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Concise Communication

Variability of surgical prophylaxis in penicillin-allergic children

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Abstract

We retrospectively evaluated the effect of penicillin adverse drug reaction (ADR) labeling on surgical antibiotic prophylaxis. Cefazolin was administered in 86% of penicillin ADR-negative (−) and 28% penicillin ADR-positive (+) cases. Broad-spectrum antibiotic use was more common in ADR(+) cases and was more commonly associated with perioperative adverse drug events.

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Materials and methods

Population and setting

A retrospective study was performed extracting data from a surgical bundle reliability report for the period from January 1, 2011, to December 31, 2013. The surgical bundle reliability report is generated from the hospital electronic medical records as part of a national quality improvement collaborative. All operating room procedures lasting >5 minutes are included in the report. For this study, only patients who received at least 1 dose of an intraoperative antibiotic were included. The data collected included age, race, gender, surgery month/year, surgical procedure, isolation status (ie, evidence of methicillin-resistant S. aureus (MRSA) carrier status), wound class (ie, clean, clean/contaminated, contaminated, dirty/infected), and antibiotic(s) administered during surgery. The Children’s Mercy Institutional Review Board approved this protocol.

Penicillin ADR label

Penicillin ADR type was defined as allergy or hypersensitivity or side effect, and severity was defined as follows: mild, implicated drug continued; moderate, implicated drug discontinued and/or ADR treatment required; and severe, life-threatening or need for hospitalization. ADR type and severity data were available in the electronic medical record (EMR) at the time of surgery. These data are readily available to prescribers; however, attention to this qualifier is user dependent and likely variable. Documentation of penicillin ADRs included any of the following antibiotics: amoxicillin, oxacillin, penicillin, amoxicillin-clavulanate, ampicillin, ampicillin-sulbactam, piperacillin-tazobactam. Patients with a penicillin allergy or hypersensitivity but undocumented severity were included as ‘unknown’ severity. Patients with a documented cephalosporin ADR were excluded.

Potential perioperative adverse drug event (ADE)

Potential perioperative ADEs were based on International Classification of Diseases, Ninth Revision, Clinical Modification
In total, 137 perioperative ADEs were identified, the most common were skin eruption, documented in 59 cases (43%), allergic urticaria (N = 10; 7.3%), and drug dermatitis (N = 9; 6.6%). When cefazolin was administered, there was no difference in the perioperative ADE rate between penicillin ADR(+) allergy or hypersensitivity and ADR(–) patients (1.04% vs 0.75%, respectively; P = 0.485). Overall, vancomycin was the antibiotic most commonly associated with a perioperative ADE, occurring in 3.3% of all cases. Penicillin ADR(+) patients experienced perioperative ADEs to vancomycin (9.7%), noncefazolin cephalosporins (5.1%), and clindamycin (0.77%).

Discussion

Surgical antibiotic prophylaxis results in significant antibiotic exposure among children.6,9 Despite evidence that cefazolin is safe to use in children with a non–life-threatening penicillin ADR history, many clinicians remain reluctant. Ideally, cefazolin would be selected when indicated because it is narrow-spectrum and well tolerated and has been extensively studied. Our results demonstrate that prescribers avoid cefazolin in children labeled with a penicillin ADR, regardless of the severity of the reaction. Additionally, alternative antibiotics such as vancomycin were associated with higher rates of perioperative ADRs compared to cefazolin.

In this study, penicillin ADR(+) patients received an alternative agent instead of cefazolin in 72% of cases. This is consistent with Beltran et al9 who reported that ADR(+) children received cefazolin in only 20% of cases. We observed that penicillin ADR classification and severity did not influence antibiotic choice, suggesting that providers are not relying on ADR history to guide antibiotic selection. Clindamycin was the most common cefazolin alternative selected. Unfortunately, clindamycin has limitations due to rising resistance, making it potentially ineffective against methicillin-susceptible S. aureus for which cefazolin would be 100% effective.10

Only 1% of penicillin ADR(+) patients who received cefazolin experienced a perioperative ADE, which is consistent with previous findings.9 Our data reveal that perioperative ADEs occurred

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**Results**

In total, 17,741 operations with intraoperative AP were identified. We excluded 382 operations (2.2%) due to a documented cephalosporin allergy. These patients were predominately male (56%) and white (69%), with a median age of 7.6 years (interquartile range [IQR], 2.3–13.4). Most wounds were classified as clean (66%) or clean-contaminated (28%). The most common procedures were closed reduction of the elbow with percutaneous pinning, removal of hardware, and laparoscopic-assisted gastrostomy. A penicillin ADR label (allergy or hypersensitivity or side effect) was documented in 1,150 cases (6.6%). The prevalence of cefazolin administration in ADR negative (–) cases was significantly higher (86%) compared to ADR positive (+) allergy or hypersensitivity cases (28%; P < .001) or ADR(+) side-effect cases (48%; P < .001). After adjusting for MRSA isolation and wound class, the odds of receiving an alternative agent compared to ADR(–) cases, was significantly higher in ADR(+) allergy or hypersensitivity cases (25.4; 95% confidence interval [CI], 21.8–29.6) and ADR(+) side-effect cases (6.4; 95% CI, 3.8–11.0). Penicillin ADR severity had no effect on the likelihood of receiving an alternative to cefazolin.

Clindamycin was the most commonly prescribed alternative antibiotic prophylaxis among ADR(+) patients at 58.4%. This was significantly higher compared to ADR(–) patients (5.3%; P < .001). Penicillin ADR(+) patients also received gentamicin (4% vs 0.1%; P < .001) and vancomycin more frequently (2.8% vs 0.7%; P < .001) compared to ADR(–) patients (Fig. 1).

In total, 137 perioperative ADEs were identified, the most common were skin eruption, documented in 59 cases (43%), allergic urticaria (N = 10; 7.3%), and drug dermatitis (N = 9; 6.6%). When cefazolin was administered, there was no difference in the perioperative ADE rate between penicillin ADR(+) allergy or hypersensitivity and ADR(–) patients (1.04% vs 0.75%, respectively; P = 0.485). Overall, vancomycin was the antibiotic most commonly associated with a perioperative ADE, occurring in 3.3% of all cases. Penicillin ADR(+) patients experienced perioperative ADEs to vancomycin (9.7%), noncefazolin cephalosporins (5.1%), and clindamycin (0.77%).

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**Table 1. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Codes Used to Identify Perioperative Adverse Drug Effects**

<table>
<thead>
<tr>
<th>ICD-9-CM</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>283.9</td>
<td>Acquired hemolytic anemia</td>
</tr>
<tr>
<td>288.03</td>
<td>Drug induced neutropenia</td>
</tr>
<tr>
<td>693.0</td>
<td>Drug dermatitis</td>
</tr>
<tr>
<td>695.1</td>
<td>Erythema multiforme</td>
</tr>
<tr>
<td>708.0</td>
<td>Allergic urticaria</td>
</tr>
<tr>
<td>708.9</td>
<td>Urticaria nos*</td>
</tr>
<tr>
<td>782.1</td>
<td>Nonspecific skin eruption</td>
</tr>
<tr>
<td>995</td>
<td>Other anaphylactic reaction</td>
</tr>
<tr>
<td>995.1</td>
<td>Angioneurotic edema</td>
</tr>
<tr>
<td>995.2</td>
<td>Unspecified adverse effect of unspecified drug, medicinal and biological substance</td>
</tr>
<tr>
<td>995.27</td>
<td>Other drug allergy</td>
</tr>
<tr>
<td>995.3</td>
<td>Allergy, unspecified</td>
</tr>
<tr>
<td>e94.60</td>
<td>Local anti-infectives and anti-inflammatory drugs causing adverse effects in therapeutic use</td>
</tr>
<tr>
<td>960–961</td>
<td>Poisoning by antibiotics and other anti-infectives</td>
</tr>
<tr>
<td>E856–857</td>
<td>Adverse effects of antibiotics and other anti-infectives</td>
</tr>
</tbody>
</table>

*Not otherwise specified.
more frequently in ADR(+) patients who received vancomycin or alternative cephalosporins. Thus, data also highlight the finding that cefazolin alternatives are associated with a potential increased risk for perioperative ADEs.

Our study has several limitations. The findings are limited to a single pediatric institution and therefore may not be generalizable. This study was retrospective in nature, and perioperative ADEs were documented based on ICD-9-CM and E codes. Conversely, ICD-9-CM and E codes have proven effective in identifying ADEs in hospitalized patients, including surgical patients. The selected codes were likely not all-inclusive for antibiotic-associated ADEs and could have resulted in an underrepresentation of ADEs. Attributing a perioperative ADE specifically to an antibiotic is difficult without subsequent drug rechallenge or skin testing. Most of the documented penicillin ADRs were unknown in severity, which made it challenging to determine whether cefazolin would be indicated using ADR label alone. Notably, a review of the surgical procedures included in our study’s patient population revealed that many do not routinely require antibiotic prophylaxis (ie, circumcision, tympanoplasty). This finding highlights the lack of standardization for routine antibiotic prophylaxis and demonstrates that additional work is needed to limit antibiotic exposure and ADE risk for procedures without prophylaxis indications. Regardless, our data strongly indicate that perioperative antibiotic prescribing is highly variable among children with a documented penicillin ADR. Further research is needed to optimize clarification and interpretation of an ADR history to safely standardize care, to provide the antibiotic of choice when possible, and to utilize a safe alternative when truly needed.

In conclusion, our study demonstrates that surgical AP varies significantly in children with documented penicillin allergic and minimize the avoidance of cefazolin in cases when it can be safely administered.

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Conflicts of interest. All authors report no conflicts of relevant to this article to disclose.

References

Fig. 1. Antibiotic prophylaxis exposure based on penicillin allergy classification and associated perioperative adverse drug reactions (ADR).

