy demonstrated a low anastomotic leak rate of 4.9%, in keeping with prior published rates from patients receiving MBP.⁵² This report was followed in 2007 by a case-controlled study of 52 consecutive rectal cancer patients undergoing surgery without MBP.⁵³ The authors reported a higher overall morbidity rate in patients who had MBP than in those that did not. Though peritonitis occurred more frequently in the no MBP group, the difference was not statistically significant. The authors observed a trend toward higher rates of infectious complications in patients receiving MBP and a statistically significantly higher rate of infectious extraabdominal complications and longer mean hospital stay in the MBP group. They concluded that elective rectal cancer surgery without MBP may be associated with reduced postoperative morbidity.

The most thorough and current meta-analysis on the subject was recently published by Pineda and colleagues from Stanford, who completed a systematic review of the literature through early 2008 and found 13 prospective trials available with a total of 4601 patients, the largest number of patients available to date.⁶⁰ In this meta-analysis, the authors analyzed two primary outcomes— Anastomotic leaks and wound infections. They found no statistically significant difference between 2304 patients receiving MBP compared with 2297 patients receiving no MBP in either outcome. Anastomotic leaks were reported in 97 patients (4.2%) with MBP and 81 patients (3.5%) without MBP ($p = 0.206$). Wound infections occurred in 9.9% versus 8.8% ($p = 0.155$). This lack of any statistically significant difference between the two arms in the largest meta-analysis yet performed prompted the authors to conclude that MBP is of no benefit to patients undergoing elective colorectal resection. Though the authors acknowledge certain scenarios when the use of MBP is warranted, such as the anticipated need for intraoperative colonoscopy, they propose that routine MBP need not be considered a “prerequisite of safe colorectal surgery.”

SUMMARY

As scientific evidence mounts to question the utility of MBP and its role in elective colorectal surgery, it remains to be seen whether the growing body of literature will influence surgeons' behaviors. Recent studies that suggest equivalence or an even detrimental effect of MBP compared with no MBP have not yet led to any significant

changes in clinical practice patterns, and many national and international societies still include MBP among accepted recommendations. At present, no national society has publicly endorsed the abandonment of MBP in elective colorectal surgery. Whether historical doctrine or unsubstantiated dogma, routine MBP may require further scrutiny and debate before it is relegated to an antiquated practice.

DISCLAIMER

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.

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