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Review Article

Prevention of infectious complications after elective colorectal surgery in children: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee comprehensive review

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ABSTRACT

Objective: This goal of this review was to examine the clinical evidence in support of commonly utilized measures intended to reduce complications following elective colorectal surgery.
Data source: Literature searches were performed to identify relevant studies from Medline, PubMed, and Cochrane databases.
Study selection: The American Pediatric Surgery Association Outcomes and Clinical Trials Committee selected eight questions to address this topic systematically in the context of three management areas: 1) appropriate utilization of systemic antibiotics for colorectal procedures, 2) reduction of stool burden through mechanical bowel preparation, and 3) intraluminal gut decontamination through use of enteral nonabsorbable antibiotics. Primary outcomes of interest included the occurrence of infectious and mechanical complications related to stool burden and intraluminal bacterial concentration (incisional surgical site infection, anastomotic leakage, and intraabdominal abscess).
Results: The evidence in support of each management category was systematically reviewed, graded, and summarized in the context of the review's primary outcomes. Practice recommendations were made as deemed appropriate by the committee.
Conclusions: Clinical evidence in support of interventions to reduce infectious complications following colorectal surgery is derived almost exclusively from the adult literature. High-quality evidence to guide clinical practice in children is sorely needed, as the available data may have only limited relevance to pediatric colorectal diseases.

Surgical site infections (SSIs) are a costly and potentially preventable source of morbidity, representing the most common cause of hospital-acquired infection in the surgical population [1–3]. Along the spectrum of elective procedures, colorectal operations have been associated with the highest risk of SSI and other infectious complications owing to the heavy bacterial load of the colon and rectum [3,4]. Although the rate of SSI associated with colorectal surgery is difficult to estimate, rates in excess of 25% have been reported from several large series [1,3]. Inpatient hospital costs for patients undergoing a colorectal procedure complicated by an incisional SSI are approximately twice that for patients without an SSI, and deep organ-space infections may increase costs by nearly four-fold [5–7]. Although these epidemiological data are derived exclusively from the adult population, bacterial colonization of the colon occurs by the second week of life, and the concentration and

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microbiological profiles of stool are similar in adults and children [8,9]. It is therefore likely that colorectal procedures are similarly responsible for a disproportionate burden of perioperative complications and excess hospital cost within the scope of pediatric surgical practice.

In response to the relatively high rate of morbidity associated with colorectal surgery, three main categories of prophylactic strategies have evolved with the goal of reducing infectious complications: 1) appropriate utilization of systemic antibiotic prophylaxis before, during, and following operative procedures, 2) reduction of stool burden through the use of mechanical bowel preparation, and 3) intraluminal decontamination of the colon and rectum through the use of enteral, nonabsorbable antibiotics. Although the pediatric surgical community has broadly adopted a consensus opinion favoring systemic antimicrobial prophylaxis for reducing infectious complications, there remains little agreement regarding the choice and optimal timing of these agents nor the role and efficacy of enteral antibiotics and mechanical bowel preparation as adjunct therapies [10,11]. Therefore, the purpose of this review was to examine the available evidence regarding these interventions (and combinations of interventions when available) and to propose recommendations based on the strength of available data. The American Pediatric Surgery Association Outcomes and Clinical Trials Committee selected the following eight questions to review the three categories cited above:

1. Which parenteral antibiotics should be used prophylactically and at what dose should they be administered?
2. When should parenteral antibiotics be administered relative to the operative incision for optimal prophylaxis?
3. How often should parenteral antibiotics be redosed during colorectal procedures?
4. How long should parenteral antibiotics be continued following colorectal procedures?
5. Does preoperative administration of enteral, nonabsorbable antibiotics combined with a mechanical bowel preparation reduce infectious complications?
6. Does the administration of preoperative mechanical bowel preparation without enteral antibiotics reduce infectious complications?
7. Does the administration of enteral antibiotics without a mechanical bowel preparation reduce infectious complications?
8. Does preoperative enema administration reduce infectious complications in colorectal procedures involving the rectum?

1. Methods

Literature searches were performed to identify English language publications using Medline, PubMed, and pertinent Cochrane reviews without a defined date range. Searches were conducted using the following search terms: colorectal surgery, antibiotic prophylaxis, infection control and prevention, mechanical bowel preparation, surgical site infection, anastomotic leakage, intraabdominal abscess and deep-space infection. Additional literature searches were conducted relating to the specific review questions. Studies were included in the review if they met criteria for providing either Class I or Class II evidence as defined by the Oxford Centre for Evidence-Based Medicine (Table 1) [12]. Very little data were found in the pediatric literature to support practice recommendations across all eight review questions, and none of the published studies including children provided Class I or higher-quality Class II evidence. However, given the similarities between the adult and pediatric populations with respect to fecal bacterial concentration and microbiological profiles, it was the committee's consensus that data from adult studies should be considered relevant to the pediatric population, and so chose to include adult-focused studies in this review. The primary outcomes of interest included infectious and mechanical complications plausibly related to stool burden and intraluminal bacterial concentration (incisional surgical site infection, anastomotic leakage and intraabdominal abscess). The evidence supporting each management question was reviewed and graded on the basis of established guidelines, and practice recommendations were made based on the strength of available evidence.

2. Literature review

2.1. Optimal use of parenteral antibiotics

The role of prophylactic intravenous antibiotic administration prior to elective colonic surgery is well established and has long been considered the standard of care in adult colorectal surgery. In a 2009 Cochrane review of ten clinical trials comparing outcomes in patients receiving parenteral antibiotic prophylaxis to none (or placebo), a significant reduction in the risk of SSI was observed in eight of the ten trials, with a reduction in relative-risk (RR) ranging from 59% to 88% [13–20]. A meta-analysis of all ten trials demonstrated a statistically significant benefit in favor of parenteral antibiotic prophylaxis, with a reduction in the aggregate SSI rate from 39% to 10% (RR 0.30, 95% CI 0.22–0.41) [21].

At the time of this review, no Class I data were available in the literature to make a similar statement regarding the efficacy of prophylactic antibiotics in pediatric colorectal surgery. No clinical trial was found that included children in the Cochrane review cited above or in a similarly directed MEDLINE search strategy when cross-referenced to the pediatric population. Pediatric surgeons have thus far had to rely on adult derived data to make choices regarding intravenous (IV) antimicrobial prophylaxis, and consequently, the data utilized to support the conclusions in the following section are derived almost exclusively from the adult literature.

2.1.1. Which parenteral antibiotics should be used prophylactically and at what dose should they be given?

Effective use of prophylactic IV antibiotics in elective colorectal surgery requires that the drug (or drugs) has activity against a broad range of colonic flora. Preoperative IV antibiotics used in elective colorectal surgery must therefore cover both the aerobic and anaerobic bacteria commonly found in the colon and rectum. Agents that solely target anaerobic or aerobic bacteria have been shown to be inferior to broad spectrum agents in a multitude of clinical trials and a large meta-analysis [21]. In a Cochrane review of 15 such trials, the addition of anaerobic coverage to antimicrobial agents primarily effective against aerobic organisms resulted in a nearly 50% further reduction in the risk of SSI for colorectal procedures (RR 0.55, 95% CI 0.35–0.85) [21]. Similarly, a nearly 60% further reduction in SSI rates was observed with the addition of aerobic gram-negative coverage to agents that principally covered anaerobic bacteria (RR 0.41, 95% CI 0.23–0.71) [21].

Although the efficacy of broad-spectrum IV antibiotic prophylaxis is now well-established, the optimal choice of antibiotic agents remains controversial. In a systematic review of 147 clinical trials including more than 70 antibiotic combinations, Song and Glenny found no significant differences in the prevention of SSIs within the majority of trials

Table 1
Grading classification for levels of clinical evidence and grades of recommendation according to the Oxford Centre for Evidence-based medicine*.

Classes of evidence	Grades of recommendation
I Systematic review of RCTs or with one RCT with narrow CI	A – Consistent Level 1 studies
II Cohort studies, low quality RCTs, outcomes research	B – Consistent Level 2 or 3 studies or extrapolation from Level 1 studies
III Case–control studies	C – Level 4 studies or extrapolations from Level 2 or 3 studies
IV Case series	D – Level 5 evidence or inconsistent or inconclusive studies
V Expert opinion	

RCT: randomized controlled trial, CI: confidence interval.
* www.cebm.net.