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Preoperative bowel preparation

AARON L. KLINGER AND DAVID A. MARGOLIN

CHALLENGING CASE

A 57-year-old man with a sigmoid colon cancer found via colonoscopy for a history of anemia and weight loss is awaiting surgery. The patient had a mechanical and oral antibiotic bowel preparation ordered. While you are seeing the patient in the preop holding area, he tells you that he took the oral antibiotics, but "I tried drinking that prep last night and after only half a glass I got sick and threw up. I just couldn't take it." Do you perform elective surgery?

CASE MANAGEMENT

Yes. Multiple studies have demonstrated the safety of elective bowel surgery in the absence of a mechanical bowel preparation.

INTRODUCTION

In 1887, Halsted published his landmark study, "Circular Suture of the Intestine" (1). Here he further supported the novel realization that microorganisms, not air exposure, lead to peritonitis and noted the high rate of death at the time following bowel surgery. He concluded that "the chief danger of infection of the peritoneal cavity is manifestly from the contents of the intestine, in case they find their way through the wound in the intestine or along the lines of suture." Since then the idea of cleaning the bowel to reduce bacterial burden and prevent infectious

complications has been adapted into surgical dogma, but practice continues to be challenged.

Rates of surgical site infection (SSI) following elective colon and rectal resection remain among the highest of the general surgical procedures with estimates at 20% or higher (2–4). This is due largely to the high concentration of aerobic and anaerobic bacteria that reside within the gut. Surgical wound infection has been shown to increase length of stay by 1 week and hospital costs by over \$17,000 (4). Currently, to help mitigate these infectious complications, IV antibiotics with the addition of a preoperative bowel preparation consisting of mechanical bowel preparation (MBP), oral antibiotics (OAP), or a combination of the two have become common practice. The purpose of bowel preparation is to decrease the bacterial load in the gut in order to reduce rates of infectious complications including wound infection, abscess, and anastomotic leaks. Suggested secondary benefits of bowel preparation include ease of bowel handling (especially in minimally invasive surgery) and facilitation of intraoperative endoscopy. Those who question the benefits of preoperative bowel preparation note suboptimal patient compliance, associated patient discomfort, potential electrolyte imbalances, as well as the aspiration risk associated with consuming large volumes of liquid.

SYSTEMIC ANTIBIOTIC PROPHYLAXIS

There is no debate regarding the importance of systemic antibiotic prophylaxis in colorectal surgery. In the 1860s Joseph Lister, having been made aware of the work of Louis Pasteur, began work on antiseptic techniques for wounds (5). He famously sprayed incisions, dressings, and instruments with carbolic acid in hopes of preventing infection. Experimentation with preoperative systemic antibiotic prophylaxis began in the 1940s following the release of penicillin, a time when SSI following colon surgery was as high as 90% (6). Use of perioperative penicillin was common practice by the mid-1950s, and its use became expected by the general public. This prompted Altemeier to state in 1955 that “antibiotics are most effective prophylactically when used as adjuvants to careful and adequate surgery but not as substitutes for it.” He noted that the evidence at the time supported the use of antibacterial agents in select conditions, including surgical procedures through contaminated areas such as the gastrointestinal tract, and warned of rising antibiotic resistance (7).

Song and Glenny, in their landmark review, evaluated 147 trials of antibiotic prophylaxis in colorectal surgery performed between 1984 and 1995. They showed that the infection rate of those receiving prophylaxis had improved significantly from 22% (mean rate 1965–1980) to 11% (1984–1995). Pooled data from four trials showed a much higher infection rate in patients receiving no prophylaxis than in those receiving any systemic antibiotics (40% versus 13%). They also concluded from their review of 17 trials that there is no benefit to multiple antibiotic doses compared with a single preoperative dose. Oral antibiotics alone were shown to be significantly worse at preventing SSI than oral antibiotics with additional systemic antibiotics (odds ratio [OR] 3.34). They concluded that oral antibiotics alone were inadequate prophylaxis, that the regimen chosen must provide adequate coverage of aerobic and anaerobic bacteria, and that parenteral antibiotic administration must be timed to assure that tissue concentration of antibiotics is sufficient at the time of bacterial contamination (8).

In addition to recommending combined OAP and MBP prior to colorectal surgery, the 2013 guidelines from the Surgical Infection Society strongly recommend the use of preoperative IV antibiotics (3). They note infectious complication rates as high as 30%–60% without antibiotics compared to <10% with prophylaxis. Pooled data analysis by this group also shows a significantly decreased mortality rate with the use of preoperative IV antibiotics (11.2% versus 4.5%). The authors echo that systemic antibiotics should offer coverage for both aerobic and anaerobic bacteria. Recommended regimens include a single dose of a second-generation cephalosporin with appropriate coverage (cefoxitin or cefotetan) or cefazolin plus metronidazole. Alternative regimens are provided for those in resistant communities or with allergies to recommended agents. It is noted that ertapenem has been shown to be superior to cefotetan at preventing SSI (18.1% versus 31.1%), but its use remains controversial due to concern of creating resistant organisms and potential for *Clostridium difficile* infection (increased, but not statistically significant rates have been reported). Systemic prophylaxis should be provided within 1 hour to the start of surgery, drugs with shorter half-lives may require re-dosing for longer operations. This can be avoided by using an antibiotic with a longer half-life.

To better determine the ideal prophylactic IV antibiotic regimen, Poeran et al. analyzed 90,725 patients receiving open colectomies at 445 hospitals between 2006 and 2013 (9). The overall SSI prevalence for the study was 5.2%. Although cefoxitin was the most commonly used preoperative antibiotic (42% of cases), they found ampicillin-sulbactam (OR 0.71), ertapenem (OR 0.65), and metronidazole with

cefazolin (OR 0.56) all to be superior in preventing SSI. The authors confirmed lack of benefit to providing antibiotics beyond the day of surgery.

MECHANICAL BOWEL PREPARATION

Physical clearance of the colonic lumen before surgery has been common practice for over a century. Historic preparations included extended period dietary restriction, cathartics, whole bowel irrigation, and enemas (6). Today several oral preparations are available for bowel cleansing. While these have U.S. Food and Drug Administration (FDA) indications for cleansing for colonoscopy and radiologic studies, none are approved for preoperative cleansing for surgery. Available preparations vary from large volume isotonic preparations to smaller hyperosmotic solutions. Osmotic agents include polyethylene glycol (PEG), sodium phosphate (NaP), sodium sulfate, sodium ascorbate, and sodium picosulfate.

PEG is an inert osmotically active polymer that is mixed with an electrolyte solution, typically to a volume of 4 L, which a patient is instructed to ingest over 2–3 hours. The added electrolyte content in concert with the osmotic activity of PEG prevents net absorption or excretion of water and electrolytes acting to clear bowel contents without causing significant fluid shifts or electrolyte abnormalities in most patients. Due to the potential for these imbalances, however, special care needs to be taken in elderly patients, patients with congestive heart failure, and patients with renal insufficiency. A modified, reduced volume prep consists of 2 L PEG solution taken with four bisacodyl tablets. While not FDA approved, some surgeons have begun using a “MiraLAX prep,” which consists of over-the-counter electrolyte-free PEG solution dissolved in a sports drink (i.e., Gatorade). This prep with the addition of bisacodyl utilizes less volume than traditional PEG and is more palatable for patients, allowing for better compliance (10).

NaP is a sodium-based hyperosmolar oral laxative. Its use requires smaller volumes than PEG, which like the “MiraLAX prep” may result in better patient compliance. This regimen consists of 45 mL NaP in 240 mL clear liquids taken twice, 10 hours apart. Patients should be instructed to take their prep early so that they are not kept awake the night prior to their procedure. Alternatively, patients can take NaP in tablet form—4 tablets and 240 mL clear liquids are taken every 15 minutes until 28 tablets have been consumed. The FDA issued a black box warning in May 2006 regarding the use of oral NaP for bowel preparation in elderly patients, those

with underlying kidney disease, those with dehydration, or those taking medications that alter renal perfusion (such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics, and nonsteroidal anti-inflammatory drugs). This population is at an increased risk for development of acute renal failure, or nephrocalcinosis, secondary to fluid shifts, phosphate load, and decreased intravascular volume when taking NaP prep. This complication can be avoided by consuming a larger (2–3 L) volume of clear liquids while taking this prep. However, oral NaP solutions are not currently commercially available.

The efficacy of MBP in reducing infectious complications has recently been questioned. Multiple randomized controlled trials and meta-analyses have failed to show a benefit to MBP alone. In a 2011 Cochrane Review, Güenaga et al. compared 5,805 patients from 18 trials who underwent elective colorectal surgery (11). Of these, 2,906 received MBP, and 2,899 received no preparation. All patients received IV antibiotics. They found no significant difference between these groups in rates of anastomotic leakage or wound infection in low anterior resection or colonic resection.

Despite these findings, MBP remains common practice in colorectal surgery. A survey of members of the American Society of Colon and Rectal Surgeons (ASCRS) performed by Beck and Fazio in 1990 showed 100% of respondents using some form of mechanical (most commonly enemas and cathartics) and antibiotic preparation, most using combined oral and parenteral agents (12). A repeat survey in 1997 by Nichols again found 100% compliance with some form of MBP prior to elective colorectal surgery with the majority using PEG solutions. Eighty-seven percent of respondents used both oral and parenteral antibiotics (13). A 2005 survey by Lassen et al. of colorectal surgeons in five Northern European countries found over 90% using some form of mechanical prep prior to elective left colectomy (14). Finally, a survey of ASCRS surgeons in 2016 found that 94.3% of respondents used a mechanical bowel preparation always or selectively (15).

It is difficult to establish the true value of MBP in isolation of other factors. A common endpoint in most studies is SSI, which as discussed previously and in the following section is influenced by the use of oral and/or systemic antibiotics.

ORAL ANTIBIOTIC BOWEL PREPARATION

Attempts to reduce the colon's bacterial load with poorly absorbed oral antibiotics