Surgical Site Infections in Children with Beta-Lactam Allergy: A Matched Cohort Study

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Abstract

BACKGROUND: Surgical site infections (SSIs) are a significant cause of morbidity and mortality. The administration of appropriate pre-operative antimicrobial prophylaxis (AMP) reduces SSI risk and beta-lactam antibiotics are considered the most effective agents. Studies in adult patients found increased SSI risk in patients with documented beta-lactam allergy (BLA) due to use of second line AMP agents. The SSI risk in BLA pediatric patients is not well-described.

METHODS: We conducted a retrospective matched cohort study of patients (1-19 years-old) who underwent a surgical procedure at a quaternary pediatric hospital during 2010-2017. Patients with documented BLA at the time of surgery were matched 1:1 to patients with no BLA by age at surgery, National Surgical Quality Improvement Program (NSQIP) category, surgical calendar year, and presence of complex chronic conditions (CCC). AMP by BLA status was considered appropriate if recommended by the 2013 American Society of Health-System Pharmacists (ASHP) guidelines, antibiotic class appropriate, or recommended by an infectious disease physician. McNemar's test was used to assess differences in SSI rates and antibiotic regimen appropriate for BLA status between BLA and no BLA groups.

RESULTS: Of the 11878 surgical procedures among 9781 patients during the study period, 1021(9%) of patients had a reported BLA and we matched 972. SSI was rare in both groups and there was no significant difference in rates (18 (1.9%) in no BLA, 17 (1.8%) in BLA, p=1.0). BLA were more likely to receive an antibiotic regimen considered inappropriate for BLA status (22%) compared to no BLA (3%) with 89% receiving a beta-lactam-containing AMP regimen (p<0.01).

CONCLUSION: BLA was not associated with increased SSI risk in the pediatric patients studied. Interestingly, a significant proportion of children with a documented allergy received a beta-lactam for AMP. This suggests some providers recognize that allergy labels are inaccurate and may be comfortable administering beta-lactam AMP regardless of allergy status.

Introduction

- Surgical site infections (SSI) are a significant cause of morbidity and mortality in hospitalized patients.
- In pediatric patients, SSIs comprise 6-30% of HAIs and occur in 1-2% of surgical patients.
- The appropriate use of antimicrobial prophylaxis (AMP) significantly decrease the incidence of SSIs for procedures that require perioperative antibiotics.
- Beta-lactam antibiotics are preferred and cefazolin is usually the first-line choice due to its bactericidal activity, pharmacokinetics, and antimicrobial coverage.
- However, up to 10% of patients report a beta-lactam allergy (BLA) and subsequently receive a non-beta-lactam antibiotic perioperatively.
- Evidence suggests that 90-99% of patients with a reported BLA do not have a true allergy.
- BLA has been associated with an increased risk of HAIs and few studies have addressed SSI risk in surgical patients, adult or pediatric, with BLA.

Hypothesis

- Gap: Few studies evaluate SSI risk in pediatric patients with reported BLA.
- Hypothesis: Reported BLA in pediatric patients increases the risk of SSI.
- Aims:
  1. Assess perioperative AMP choice based on BLA status.
  2. Evaluate SSI risk in pediatric surgical patients with BLA

Methods

Data Source
- We conducted a retrospective cohort study of pediatric patients 1-19 years of age at a large quaternary pediatric institution from 2010-2017.
- Excluded patients were <1-year-old, had previous bone marrow transplant, or underwent procedures that did not warrant AMP.
- Data was extracted from Epic and Pediatric Health Information System (PHIS).
- We utilized institutional procedure and SSI data as reported to National Surgical Quality Improvement Program (NSQIP).

Exposure
- BLA was defined as any documented allergy of any beta-lactam antibiotic at the time of surgery regardless of reaction type.
- We used allergy status at time of the first procedure if patient underwent multiple procedures.

Outcomes
- The primary outcome was perioperative AMP use, defined as antibiotic administration from 60 minutes prior to the procedure through the end of surgery.
- AMP was categorized as:
  1. Tier 1: if 2013 American Society of Health-System Pharmacist (ASHP) and institutional guidelines were followed.
  2. Tier 2: if a class-appropriate antibiotic was used or the plan was recommended by an infectious diseases physician
  3. Inappropriate: if not tier 1 or tier 2.
- The secondary outcome was SSI as defined and reported to the National Healthcare Safety Network (NHSN) through surveillance by the infection prevention team.
- We applied NSQIP definitions for procedure categories and final analysis.

Covariates and Confounders
- Patient demographics included age, sex, race, ethnicity, and payor category.
- Complex chronic conditions were identified using codes from PHIS.

Statistical Analysis
- Patients were matched 1:1 by age at time of surgery within calendar year, NSQIP category, surgical calendar year, and presence of complex comorbid conditions.
- We assessed AMP regimens and SSI rates by BLA status using McNemar's test.

Results

Patient Characteristics
- During the study period, there were 9,781 patients who met inclusion criteria; 1021 (9%) of patients reported BLA (**Figure 1**).
- There was a significant difference between patients with BLA and patients with no BLA based on race (p=0.002) and complex chronic conditions (p = 0.003, **Table 1**).

Outcomes
- There was a difference in antibiotic appropriateness (p<0.001) with many patients receiving "inappropriate" AMP if they had BLA (211 or 21% of BLA patients, **Table 2**).

Results

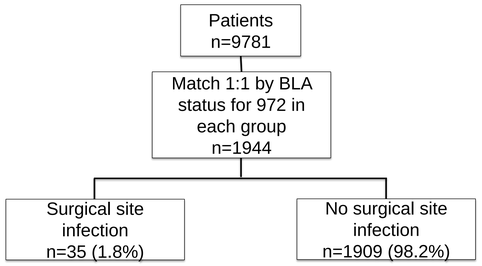

Figure 1. Consort flow diagram

Table 1. Patient Demographics

Characteristic	No BLA	BLA	P value
Age (years)	11.3 (range 6.7-15.1)	11.4 (range 6.9-15.0)	0.94
Female gender	459 (47.2%)	465 (47.8%)	0.79
Race			0.002
White	784 (81.5%)	841 (87.2%)	
Black	82 (8.5%)	48 (5.0%)	
Asian	31 (3.2%)	20 (2.1%)	
Multiracial or other	65 (6.8%)	56 (5.8%)	
Hispanic or Latino Ethnicity	32 (3.3%)	29 (3.0%)	0.678
Complex chronic condition count			0.003
0	435 (44.8%)	420 (43.2%)	
1	175 (18.0%)	190 (19.5%)	
2	143 (14.7%)	139 (14.3%)	
3	121 (12.4%)	86 (8.8%)	
≥4	98 (10.1%)	137 (14.1%)	
Payor Category			0.53
Private	637 (65.5%)	650 (66.9%)	
Public	335 (34.5%)	322 (33.1%)	
NSQIP Categories			1.0
Gastrointestinal	408 (42.0%)	408 (42.0%)	
Genitourinary	102 (10.5%)	102 (10.5%)	
Head and Neck	93 (9.6%)	93 (9.6%)	
Neurosurgery	172 (17.7%)	172 (17.7%)	
Orthopedics	126 (13.0%)	126 (13.0%)	
Plastics	33 (3.4%)	33 (3.4%)	
Thoracic	38 (3.9%)	38 (3.9%)	

Table 2. Antibiotic Appropriateness by BLA Status

Characteristic	No BLA	BLA	P value
Antibiotic Appropriateness			<0.001
Tier 1	859 (88.4%)	720 (74.1%)	
Tier 2	87 (9.0%)	41 (4.2%)	
Inappropriate	26 (2.7%)	211 (21.7%)	

- There was no significant differences in SSI in patients who had BLA compared to patients without BLA (**Table 3**).

Table 3. SSI by BLA Status.

SSI Status	No BLA	BLA	Total	P value
No SSI	954	955	1909	1.0
SSI	18 (1.9%)	17 (1.8%)	35	
Total	972	972	1944	

Results

- When performing a sensitivity analysis, we noted our institution updated guidance in 2015 to encourage beta-lactam AMP in patients with BLA if there was no diagnosis of anaphylaxis.
- Children with BLA still receive less beta-lactams, however, than pediatric surgical patients with reported BLA (23.7% vs 93.7%, **Table 4**).

Table 4. Beta-Lactam AMP Receipt by BLA Status.

	No BLA	Yes BLA	Total
No beta-lactam	683 (46.7%)	779 (53.3%)	1462
Yes beta-lactam	10174 (93.7%)	242 (23.7%)	10416
Total	10857	1021	11878

- When comparing pediatric patients by beta-lactam AMP, we noted the SSI rate was lower in patients who received a beta-lactam (1.5% vs 2.1%, **Table 5**).

Table 5. SSI by beta-lactam antibiotic receipt.

	No SSI	Yes SSI	Total
No beta-lactam	1432 (97.9%)	30 (2.1%)	1462
Yes beta-lactam	10236 (86.2%)	180 (1.5%)	10416
Total	11668	210	11878

- Interestingly, pediatric patients with BLA had a lower SSI rate if they did not receive a beta-lactam antibiotic (1.4%) than if they did receive a beta-lactam agent (2.5%) whereas the converse was true in children without BLA (2.8% vs 1.7%).

Discussion

- BLA was not associated with increased SSI risk in the pediatric patients studied.
- A significant proportion of children with BLA received beta-lactam antibiotics for AMP which suggests providers recognize that allergy labels are inaccurate.
- Many clinicians may be comfortable with administering beta-lactam AMP regardless of allergy status.
- Limitiations of our study include a retrospective study design, the inability to assess all confounders in the relationship of BLA and SSI, and being underpowered due to small number of SSIs in our patient population.

Conclusions

- Pediatric surgical patients are inappropriately given BLA diagnosis and many providers are comfortable administering beta-lactam AMP regardless of BLA status.
- Aggressive BLA de-labeling is warranted.
- More data is needed to determine if non-beta-lactam AMP is associated with SSI in children.