Title: Role of Mechanical Bowel Prep and Perioperative Antibiotics in Pediatric Pull-through Procedures

Short Title: Bowel Prep in Pediatric Pull-throughs
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All authors contributed to the study design and implementation. Dr. Carpenter conducted statistical analysis with review and input from Drs. Breckler and Gray. Dr. Carpenter and Dr. Breckler both contributed significantly to the drafting of this manuscript, with review and editing from Dr. Gray.

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The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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Abstract:

Background:
There are no clear guidelines for the use of mechanical bowel prep and postoperative antibiotics in children undergoing elective colorectal pull-through surgery. The objective of this study was to determine whether preoperative bowel prep administration or duration of postoperative antibiotics impacted the rate of complications following elective pediatric pull-through surgery.

Materials and Methods:
Patients under 18 years who underwent a pull-through procedure between 2011 and 2017 were retrospectively identified. Patient data included diagnosis, procedure, administration of mechanical bowel preparation, and duration of perioperative IV antibiotics. Outcomes of interest included surgical site infections and anastomotic complications.

Results:
180 patients met inclusion criteria, of which 47.2% received mechanical bowel prep. The combined rate of infectious and anastomotic complications was 12.2%. There was no significant difference in combined complication rate among those receiving bowel prep compared to those who did not (14.1% vs. 10.5%, p=0.46). Administration of bowel prep in the perineal anoplasty subgroup was associated with higher rates of wound infection (33.3% vs 3.3%, p=0.05). 105 patients (58.3%) received perioperative IV antibiotics for 24 hours or less. This group had similar rates of complications (13.3%) compared to those receiving IV antibiotics for longer than 24 hours (11.6%, p=0.74).

Conclusion:
Although mechanical bowel prep did not affect the overall complication rate for pull-through procedures, it was associated with more wound infections in those undergoing perineal
anoplasty. Duration of postoperative IV antibiotics was not significantly associated with the rate of wound and anastomotic complications.

Keywords: Bowel prep, perioperative antibiotic prophylaxis, pull-through, pediatric colorectal, surgical site infection, anastomotic leak.
**Introduction:**

The prevention of surgical site infections (SSI) in patients undergoing elective colorectal procedures is multifaceted. Bowel preparation for elective colorectal operations in adults has been a standard of care since the 1970s as a method to decrease postoperative complications such as wound infection and anastomotic leakage.\(^1\) The use of a mechanical bowel preparation in adults has come under scrutiny when the results of several meta-analyses demonstrated an increased rate of anastomotic leakage.\(^2,3\) More recently, a large database study by Kiran and colleagues found that patients who had received mechanical bowel preparation and oral antibiotics prior to elective colorectal resections had a significant decrease in anastomotic leaks and surgical site infections (SSI).\(^1\)

There is a paucity of data in the literature regarding the use of bowel preparation in children. Several small studies done in pediatric surgical patients have shown that the use of mechanical bowel preparation without the use of oral antibiotics compared to no preparation did not result in a difference in wound infections or anastomotic leaks.\(^4,5\) These studies included patients with a variety of colorectal diseases. Use of mechanical bowel preparation and oral antibiotics can be challenging in pediatric patients. Polyethylene glycol with electrolyte solution (GoLYTELY®) is generally unpalatable for children and typically requires a nasogastric tube for administration. The usual oral antibiotics included in a standard bowel preparation (neomycin and erythromycin) are not commercially available in an appropriate liquid formulation. These factors make the use of bowel preparation difficult in children.

Current guidelines for antimicrobial use in colorectal surgery include the use of an intravenous antibiotic within 60 minutes of the incision.\(^6\) These antibiotics are recommended to
be limited to a 24-hour duration after colorectal surgery. In pediatric surgical patients, there remains variability among surgeons on the appropriate duration of intravenous antibiotics after surgery. In a survey of pediatric surgeons on current practices of bowel preparation for elective colorectal surgery, 38% of respondents indicated that intravenous antibiotics were continued for 48 hours or longer. To our knowledge, there are no studies in the pediatric population specifically examining preoperative bowel preparation for anorectal pull-through procedures. The objective of this study was to determine whether preoperative mechanical bowel prep administration or duration of postoperative antibiotics impacted the rate of complications following elective pediatric pull-through surgery. We hypothesized that administration of mechanical bowel prep and administration of IV antibiotics for greater than 24 hours would confer no benefit in decreasing anastomotic and infectious complications.

**Material and Methods:**

After Institutional Review Board approval (#1703739785) and an approved waiver for informed consent was obtained, patients 18 years or less who underwent an abdominal or perineal pull-through procedure with a rectal, anal, or perineal anastomosis between 2011 and 2017 were identified from an electronic database. The operations reviewed included the following: Hirschsprung’s Soave and Duhamel pull-through, J-pouch ileo-anal anastomosis, ileo-rectal anastomosis, posterior sagittal anorectoplasty (PSARP) for imperforate anus, and perineal anoplasty. Patients who underwent joint procedures with urology were excluded from the study. One patient received oral antibiotics as part of their bowel prep regimen and was excluded. Demographic data that was collected included gender, age at time of surgery, weight and height at surgery. Clinical data included disease state, surgical history, type of bowel preparation, perioperative antibiotic, procedure, duration of intravenous antibiotic postoperatively, time to
resumption of regular feeds, and length of stay (LOS). LOS was calculated from time of surgery to control for pre-operative admission for bowel prep administration. 30-day complications of the pull-through procedure included SSI (wound infection, dehiscence, intra-abdominal abscess), anastomotic stricture, and anastomotic leak. The Centers for Disease Control definitions for SSI were utilized.

The study group was first analyzed as a whole. Patients were then divided into comparison groups based on whether they received mechanical bowel prep preoperatively. Antibiotic administration was analyzed dichotomously, with patients receiving postoperative antibiotics for less than 24 hours compared to those who received them for longer. In our practice, patients undergoing PSARP are typically held NPO on TPN for 5 days postoperatively. To control for this, LOS analysis was performed excluding these patients. Then the study group was stratified by procedure type to determine if mechanical bowel preparation or antibiotic duration had different effects in the different procedure types.

Statistical analysis was performed using SAS 9.4 for Windows Copyright © 2013, SAS Institute Inc., Cary, NC, USA. Descriptive statistics including n values, mean values, standard error, and frequencies were calculated. Univariate analysis was performed with Chi-Square analysis or Fisher’s Exact Test, as appropriate. Stepwise multiple logistic regression was used to model dichotomous outcomes based on the original univariate analysis. In addition to bowel prep administration and antibiotic duration, variables included in regression analysis included gender, diagnosis, history of prior abdominal surgery, rectal irrigation in the OR, creation of a proximal diverting stoma, surgical approach, intraoperative blood transfusion, post-operative TPN, and stoma takedown among those patients with a stoma. LOS and time to regular feeds were not normally distributed on univariate analysis, based on the Kolmogorov-Smirnov test (p <0.01);
therefore, they were evaluated using the non-parametric Wilcoxon Rank-Sum and Kruskal-Wallis Tests. An α-level of 0.05 was used to determine statistical significance for all tests.

Results:

A total of 180 patients met inclusion criteria and underwent an elective pull-through operation at Riley Hospital for Children at Indiana University Health between 2011 and 2017. Table 1 shows the demographic data and type of pull-through procedure for this patient cohort. The overall complication rate was 16.7%. Nineteen patients (10.6%) developed infectious complications. Three patients (1.7%) developed anastomotic complications, one stricture and two leaks. Seventeen patients (9.4%) required repeat operation within 30 days. Six of these were for infectious or anastomotic complications while 10 were for small bowel obstruction or volvulus.

Eighty-five patients (47.2%) received mechanical bowel prep. Administration of mechanical bowel preparation was not significantly associated with the overall rate of complication, infectious complications, anastomotic complications, or reoperation within 30 days (Table 2). One-hundred five patients (60.3%) received postoperative antibiotics for 24 hours or less while 69 patients received postoperative antibiotics for longer. The remaining six patients were treated as outpatients and were excluded from this analysis. The most common antibiotic regimen (77% of patients) was cefoxitin. On univariate analysis, duration of postoperative antibiotics did not impact rate of overall complications, infectious complications, or anastomotic complications (Table 2). However, reoperation rates were higher in the group receiving shorter antibiotic courses (13.3% vs. 4.4%, p=0.05).

When stratified by procedure type, neither administration of mechanical bowel prep nor duration of postoperative antibiotics was associated with combined rates of SSI and anastomotic
complications or rates of reoperation. However, among patients undergoing perineal anoplasty, administration of mechanical bowel preparation was associated with increased rates of these complications (33.3% vs 3.3%, p=0.05). There was no significant association between the outcomes of interest and either mechanical bowel preparation or antibiotic duration among the other procedure types (Table 3).

After removal of PSARP patients from analysis, neither administration of mechanical bowel preparation (p=0.3070) nor IV antibiotic duration (p=0.3537) was associated with median LOS. Multiple regression revealed that creation of a proximal diverting ostomy at the time of pull-through surgery significantly increased the odds of reoperation within 30 days (Odds Ratio: 6.7 (95% C.I.: 2.2-19.9); p=0.0007). Additionally, on multiple regression intraoperative blood transfusion significantly increased the odds of developing an SSI (OR: 15.4 (95% C.I.: 2.4-100.2); p=0.0042).

**Discussion:**

Surgical site infections after colorectal procedures can lead to significant patient morbidity and mortality. In adult patients, the rate of SSI has been reported to impact 15-30% of those who undergo elective colorectal surgery. Opportunities to decrease these infections have been reported in the literature, but the most scrutiny has surrounded the use of mechanical bowel prep and oral antibiotics.

Robust data for mechanical bowel prep and oral antibiotics does not exist in the pediatric colorectal literature, confounding how adult data can be extrapolated to this population. Aldrink and colleagues reported their results of a pilot study on infectious complications in pediatric patients who received a mechanical bowel prep compared to those who did not for elective colorectal procedures. Forty-four patients were enrolled in the study from December 2010 to
February of 2013; 24 patients received a mechanical bowel prep, and 20 did not. No oral antibiotics were administered to either group. All patients received an IV dose of antibiotics prior to surgery. The use of mechanical bowel prep did not impact rate of anastomotic leak, intra-abdominal abscess or wound infection compared to those that did not. Shah and colleagues performed a prospective, randomized trial comparing outcomes between pediatric patients receiving a bowel prep to those getting no bowel prep prior to undergoing an elective bowel resection or ostomy closure.5 No preoperative antibiotics were utilized. Thirty-two patients were enrolled into the study, with 18 in the bowel prep group and 14 in the no bowel prep group. No difference in wound infections was noted between the bowel prep and no prep groups (11.1% vs. 21.4%, p=0.63). Only one anastomotic leak was noted in the study, and that was in the bowel prep group.

As in these two pediatric colorectal studies, we found that administration of mechanical bowel preparation did not significantly impact the overall complication rate, rates of infectious complications, or anastomotic complications in patients undergoing pull-through procedures. The rates of infectious complications was 11.8% of those receiving a bowel prep vs. 9.5% in the no bowel prep (p=0.62).

Two anastomotic leaks were identified in our study. As in the Shah study both leaks occurred in patients having received mechanical bowel prep.

These findings support large adult cohort studies which demonstrated that use of a mechanical bowel prep alone did not improve complication rates over no prep.1,9 Koller et al concluded that mechanical bowel prep alone for the prevention of infectious complications should be abandoned.10 Adult studies have also demonstrated the superiority of oral antibiotic prep over both mechanical bowel prep and no prep. Kiran and colleagues in 2015 collected data
from the ACS-NSQIP data base to determine the impact of no bowel prep, mechanical bowel prep, or mechanical bowel prep plus oral antibiotics on the rate of SSI.1 There were a total of 8442 patients of which 27.2% had no prep, 45.3% had a mechanical prep with no antibiotics, and 27.5% had a mechanical bowel prep combined with oral antibiotics. They found that the overall rate of SSI was significantly higher in the no prep and mechanical bowel prep only groups. In addition, anastomotic leaks were also significantly higher in the no prep and mechanical prep only groups. The conclusion of their study indicated that the use of oral antibiotics with mechanical bowel prep significantly improved outcomes. In 2018, McSorley and colleagues performed a meta-analysis of the use of oral antibiotics in combination with preoperative IV antibiotics and mechanical bowel prep on rates of SSI in adults undergoing elective colorectal procedures.11 Interestingly, they found that use of preoperative oral antibiotics plus mechanical bowel prep along with IV antibiotic prophylaxis significantly decreased the rate of SSI and anastomotic leak compared to the group who received only mechanical bowel prep and IV antibiotic prophylaxis. We were unable to determine the impact of oral antibiotic administration in our study as only one patient was given that regimen prior to surgery and was thus excluded.

Bowel prep can cause dehydration, hypocalcemia, and hypokalemia, all of which may delay return of bowel function.12 However, in our study, there was no association between bowel prep administration and LOS among those patients not intentionally held NPO. Our findings are in contrast to Kiran, who showed decreased ileus (OR: 0.57; 95% C.I.:0.48-0.68) in those receiving mechanical bowel prep, with or without antibiotics.1 McSorley in their meta-analysis noted a decreased LOS in patients who received an oral antibiotic in combination with mechanical bowel prep and IV antibiotic prophylaxis compared to the group who received only mechanical bowel prep and oral antibiotics. (mean difference -0.6, -1 to -0.3).11 The role of oral
antibiotics in decreasing length of stay further highlights the need for their study in future pediatric trials.

Our study looked at patients who underwent pull-through procedures and further stratified them into type to determine if a difference in complication rates existed among those patients who received a mechanical bowel prep and those that did not. For most procedure types, no difference was seen. Only among patients who underwent perineal anoplasty was mechanical bowel prep administration associated with increased rates of infectious wound complications. Given the small number of patients who received bowel prep prior to their perineal anoplasty, the wound infection rate in this subgroup was disproportionately high. It is unclear whether this statistical finding represents a true clinical correlation. However, we can conclude that for all pull-through procedures, mechanical bowel prep alone did not decrease complication rates. Midura and colleagues compared mechanical bowel prep with or without oral antibiotics in decreasing complications in patients undergoing right, left, or segmental colectomy. \(^{13}\) They used the ACS-NSQIP data base for extraction of data from 2012-2015. Overall complications of anastomotic leak and surgical site infection were significantly decreased in the patients who received oral antibiotics in addition to their mechanical prep, which held true across all colectomy locations. Again, as our study did not utilize oral antibiotics, we are unable to make any conclusions whether their addition would be beneficial among different pull-through procedure types.

Use of mechanical bowel prep can be uncomfortable for pediatric patients, as nasogastric tubes are often needed for administration. The availability of oral antibiotic formulations of neomycin, metronidazole, and erythromycin further compound the difficulty of administration to pediatric patients. Controversy exists on how adult guidelines can be extrapolated to pediatric
patients, as adults have elective colorectal procedures for different disease states and also have different comorbidities. A recent retrospective study of the Pediatric Health Information System (PHIS) data base concluded that utilization of an adult evidenced based bowel prep strategy to decrease complications was only 22.9%. Pediatric surgeons are in a unique position to perform randomized trials to determine the role of mechanical bowel prep and oral antibiotics in elective colorectal procedures.

National guidelines recommend limiting intravenous prophylactic antibiotics to 24 hours or less. In our study group, patients receiving prophylactic antibiotics for less than 24 hours did not have increased rates of infectious wound or anastomotic complications, as would be expected. On initial univariate analysis, prophylaxis duration less than 24 hours was associated with reoperation within 30 days. Most (10/17) of the reoperations in our study were due to early small bowel obstruction, frequently secondary to small bowel volvulus around newly created stomas. This explains the association between concomitant stoma creation and reoperation seen on multivariate analysis. Controlling for concurrent diverting stoma creation revealed that there was no true relationship between postoperative antibiotic duration and the risk for reoperation (p=0.3069). All patients in our cohort received both a single pre-incision dose of antibiotics as well as some form of postoperative IV antibiotic prophylaxis, save for those patients treated as outpatients which were excluded from this analysis. Therefore we are unable to assess the role of preoperative antibiotics alone in this patient population.

Finally, patients receiving blood transfusion during surgery had an increased risk of developing infectious complications. This is a known association, though our odds ratio was much higher than those seen in the literature for neonates receiving perioperative transfusion (OR: 2.08; 95% C.I.: 1.59-2.72) and for patients undergoing surgery for Crohn’s disease (OR =
Only five patients received a blood transfusion in our study. Given this small number and the wide confidence interval obtained, it is likely that the odds ratio we observed overstates the true risk.

We found that some patients in our series received mechanical bowel prep despite having a proximal diverting stoma in place at the time of surgery. The decision for bowel prep in patients with a stoma in place was surgeon dependent, and a clear explanation for this decision was not routinely given in the chart. Presumably, for patients undergoing PSARP there was a potential for stoma takedown during the procedure, so a bowel prep was conducted as a precaution. Of our 57 PSARP cases, 15 were primary pull throughs and 42 had a stoma in place. Among the 42 with a stoma, 3 had takedowns and 16 (38.1%) received bowel prep. For those patients undergoing colectomy with J-Pouch or ileorectal anastomosis, they likely were administered bowel prep as the stoma was being taken down to make the pouch or anastomosis. Twenty of the 42 patients who received a J-Pouch (47.62%) had a stoma in place. Seven of these 20 (35%) received bowel prep. Seven patients underwent an ileorectal anastomosis, of which 5 (71.4%) had a stoma in place at time of surgery. Of these 5, 1 (20%) received bowel prep.

This study has several limitations. The retrospective nature of the study is a limitation. Patients were not randomly assigned to mechanical preparation or antibiotic duration groups, as these decisions were based on surgeon preference. If no information was provided regarding bowel preparation, it was assumed that none was given. This may not be a correct assumption for some patients, and these patients may have been assigned incorrectly. Furthermore, many factors including social factors, such as caregiver availability, ride availability, and the distance between the patient’s home and the hospital may influence the length of stay of patients. It is difficult to assess whether these effects are randomly distributed or whether they biased the results of this
study. Due to the small number of some pull-through types performed, interpretation of results obtained from the stratified analysis may be limited.

**Conclusion**

In this study, 180 pediatric patients underwent an elective pull-through procedure at Riley Hospital for Children at Indiana University Health between 2011 and 2017. Administration of mechanical bowel prep prior to surgery did not affect complication rates or LOS for pull-through procedures. However, it was associated with an increased rate of wound infections in those undergoing perineal anoplasty. Pediatric patients undergoing elective pull-through surgery can likely be spared the burden of mechanical bowel preparation with no increased risk for postoperative complications.

Once reoperations for early SBO following proximal stoma creation were controlled for, patients receiving intravenous antibiotics for 24 hours or less after surgery had similar rates of complications, including SSIs and anastomotic complications, compared to those who received antibiotics for longer. There is likely no benefit to continuing intravenous antibiotic prophylaxis beyond 24 hours in this patient population.

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References


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