Recent trends in the use of antibiotic prophylaxis in pediatric surgery

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Abstract

Aims: The use of surgical antibiotic prophylaxis (AP) in children is poorly characterized. The aims of this study were to examine (1) trends in the use of AP for commonly performed operations, (2) appropriateness in the context of available guidelines, and (3) adverse events potentially attributable to AP.

Methods: We conducted a 5-year retrospective analysis of 22 children’s hospitals (January 2005-March 2009) for all patients younger than 18 years who underwent 1 of the 40 commonly performed general and urological procedures. Indications for AP were defined by published specialty-specific guidelines. Clostridium difficile infection and surrogate events for drug allergy (diphenhydramine and epinephrine administrations) were examined as potential antibiotic-associated adverse events.

Results: Procedures of 246,316 were identified, of which 25% met criteria for AP. Eighty-two percent of the children received antibiotics during procedures when AP was indicated (range, 60%-96% by hospital), and 40% of the patients received antibiotics when there was no indication (range, 10%-83%). The likelihood of receiving AP was significantly different between hospitals for all procedures examined ($P < .0001$ for each procedure). Adverse events were significantly more frequent in children receiving AP than in those who did not (odds ratio [95% confidence interval] $C. difficile$: 18.8 [6.9-51.5], $P < .0001$; epinephrine: 1.8 [1.7-2.0], $P < .0001$; diphenhydramine: 6.0 [5.6-6.5], $P < .0001$).

Conclusions: Significant variation exists in the use of AP in the pediatric surgical population. Many children do not receive AP when indicated, and an even greater proportion may receive antibiotics when there is no indication. These findings may have profound implications from a public health perspective when extrapolated to all children undergoing surgical procedures.

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Keywords: Antibiotic prophylaxis; Surgical site infection; Infection prevention and control; Quality improvement; Pediatric surgery; Urology

Little is known about practice patterns for the use of antibiotic prophylaxis (AP) in the current pediatric surgical population and whether trends are in line with currently...
recommended guidelines. Appropriate use of AP has been shown to reduce the incidence of surgical site infections (SSIs), a significant and preventable source of morbidity and mortality in hospitalized patients [1-10]. Increasing evidence also suggests that giving antibiotics when they are not indicated is a potentially harmful practice, exposing patients to the unnecessary risk of side effects and antibiotic-associated complications such as *Clostridium difficile* infection [11-13]. Furthermore, this practice has been strongly linked to facilitating the emergence of resistant organisms [11,14-17].

With the considerations above, there may be significant public health implications surrounding the appropriate use of surgical AP from a population-based perspective. The goal of this analysis was to characterize practice patterns for the use of surgical AP in children by way of 3 specific aims: (1) to characterize national variation in the use of AP for commonly performed pediatric general and urologic surgical procedures, (2) to characterize the appropriateness of these trends in the context of currently available guidelines, and (3) to examine adverse events potentially attributable to the use of surgical AP in children.

### 1. Methods

We conducted a retrospective cohort study by performing a 6-year audit (January 2003-March 2009) of perioperative antibiotic-use rates using the Pediatric Health Information System (PHIS) database. Pediatric Health Information System is an administrative database managed by the Child Health Corporation of America (CHCA; Shawnee Mission, KS) that contains a wide array of discharge-level data from 42 freestanding children’s hospitals collectively representing a broad geographic and socioeconomic population. Information contained within the PHIS database includes primary and secondary *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnostic and procedural codes, demographic information, and detailed billing data for all inpatient and outpatient surgical encounters. This includes date-stamped pharmacologic billing data that can be used to identify antibiotic agents and their respective administration dates during the hospital encounter. We limited our analysis to the 22 of 42 PHIS hospitals that submitted outpatient procedure and complete pharmacologic data during the period of study. This study was approved by the Children’s Hospital Boston Institutional Review Board.

#### 1.1. Study population

All patients younger than 18 years who underwent 1 of the 40 most commonly performed pediatric general and urologic procedures were identified. To limit the analysis to cases where AP would be potentially relevant, we excluded cases where patients were already receiving antibiotics for preexisting infections (defined by receiving any type of antibiotic at least 1 day before the procedure), cases where intraoperative cultures were obtained (indicating the possibility of a contaminated case), and procedures that would be classified by the Centers for Disease Control and Prevention as a contaminated or dirty case (suggesting that antibiotics were given for treatment rather than prophylactic indications) [18]. Of note, patients receiving antibiotics associated with bowel preparations (eg, erythromycin) before the date of surgery were not excluded. We also excluded cases where the decision to use AP may have been influenced by an underlying condition associated with immunodeficiency. These included patients with a diagnosis of an immunodeficiency disorder, cancer, diabetes mellitus, malnutrition, and those receiving oral or intravenous steroids during the perioperative period. Finally, we excluded cases where multiple procedures were performed at the same time to ensure the use of AP could be associated with a single procedure.

#### 1.2. Calculation of procedure-specific use rates for AP

Antibiotics administered during the perioperative period were considered prophylactic if they were given parentally during the same calendar day as the surgical procedure. Procedure-specific AP use rates were calculated for all 40 procedures by dividing the number of patients undergoing a specific procedure that received AP by the total number of patients undergoing the procedure. Procedure-specific use rates were calculated for the entire cohort and for each of the 22 centers individually. \( \chi^2 \) Tests were used to compare procedure-specific AP use rates between hospitals (SAS v. 9.0; SAS Institute, Cary, NC).

#### 1.3. Calculation of use rates based on appropriate and inappropriate indications

To define which procedures would be considered appropriate for AP, we conducted an extensive literature search of consensus statements and specialty-specific guidelines using the PubMed search engine and cross-referenced these with Centers for Disease Control and Prevention recommendations [3,18-26]. From these sources, we defined appropriate indications as all clean-contaminated procedures (where the gastrointestinal, genitourinary, or respiratory tract was entered with minimal soilage) and clean procedures where the potential morbidity of an infectious complication was excessively high (procedures involving the central nervous system, open fractures, and the insertion of central lines and other prosthetic devices). The administration of perioperative antibiotics was considered inappropriate for AP if they were given outside these indications.

The rate of appropriate AP use was calculated by dividing the number of patients receiving perioperative antibiotics for all procedures meeting the indication criteria for AP by the
total number of patients undergoing these procedures. Similarly, the rate of inappropriate AP use was calculated by dividing the number of patients receiving perioperative antibiotics for all procedures not meeting the indication criteria for AP by the total number of patients undergoing these procedures. The rates of appropriate and inappropriate AP use were calculated for the entire cohort and for each of the 22 hospitals individually.

1.4. Calculation of adverse event rates

To characterize the incidence of adverse events potentially associated with the administration of AP, we identified all patients with a diagnosis of *C difficile* infection within 30 days of their index procedure and those receiving diphenhydramine or epinephrine during the perioperative period (as surrogate events for allergic reaction). Data are quoted as median (range). χ² Tests were used to compare the proportions of patients with these events between the cohort of patients who received AP and those that did not. *P* ≤ .05 was regarded as significant.

2. Results

Our search criteria identified 246,316 cases with a median number of 23,435 cases per hospital (range, 4212-36,129). Seventy-five percent (185,552) were male, and the median age was 3.3 years. Fifty percent of all patients in the study cohort received perioperative antibiotics the same day as their procedure, and this proportion ranged from 33% to 75% across hospitals. Procedure-related AP rates ranged from 20% for patients undergoing abdominal wall hernia repairs to 98% for patients undergoing colectomies (Fig. 1). The greatest variation in procedure-specific AP rates between hospitals was observed for circumcision, meotatomas, penile reconstructions, and epispadias repairs, whereas the least variation was observed for colectomies, small bowel resections, and appendectomies (nonperforated). Procedure-specific AP rates were significantly different between hospitals for all 40 procedures examined in this study (*P* < .001 for each procedure; Fig. 1).

Twenty-five percent (61,579) of all cases met indication criteria for AP, and 82% (50,494) of these patients received antibiotics in the perioperative period. Of the 75% (184,737) of cases that did not meet indication criteria for AP, 40% (73,895) of patients received perioperative antibiotics. The proportion of children receiving perioperative antibiotics for procedures when AP was indicated was significantly different between hospitals (range, 60%-96% by hospital; *P* < .001; Fig. 2), as was the proportion receiving antibiotics when AP was not indicated (range, 10%-83% by hospital; *P* < .001; Fig. 2).

The incidence of adverse events was significantly higher in patients receiving AP than in those who did not, including a higher odds ratio (OR) of *C difficile* infection (AP, 0.061% [76/123,604] vs non-AP, 0.003% [4/122,632]; OR, 4.1; 95% confidence interval [CI], 6.9-51.5; *P* < .0001), a higher OR of receiving epinephrine (AP, 2.33% [2878/120,804] vs
non-AP, 1.28% [1571/121,065); OR, 1.8; 95% CI, 1.7-2.0; \( P < .0001 \), and a higher OR of receiving diphenhydramine (AP, 3.84% (4755/118,925) vs non-AP, 0.66% (810/121,826); OR, 6.0; 95% CI, 5.6-6.5; \( P < .0001 \)).

3. Discussion

Surgical site infections remain a significant source of preventable morbidity and mortality in hospitalized patients [10,27]. The appropriate use of AP has been shown to decrease the incidence of SSIs and the costs associated with them from increased length of stay, antibiotic treatment, and infection-related diagnostic testing. At the same time, considerable effort has been put forth to educate both physicians and the public alike to the hazards of prescribing unnecessary antibiotics [15-17,28]. Despite the availability of consensus guidelines designed to facilitate the appropriate use of AP, we found a significant variation in this practice for the most commonly performed operations in pediatric surgery. In this regard, many children did not receive antibiotics when prophylaxis was indicated, and a relatively greater proportion may have received antibiotics when there was no clear benefit.

The results of this study are consistent with previous reports characterizing variation in the use of surgical AP [29-36]. Specific to the pediatric population, 62% of patients who underwent orthopedic procedures continued to receive antibiotics without a documented infection [37]. In a survey of pediatric cardiothoracic surgeons in the United States, 68% reported continuing prophylactic antibiotics for longer than 2 days despite evidence from the adult literature demonstrating similar efficacy with 24 hours of coverage [38,39]. To our knowledge, this is the first study specifically focusing on procedures within the scope of pediatric general and urologic surgical practice. Furthermore, we are not aware of any study that has used a large multicenter administrative database to characterize AP use trends on a national level.

The implications of overuse and underuse of surgical AP cannot be overstated. Underuse may increase the rate of SSIs and considerably increase infection-related hospital costs. In fact, major infectious complications may increase the duration of hospitalization as much as 20-fold and the cost of hospitalization nearly 5-fold [40]. On the other hand, overuse of AP can lead to the emergence of resistant organisms and increased hospital costs associated with the diagnosis and treatment of antibiotic-associated adverse events. The observation in our study that perioperative antibiotics significantly increased the odds of developing \textit{C difficile} infection provides yet more compelling evidence that giving even a single dose of prophylactic antibiotics is not without risk. This finding is in line with other studies that have characterized an increased risk of \textit{C difficile} infection with the use of surgical AP [41-43].

There are several potential explanations for the variation in AP use rates observed between hospitals. Diagnostic uncertainty, increasing pressure from hospitals and regulatory agencies to reduce nosocomial infection rates, inexperienced clinicians, and patient preferences have all been found to influence decision making in this regard [44]. Furthermore, the decision to use prophylactic antibiotics may

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**Fig. 2** Interhospital variation in the likelihood of receiving perioperative antibiotics for procedures when antimicrobial prophylaxis (AP) was indicated and not indicated by currently recommended guidelines. Each set of bars represents a single hospital and reflects the proportion of patients receiving perioperative antibiotics for all procedures based on indication criteria for AP.
also hinge upon a patient’s condition and comorbidity profile. In fact, the American Society of Anesthesiologists score and the National Nosocomial Infection Surveillance System risk index score have both been shown to have predictive value in determining the rate of postoperative infections [45]. However, neither of these prediction tools has been factored into indication criteria for currently existing surgical AP guidelines.

Other factors underlying variation in the use of surgical AP in children may be unique to the pediatric population. In this regard, many of the current guidelines and specialty-specific recommendations used for the pediatric population are based on adult clinical data from 1979 and 1989. It is plausible that some surgeons may not find current guidelines relevant to their pediatric patients. Furthermore, confusion may exist as to what constitutes “best evidence” on which to base surgical AP decision making when adult-derived consensus guidelines and pediatric-focused observational data are not in agreement. Inguinal hernia repair and pyloromyotomy are examples of such procedures. Single-institutional case series have suggested some benefit for prophylactic antibiotics for these procedures, although they are technically clean cases where AP would not otherwise be indicated [23,46].

The results of this study must be carefully considered in the context of its limitations. First and foremost, the results of this study were based on the analysis of administrative data. The misclassification or miscoding of surgical procedures, antibiotic administration data, and outcomes of interest within the PHIS database is certainly possible. Furthermore, our analysis assumes that antibiotics administered on the day of the procedure were given for prophylactic indications. Although this is likely to be the case in most cases, we cannot determine from the database whether antibiotics were given for prophylactic indications or for some other considerations. Finally, the generalizability of our findings to pediatric surgical care outside the PHIS hospital network may be limited. In this regard, the PHIS database serves a consortium of tertiary-care, freestanding academic teaching hospitals. These institutions may differ from community and other nonacademic hospitals in their use patterns for AP.

In conclusion, we found a significant variation in the use of AP between freestanding children’s hospitals for commonly performed general pediatric and urologic surgical procedures. Many children may not be receiving antimicrobial prophylaxis for procedures where there is proven benefit, and a relatively greater proportion may be receiving antibiotics when there is no clear indication for prophylaxis. Further efforts should explore the nature of this variation and develop strategies to bring practice patterns more in line with current use guidelines. Use trends should also be examined for the pediatric surgical subspecialties to establish the need for multidisciplinary collaboration. Given the public health implications of our findings when extrapolated to the national and global population, strategies to facilitate compliance with use guidelines will be critical for preventing SSIs while at the same time controlling costs, minimizing adverse events, and mitigating the emergence of resistant organisms.

References


