Impact of standardization of antimicrobial prophylaxis duration in pediatric cardiac surgery

Sundeep Bath, PharmD,[a,b] Jason Lines, PA,[b] Ann M. Loeffler, MD,[b] Ashim Malhotra, PhD,[a] and R. Brigg Turner, PharmD[a,b]
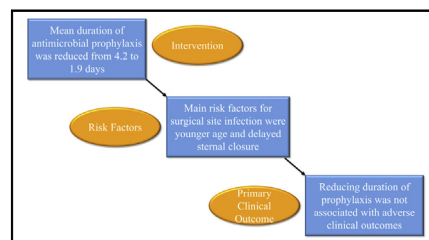
ABSTRACT

Objectives: The optimal duration of antimicrobial prophylaxis following pediatric cardiac surgery is still debated. Adult studies suggest that shorter durations are adequate, but there is a paucity of data on pediatric patients.

Methods: This quasi-experimental study reviewed the charts of patients 18 years and younger who underwent cardiac surgery from April 2011 to November 2014 at a single institution. Starting in April 2013, a protocol was implemented to limit antimicrobial prophylaxis to 48 hours following sternal closure. Two analyses were performed: (1) identification of risk factors for surgical site infections from the entire cohort, and (2) comparison of surgical site infection incidence in the pre- and postprotocol groups.

Results: In the entire cohort, delayed sternal closure (adjusted odds ratio [OR], 5.7; 95% confidence interval [CI], 1.8-17.9) and younger age (adjusted OR, 2.1; 95% CI, 1.1-3.8) were associated with incidence of surgical site infection. Following the protocol change, duration of antimicrobial prophylaxis decreased from 4.2 ± 2.7 to 1.9 ± 1.3 days ($P < .0001$). After adjusting for age and delayed sternal closure, the postprotocol group had an adjusted OR of 0.98 (95% CI, 0.32-3.00) for occurrence of surgical site infection. Other outcomes were not altered following the protocol change.

Conclusions: Restricting antimicrobial prophylaxis to 48 hours following pediatric cardiac surgery did not increase the incidence of surgical site infection at our institution. Further study is needed to validate this finding and to identify practices that reduce surgical site infections in those with delayed sternal closure. (J Thorac Cardiovasc Surg 2016;152:1115-20)

Summary of risk factors, intervention, and main result.

Central Message

Limiting antimicrobial prophylaxis to 48 hours after pediatric cardiac surgery did not increase incidence of surgical site infection.

Perspective

The optimal duration of antimicrobial prophylaxis following pediatric cardiac surgery is still debated. Limiting antimicrobial prophylaxis to 48 hours following surgery did not increase the incidence of surgical site infection. Efforts should be made to limit antimicrobial prophylaxis duration while identifying strategies to prevent infection in those patients who require delayed sternal closure.

Antimicrobial prophylaxis for cardiac surgery is a widely accepted practice that has demonstrated substantial reductions in postoperative morbidity and surgical site infections (SSIs), especially for difficult to treat cardiothoracic infections such as mediastinitis and endocarditis.[1] However, the optimal duration of antimicrobial prophylaxis in pediatric cardiac surgery has not been determined. Recently published consensus guidelines by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America recommend antimicrobial prophylaxis to be continued up to 24 hours postoperatively in adult cardiac surgery.[2] This guideline identifies a deficit of data in pediatric patients and recommends prophylaxis in pediatrics be based on findings from adult studies. Other guidelines from the Society of Thoracic Surgeons recommend prophylaxis up to 48 hours postoperatively but also do not have formal recommendations for pediatric patients.[3,4] Basing decisions for pediatric patients on

Scanning this QR code will take you to the article title page.

> **Abbreviations and Acronyms**
> ICU = intensive care unit
> IV = intravenous
> SSI = surgical site infection

studies comprised mainly of adults can be problematic[5] because the occurrence of SSIs in pediatric cardiac procedures has been reported to be higher than in adult patients in several studies.[6-8] Whereas adequate duration of antimicrobial therapy is necessary to prevent SSIs, extended prophylaxis may be associated with complications such as alteration of patient bacterial flora leading to increased colonization with resistant bacteria, superinfections including *Clostridium difficile* infection, and exacerbated drug toxicity.[9] For this reason, selecting the shortest duration possible for antimicrobial surgical prophylaxis is preferred.[4] We hypothesized that limiting antimicrobial prophylaxis postoperatively would result in a similar incidence of SSIs while also reducing overall antibiotic exposure. The purpose of this study was to evaluate the clinical impact after implementation of a protocol that limited postoperative prophylaxis to 48 hours following sternal closure in pediatric cardiac surgery.

PATIENTS AND METHODS
Study Design
This quasi-experimental study evaluated patients treated from April 2011 to November 2014, at Randall Children's Hospital in Portland, Oregon. Randall Children's Hospital is a 165-bed children's hospital with 24 pediatric intensive care unit (ICU) beds and a level 3 neonatal ICU with 46 beds. All patients who undergo cardiac surgery at our facility are taken immediately postoperatively to the ICU from the operating room. Incisions are protected from contamination by application of 2-octyl-cyanoacrylate adhesive. In addition, bacitracin irrigation is performed prior to sternal closure in all patients. The same surgeons performed all cardiac procedures throughout the study period. Starting in April 2013, a protocol was implemented limiting antimicrobial prophylaxis to 48 hours following sternal closure; however, the decision on length of prophylaxis was ultimately at the discretion of the treating medical team. Before the protocol, the duration of antimicrobial prophylaxis was decided by each practitioner and varied substantially. This protocol was developed in response to a hospital-wide antimicrobial stewardship effort and was initiated by the cardiac surgeons and medical teams providing care for these patients with the intent to standardize care. Two separate analyses were performed. First, factors associated with incidence of SSI were identified from the entire cohort. Second, incidence of SSI was compared between the preprotocol (prior to April 2013) and postprotocol (after April 2013) groups. The Legacy Health Institutional Review Board granted a waiver of informed consent for this study.

Inclusion/Exclusion Criteria
Patients who were 18 years or younger and underwent cardiac surgery during the dates specified were screened for inclusion. Patients were excluded if they died or were discharged within 48 hours of surgery, had repeat surgery within 7 days of original surgery except for exploration for suspected infection, were receiving antimicrobials prior to surgery, or if surgery was limited to pacemaker implantation. Patients who underwent an additional surgery within 30 days of the original surgery were only included once in the study.

Outcomes
The primary outcome was incidence of SSI as defined by the Centers for Disease Control and Prevention/National Healthcare Safety Network guidelines.[10] Secondary outcomes included hospital, ICU, and infection-related length of stay; incidence of receipt of additional antimicrobials for suspected infection; and mortality. Mortality was defined as all-cause death occurring during the admission or within 30 days of surgery.

Data Collection
Data were retrospectively collected through a hospital database which is maintained for submission of information biannually to the Congenital Heart Surgery Database of the Society of Thoracic Surgeons as well as by data extraction from the electronic health record. Appropriate prophylaxis was defined as receipt of intravenous (IV) cefazolin at a dose of 25 mg/kg or greater within 60 minutes before incision with re-dosing every 4 hours during surgery. IV vancomycin was also considered appropriate for prophylaxis for those with penicillin allergy or documented methicillin-resistant *Staphylococcus aureus* on a preoperative nasal swab. Weight for age percentile was calculated for each patient at the time of surgery. The Society of Thoracic Surgery-European Association for Cardio-Thoracic Surgery congenital heart surgery mortality score was determined by the type of procedure being performed.[11] Infection-related length of stay was calculated as the time from receipt of additional antimicrobials (not prophylaxis) until the time of discontinuation or until hospital discharge.

Statistics
Demographic and baseline data were analyzed by t test, Wilcoxon-Mann-Whitney, chi-square, and Fisher exact tests as appropriate. Univariate analysis was performed to identify factors associated with SSI in the entire cohort. Factors with $P < .2$ on univariate analysis were included in a stepwise logistic regression model with backward elimination with $P > .2$ used for elimination. Incidence of SSI and other outcomes were then compared between the pre- and postprotocol groups using t test, Wilcoxon-Mann-Whitney, chi-square, and Fisher exact tests as appropriate. A multivariate logistic regression model was performed to identify if the postprotocol group was associated with higher incidence of SSI after controlling for factors identified in the stepwise logistic regression model. A final model, adjusting for factors identified in the stepwise logistic regression model, was performed to identify any effect of duration of antimicrobial prophylaxis on SSI. Data with $P < .05$ were considered significant. All analyses were performed in Stata version 13 (StataCorp 2013. Stata Statistical Software: Release 13. College Station, Tex: StataCorp LP).

RESULTS
A total of 528 patients met the initial inclusion criteria and 82 were subsequently excluded. Thus, 446 patients were included in the final analysis (see Figure 1). Of these patients, almost all (96.2%) underwent a procedure requiring sternotomy. Fifteen (3.4%) patients developed an SSI, with 11 defined as superficial and 4 as deep incisional. Univariate analysis revealed several factors to be associated with the incidence of SSI (Table 1). Stepwise logistic regression identified younger age and delayed sternal closure to be independently associated with SSI (Table 2). The incidence of SSI in patients with delayed sternal closure was 17.6% versus 1.5% in those without delayed sternal closure ($P < .0001$). In addition,