

# Effect of Preadmission Bowel Preparation on Outcomes of Elective Colorectal Procedures in Young Children

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## Abstract

**Background:** The utility of mechanical bowel preparation (MBP) to minimize infectious complications in elective colorectal surgery is contentious. Though data is scarce in children, adult studies suggest a benefit to MBP when administered with oral antibiotics (OAB).

**Methods:** After IRB approval, the Pediatric Health Information System (PHIS) was queried for young children undergoing elective colon surgery from 2011-2014. Patients were divided into: no bowel preparation (Group 1), MBP (Group 2), and MBP plus OAB (Group 3). Statistical significance was determined using univariate and multivariate analysis with GEE models accounting for clustering by hospital.

**Results:** 1581 patients met study criteria: 63.7% in Group 1, 27.1% in Group 2, and 9.2% in Group 3. Surgical complication rate was higher in Group 1 (23.3%) compared to Groups 2 and 3 (14.2% and 15.5%;  $p < 0.001$ ). However, median length of stay was shorter in Group 1 (4, IQR 4 days) compared to Group 2 (5, IQR 3) and Group 3 (6, IQR 3) ( $p < 0.001$ ). 30-day readmission rates were similar. In multivariate analysis compared to patients in Group 1, the odds of surgical complications were 0.72 (95% CI 0.40 – 1.29,  $p = 0.28$ ) with MBP alone (Group 2), 1.79 (95% CI 1.28 – 2.52,  $p = 0.0008$ ) with MBP+OAB (Group 3), and 1.13 (95% CI 0.81 – 1.58,  $p = 0.46$ ) for the aggregate Group 2 plus 3.

**Conclusion:** Utilization of bowel preparation in children is variable across children's hospitals nationally, and the benefit is unclear. Given the discrepancy with adult literature, a three-armed pediatric-specific randomized controlled trial is warranted.

**Key Words:** Bowel preparation, surgical complication, surgical site infection, colorectal surgery, anastomotic leak

**Level of Evidence:** Level III treatment study – retrospective comparative study

**Abbreviations:** MBP, mechanical bowel preparation; OAB, oral antibiotics; PHIS, Pediatric Health Information System; SSI, surgical site infections; CI, confidence interval; IQR, interquartile range

## Introduction

Surgical site infections (SSI) occur in 13-25% of children after elective colorectal surgery, with significant resulting morbidity for patients and costs to the healthcare system [1-3]. Mechanical bowel preparation (MBP) prior to surgery has been utilized routinely since the 1970's to theoretically minimize infectious and anastomotic complications. The specific regimen used for preparation has evolved over the years, along with its perceived efficacy. MBP with oral antibiotics (OAB) was originally used and widely popularized by Nichols and Condon [4, 5]. MBP alone has also been used extensively and has over time become the preferred method by most surgeons. The efficacy of bowel preparation in reducing post-operative complications, length of stay (LOS), and readmission rates has been disputed in multiple trials,

which has resulted in a significant reduction in the utilization of MBP [6-9]. However, more recent high quality, randomized trials in adults have shown a benefit to MBP+OAB compared to MBP alone, and suggested that bowel preparation may in fact be beneficial when administered as MBP+OAB [10-15].

There has been a paucity of studies in the pediatric population on the utility of bowel preparation, so current recommendations in pediatric surgery are based largely on adult literature. Breckler et al. in 2010 found no difference in SSI incidence in pediatric patients who underwent MBP with or without OAB [16]. Current trends in pediatric hospitals continue to favor the use of no preparation over MBP alone or MBP+OAB [17, 18].

The purposes of this study are (1) to assess the current use of bowel preparation regimes for elective colorectal surgeries in young children using a national administrative database and (2) determine the association between bowel preparation regimens and post-operative complications. This large, retrospective database study aims to clarify whether adult guidelines are clearly applicable to pediatric patients or whether additional, prospective data is needed to establish pediatric guidelines.

## **1. Methods**

### *1.1. Data search*

Data for this study were obtained from the Pediatric Health Information System (PHIS), an administrative database that contains inpatient, emergency department, ambulatory surgery and observation encounter-level data from over 45 not-for-profit, tertiary care pediatric hospitals in the United States. These hospitals are affiliated with the Children's Hospital Association (Overland Park, KS). Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. Portions of the data submission and data quality processes for the PHIS database are managed by Truven Health Analytics (Ann Arbor, MI). For the purposes of external benchmarking, participating hospitals provide discharge/encounter data including demographics, diagnoses, and procedures. Nearly all of these hospitals also submit resource utilization data (e.g. pharmaceuticals, imaging, and laboratory) into PHIS. Data are de-identified at the time of data submission, and data are subjected to a number of reliability and validity checks before being included in the database. For this study, data from 45 hospitals was included. Although de-identified, records contain an encrypted medical record number that allows tracking of individual patients across multiple inpatient and outpatient encounters

The PHIS database was queried from 1/1/2011 to 12/31/2014 for patients younger than 10 years of age undergoing elective procedures involving a colonic anastomosis. Analysis was limited to children <10 years of age because it is only possible to capture bowel preparations administered in the inpatient setting. Older children who were more likely to have had a bowel preparation as outpatients were excluded. Analysis was also limited to children who underwent their primary procedure on hospital day 0, 1, or 2. Patients were considered to have a bowel preparation if their procedure was on day 1 or 2 and they had pharmacy charges for MBP (polyethylene glycol or magnesium citrate) and/or OAB (neomycin or erythromycin) beginning on day 0 or 1. Patients were not assumed to have a bowel preparation just because they were pre-admitted prior to surgery.

Patients undergoing colonic anastomosis were identified based on ICD-9 procedure codes 17.33, 17.35, 45.71, 45.72, 45.76, 45.79, 45.81, 45.82, 45.83, 45.94, 46.52. Patients undergoing anorectal anastomoses were excluded given the study design's inability to discern if they had a pre-existing proximal diverting ostomy at the time of surgery. We identified 2632 patients meeting initial inclusion and exclusion criteria. Among these 2632 patients, 32 received a bowel preparation consisting of oral

antibiotics alone. This number was considered too small for analysis, so these patients were excluded from further analysis.

### *1.2. Experimental groups*

Included patients were divided into three groups for analysis: Group 1: No bowel preparation; Group 2: MBP alone; Group 3: MBP+OAB. The primary outcome measure was aggregate surgical complications. This flag is identified in PHIS based on the presence of one or more ICD-9 diagnosis codes referenced in PHIS Flag Code Lists - FY 2013 [19]. Complications were further characterized based on PHIS flags (infectious complication), and/or specific ICD-9 codes (wound infection, anastomotic leak, wound dehiscence). Secondary outcome measures were hospital length of stay (LOS) and readmission within 30 days (to the emergency department, observation unit, or inpatient care unit).

### *1.3. Statistical analysis*

Categorical variables were compared by chi-square analysis. Length of stay was not normally distributed. Medians were therefore compared between groups using the Independent Samples Kruskal-Wallis test. Multivariate analysis was performed using general estimating equations (GEE). Odds ratios were obtained from GEE models accounting for the clustering within hospitals and adjusted for gender, race, ethnicity, payer, and procedure level.  $P < 0.05$  was considered significant.

## **2. Results**

### *2.1 Demographics*

1581 patients met study criteria and were included in the analysis. 952 (60.2%) were male. 964 (61.0%) patients were white, 220 (13.9%) black, 79 (5.0%) Asian, and 318 (20.1%) other or unknown. 295 (18.7%) were of Hispanic ethnicity. The primary payer was commercial insurance in 637 (40.3%) and government insurance in 875 (55.3%). The majority of patients were less than one year of age (839, 53.1%). Mean age was  $1.7 \pm 2.6$  years.

Among these 1581 patients who underwent colonic anastomosis, 1007 (63.7%) received no preoperative bowel preparation, 429 (27.1%) had MBP alone and 145 (9.2%) received MBP+OAB. The demographic characteristics of patients in each treatment group are compared in Table 1. Patients who were older than 1 year of age, White race, or non-Hispanic ethnicity were more likely to get MBP±OAB. Hospital variations in bowel preparation strategy is shown in Figure 1, with some hospitals using no preparation as the only strategy and others using MBP alone or with OAB for all their patients.

### *2.2 Outcomes*

In univariate analysis, the incidence of surgical complications was higher for the no preparation group 235 (23.3%) compared to 61 (14.2%) with MBP or 23 (15.5%) MBP+OAB ( $p < 0.001$ ) (Table 2). On the other hand, median LOS was shorter in the no preparation group compared to MBP alone or MBP+OAB,  $p < 0.001$ . 30-day readmission rates were similar between the three treatment groups.

Colostomy closure was the most commonly performed operation in this dataset, accounting for 988 of the cases. In this subgroup, surgical complication occurred in 106 (17.3%) with no preparation, 24 (8.5%) with MBP alone, and 15 (15.6%) with MBP+OAB ( $p = 0.002$ ). As in the overall cohort, LOS was shorter in Group 1, but 30-day readmission rates were not significantly different (Table 3).

### *2.3. Multivariate analysis*

In multivariate analysis accounting for clustering by hospital, the odds ratio (OR) for surgical complication was 0.72 (95% CI 0.40 – 1.29,  $p = 0.28$ ) with MBP alone and 1.79 (95% CI 1.28 – 2.52,

p=0.0008) for MBP+OAB compared to the referent group who received no preparation. When patients who received MBP with or without OAB were grouped together, their odds of surgical complication was 1.13 (95% 0.81 – 1.58, p=0.46) compared to patients who received no preparation. There was also no difference in risk of 30 day readmissions for MBP alone (OR 0.95; 95% CI 0.72 – 1.25, p=0.70), MBP+OAB (OR 0.93; 95% CI 0.75 – 1.16, p=0.53), or MBP±OAB (OR 0.94; 95% CI 0.76 – 1.16, p=0.57) compared to no bowel preparation.

### 3. Discussion

In this retrospective review of a national administrative dataset incorporating data from many of the largest children's hospitals in the country, we found no definitive benefit to any of the three strategies for preparing young children for elective colon surgery. There was considerable variation between institutions regarding the utilization of bowel preparation. In univariate analysis, MBP alone, but not MBP+OAB was associated with a lower risk of surgical complications. However, in a random-effects model accounting for hospital clustering, there was no difference in either surgical complications or 30-day readmission rates between those who underwent MBP with or without OAB compared to those who underwent no preparation. Clustering by hospital takes into account inter-hospital variations that may be unrelated but bias the results during data mining. In our case, surgeon or hospital-specific complication rates, pre- and post-operative care, and baseline differences in patient population may influence the outcome. For example, in hospitals where only no preparation was used, a higher infection rate because of poor technique may disproportionately increase the infection rate for the "no preparation" group without affecting the other two groups. Clustering by hospital takes this into account and compares similar groups to each other.

Mechanical bowel preparation was considered standard of care by colorectal surgeons for almost half a century until data emerged in the early 2000's questioning the utility of this strategy. That data is summarized by two large meta-analyses of randomized controlled trials. Slim et al. evaluated the role of any MBP regimen vs no MBP on anastomotic leakage and other septic complications looking at 14 trials, including 4859 patients. They found no difference in anastomotic leak, no harmful effects with MBP, and concluded that bowel preparation should be omitted [20, 21]. Similarly, Guenaga et al. analyzed 18 trials with 5805 patients, grouped as any MBP vs no MBP, and found no difference in anastomotic leak rate or wound infections after colonic or colorectal surgery [22, 23]. These trials provided the evidence-base for subsequent Enhanced Recovery After Surgery guidelines for colorectal surgery, which recommend no bowel preparation prior to elective surgery [24]. An important limitation of both of these meta-analyses as well as the cohort of trials published during that era is their lack of differentiation between mechanical bowel preparation groups with and without oral antibiotics. In these studies, oral antibiotics were only administered to 7-10% of patients. More recent trials have addressed this factor. Englesbe, published a large, prospective cohort of 2011 patients comparing MBP+OAB vs. MBP alone and found a decrease in SSI and organ space infections in the MBP+OAB group, with no changes in the rates of *C. difficile* colitis [25]. Finally, Chen et al. in 2016 published a meta-analysis of randomized controlled trials that stratified patients to MBP+OAB vs MBP alone. Seven trials were included and superficial/deep SSI were reduced in the MBP+OAB group compared to MBP alone, with no difference in organ space infections.

Pediatric data on this topic remains sparse, with no large, randomized controlled trials available. Data available from retrospective trials has demonstrated mixed results. Breckler et al. published a retrospective trial in 2010 with differentiation between MBP vs MBP+OAB and showed no difference in SSI. Since then, there have been two studies that found no benefit of MBP compared to no bowel preparation in children [26, 27]. Serrurier et al. in a retrospective analysis of 272 patient study in 2012

showed an increase in SSI in the MBP±OAB group compared to no preparation, and no difference in LOS [27]. Neither of these studies controlled for the use of OAB as part of the preoperative bowel preparation.

In a recent survey of bowel preparation practices among pediatric surgeons, 31% utilized MBP alone, 27% utilized diet modification alone, 20% utilized MBP+OAB, 12% used no preparation, and 5% used OAB alone. The trend over time was towards adopting no preparation or diet modification alone as the strategy of choice [18, 28]. Utilization of bowel preparation in our study was generally comparable to what was reported in this survey, although OAB usage was higher in the survey than in our results. Our study serves as a three-armed comparison of the main preparation strategies, accounting for the use, or lack thereof, of OAB. In agreement with retrospective institutional data from Breckler et al., we found no significant benefit to MBP in the pediatric population after clustering by hospital type. However, the trend towards a benefit to MBP alone in the univariate analysis, suggests that further investigation of this topic is warranted. In agreement with Serrurier et al., our data also suggests – perhaps counter-intuitively - that there may be a detrimental effect of OAB. Given the disparity between the pediatric and adult literature, this study supports the need of a pediatric randomized controlled trial.

The study is limited by the retrospective design and the inherent issues with administrative data. Surgical complications are captured based on reported billing codes, and not based on clinical chart review. It is well-established that clinical chart review, as done for the National Surgical Quality Improvement Project (NSQIP) database, identifies many complications that were not captured by administrative data in both adult and pediatric patient populations [29, 30]. In addition, because the administrative data only allowed for capture of bowel preparations performed on an inpatient basis, we excluded children 10 years-of-age or older who were more likely to have undergone outpatient bowel preparation. While many young children require a nasogastric tube to administer a MBP, it is certainly possible that some patients received a modified outpatient MBP. These patients would have been erroneously categorized as having received no MBP. Therefore, our study design prevents the direct application of our findings to older pediatric patients. Finally, the same questions about MBP apply to patients undergoing anorectal operations. However, this dataset was not appropriate for studying those patients because of the inability to distinguish those with an existing protective colostomy in whom bowel preparation may not be applicable.

#### **4. Conclusion**

For young children managed at large children's hospitals across the U.S., there is wide variability in the utilization of mechanical bowel preparation, with or without oral antibiotics, prior to elective colon surgery. After accounting for clustering between hospitals in multivariable analysis, there is no clear benefit to MBP, and the addition of oral antibiotics may in fact increase surgical complications. A three-armed pediatric-specific randomized controlled trial is needed to more definitively determine the optimal preoperative regimen for children.

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