Retrospective observational study of penicillin cross-sensitivity in patients with confirmed perioperative allergic hypersensitivity reactions to cefazolin.

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Abstract

Concern about possible cross sensitivity between cefazolin and penicillin leads to restrictions on the use of penicillin in patients with cefazolin hypersensitivity reactions and no history of penicillin allergy. Our study aims to document the prevalence of penicillin cross sensitivity in this patient cohort. Sixty-eight adult patients who were seen at our clinic with confirmed cefazolin hypersensitivity reactions during the ten-year study period (2009–2018) were investigated for allergy to penicillin. Demonstration of penicillin tolerance was by a combination of penicillin skin testing, penicillin drug provocation testing (DPT) and community exposure to penicillin. There were no positive penicillin DPTs or reported reactions to penicillins in the community in our cohort. There were six false positive penicillin skin test results. Four patients were lost to follow up. We conclude that allergy to penicillin is uncommon in patients with confirmed hypersensitivity to cefazolin. Penicillin skin testing in this cohort of patients is time consuming, costly, and unreliable with a significant rate of false positives which may lead to patients being inappropriately labelled as penicillin allergic.

Retrospective observational study of penicillin cross-sensitivity in patients with confirmed perioperative allergic hypersensitivity reactions to cefazolin.

Short title: Penicillin Cefazolin Cross-sensitivity

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Acknowledgments

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Abstract

Concern about possible cross sensitivity between cefazolin and penicillin leads to restrictions on the use of penicillin in patients with cefazolin hypersensitivity reactions and no history of penicillin allergy. Our study aims to document the prevalence of penicillin cross sensitivity in this patient cohort. Sixty-eight adult patients who were seen at our clinic with confirmed cefazolin hypersensitivity reactions during the ten-year study period (2009–2018) were investigated for allergy to penicillin. Demonstration of penicillin tolerance was by a combination of penicillin skin testing, penicillin drug provocation testing (DPT) and community exposure to penicillin. There were no positive penicillin DPTs or reported reactions to penicillins in the community in our cohort. There were six false positive penicillin skin test results. Four patients were lost to follow up. We conclude that allergy to penicillin is uncommon in patients with confirmed hypersensitivity to cefazolin. Penicillin skin testing in this cohort of patients is time consuming, costly, and unreliable with a significant rate of false positives which may lead to patients being inappropriately labelled as penicillin allergic.

Keywords: cefazolin, penicillin, allergy, anaphylaxis, cross-sensitivity

Surgical site infections (SSIs) are a major preventable cause of morbidity and mortality after surgery and one of the mainstays of prevention is the use of appropriate antimicrobial prophylaxis. In many parts of the world the recommended first-line antibiotic for surgical antimicrobial prophylaxis is cefazolin.

It is well documented that unnecessary restriction of antibiotic usage due to unfounded concerns about cross sensitivity and allergy results in increased healthcare costs, increased morbidity, and increased mortality for patients. This problem has been highlighted in patients with reported penicillin allergy.

There has long been concern about cross sensitivity between cephalosporins and penicillins because of the common beta lactam ring. Patients who had anaphylaxis to a cephalosporin or a penicillin were often advised to avoid all beta lactam antibiotics. In the perioperative context this resulted in increased use of second-line antibiotics, such as clindamycin and vancomycin, leading to an increase in surgical site infections and other adverse effects from the alternative antibiotics administered.

There is growing evidence that, in patients with immediate hypersensitivity reactions to penicillins and cephalosporins, cross sensitivity is more likely related to similarities in side chains rather than to the common beta lactam ring. Cefazolin has unique side chains that are distinct from all other currently available cephalosporins and penicillins apart from ceftezole, which is not available in New Zealand, Australia, Canada, or the United States. This has resulted in changes in clinical practice. Vorobeichik et al report the implementation of an algorithm for deciding whether or not to administer cefazolin perioperatively to patients with a history of penicillin allergy. The only circumstance in which cefazolin is not allowed is in patients with a history of a life-threatening delayed hypersensitivity reaction to penicillin. Subsequently Grant et al report that, following implementation of the new guideline, cefazolin usage increased by 18.2%, vancomycin and clindamycin usage decreased by 11.4% and 62.0% respectively and no anaphylaxis was documented in penicillin-allergic patients receiving cefazolin.

Few publications specifically report on penicillin allergy in patients with confirmed cefazolin anaphylaxis. A recent systematic review and meta-analysis assessed the frequency of what the authors called dual allergy to penicillins and cefazolin. They identified eight primary studies that looked at penicillin allergy in a total of 104 surgical patients with confirmed cefazolin allergy. In this group 2.7% (95% CI 0.8-3.9%; I squared 0.9%) had penicillin allergy confirmed by penicillin skin testing and/or penicillin challenge. There are some significant limitations. One of the bigger included studies describes patients with positive screening skin tests for cefazolin and penicillin. None of these patients had experienced a reaction to cefazolin or penicillin and none of them were subsequently given either drug. This study accounts for 11 of the 13 included cases of penicillin allergy. Li et al report 40 cases of cefazolin anaphylaxis, all of which tolerate penicillin DPT, but in the meta-analysis one of these patients is described as penicillin allergic. The remaining case of penicillin allergy.
allergy is from a case series of 3 patients with cefazolin anaphylaxis, one of whom has positive penicillin skin testing.\textsuperscript{15}

The primary aim of our study is to document the prevalence of penicillin cross sensitivity in patients with cefazolin hypersensitivity and no prior history of penicillin allergy. Our secondary aims are to evaluate our investigation of and advice to patients with cefazolin hypersensitivity with particular attention to any unintended negative consequences and to review and update the advice given in our institutional surgical antimicrobial prophylaxis guidelines regarding these patients.

Methods

Institutional Review Board ethical approval (Reference 19/STH/167) was provided by the New Zealand Health and Disability Ethics Committee.

This is a retrospective observational cohort study conducted at a multidisciplinary anaesthetic allergy clinic at a metropolitan university hospital in New Zealand involving anaesthetists and immunologists with technical support from experienced laboratory staff. The recruitment period was from 1st January 2009 to 31st December 2018. Follow up was from 1st January 2009 to 30th May 2019 to capture any reactions occurring in late 2018. The data were obtained by reviewing the referral form or letter, the anaesthetic allergy clinic letter, the anaesthetic chart, blood test results and results of skin testing. All data collected were de-identified and stored in a password protected database.

Participants were all adult patients with confirmed perioperative allergic hypersensitivity reactions to cefazolin during the study period who were seen at our clinic. A subset of 35 of these patients who had their reactions at institutions that use an electronic record keeping system intraoperatively (SAFERsleep)\textsuperscript{16} have been reported on in a paper looking at the incidence of perioperative hypersensitivity reactions to cefazolin.\textsuperscript{16}

The eligibility criteria included age \([?]\) 16 years at the time of the reaction and the diagnosis of an allergic hypersensitivity reaction to cefazolin. Exclusion criteria were age < 16 years at the time of the reaction and a prior history of penicillin allergy.

During the study period our standard practice was to investigate the possibility of penicillin cross-sensitivity in these patients with penicillin skin testing and to offer a penicillin challenge to all patients with negative penicillin skin testing. All patients who had not had these tests performed were invited to return for skin testing and/or oral penicillin challenge as appropriate. Other evidence of penicillin tolerance was sought by reviewing electronic records for prescriptions for antibiotics after the date of the reaction.

The diagnosis of an allergic hypersensitivity reaction to cefazolin was based on a combination of clinical features consistent with a hypersensitivity reaction, the administration of cefazolin within 60 minutes prior to the onset of symptoms, and skin testing positive for cefazolin and negative for all other agents given prior to the reaction. Positive serum tryptase, as defined by peak tryptase \([?]\) \(1.2 \times \text{nadir value} + 2 \mu g.l^{-1}\),\textsuperscript{17} was regarded as corroborative evidence. A negative tryptase did not exclude the diagnosis.

Skin testing was done in compliance with ANZAAG (Australian and New Zealand Anaesthetic Allergy group) skin testing guidelines.\textsuperscript{18} A skin prick test (SPT) was considered positive if the maximum diameter of the wheal was at least 3 mm. An intradermal test (IDT) was considered positive if the maximum diameter of the wheal had an increase of more than 3 mm compared with the negative control wheal size. Histamine was used as a positive control for SPT, and saline was used as a negative control for SPT and IDT. Results were read after 15–20 minutes.

Cefazolin concentrations used for skin testing were 20 mg.ml\(^{-1}\) for SPT and 0.2, 2 and 20 mg.ml\(^{-1}\) for IDT.\textsuperscript{19,20} Our penicillin SPT and IDT panel included the Diater\textregistered PPL (benzylpenicilloyl-polylysine), Diater\textregistered MDM (minor determinant mixture), benzylpenicillin BP and either amoxicillin or amoxicillin/clavulanic acid. Solutions used did not exceed published non-irritant concentrations.\textsuperscript{21}

The following terms are defined as per the World Allergy Organization revised nomenclature for allergy for global use.\textsuperscript{22}
• Hypersensitivity is used to describe objectively reproducible symptoms or signs, initiated by exposure to a defined stimulus at a dose tolerated by normal subjects.
• Allergy is a hypersensitivity reaction initiated by specific immunologic mechanisms.
• Anaphylaxis is a severe, life-threatening, generalised, or systemic hypersensitivity reaction.

The main measure of interest in our study is the proportion of patients with a confirmed hypersensitivity reaction to cefazolin who also have evidence of hypersensitivity to penicillin. Other variables relate to the characteristics of our population and the process by which they are investigated, as contained in the Results section below.

The R statistical environment is used for analysis (R Foundation, Vienna, Austria). Binomial confidence intervals for the proportion of patients with cefazolin hypersensitivity who also have penicillin allergy are calculated using the Agresti-Coull method of the binom.confint() function 23. A best-case sensitivity analysis is performed allocating all patients who were lost to follow-up as “negative”. A worst-case sensitivity analysis is also performed, allocating all patients who were lost to follow-up as “positive”, and similarly determining confidence intervals.

Results

Eighty-three patients were adjudged to have had an allergic hypersensitivity reaction to cefazolin. Eight of the 83 patients had a history of penicillin allergy and are thus considered separately, as discussed below. One patient had a time to onset of symptoms of greater than 60 minutes (about 10 hours) and was excluded. Six patients who had grade one reactions; tryptases that were either negative, not done or unable to be interpreted due to poor timing and who only tested positive at the highest IDT concentration (20 mg.ml⁻¹) were excluded. Although cefazolin avoidance was advised for these six patients in the clinical setting, it is possible that the skin tests were false positives. Supplementary table (S1) contains details of these 6 patients. The remaining 68 patients were included in the study.

Demographics and clinical characteristics of the cohort and features of their reactions are summarised in Table 1. All patients had clinical features consistent with a hypersensitivity reaction. Most patients had more than one clinical feature. The clinical features are as reported by the referring clinician and/or as documented on the anaesthetic record. They have been grouped into categories as follows: mucocutaneous (rash, urticaria, flushing, itching, oedema), cardiovascular (hypotension, tachycardia, bradycardia, cardiac arrest) and respiratory (difficulty breathing, difficulty with ventilation, bronchospasm, raised airways pressures, decreased oxygen saturation).

The results of investigations leading to the diagnosis of an allergic hypersensitivity reaction to cefazolin are summarised in Table 2.

The results of investigations into the possibility of cross sensitivity with penicillin are summarised in Table 3 and the best available evidence for penicillin tolerance in each patient is summarised in Diagram 1. Supplementary table (S2) contains details of investigations for each individual patient organised according to severity of reaction.

Penicillin skin testing was done for 59 of the 68 patients. Fifty-two of the 59 patients who had penicillin skin testing were negative. Forty-two of these patients had penicillin tolerance confirmed, either with a formal DPT (32) or through community exposure (10). The other 10 patients were invited to have a DPT but either declined or were lost to follow up. There were no positive DPTs or reports of reactions to penicillin in the community.

Seven of the 59 patients had penicillin skin testing that was positive (six) or equivocal (one). The patient with equivocal skin testing died of unrelated causes before repeat skin testing or a DPT could be performed. Five of the six patients with positive penicillin skin testing subsequently had penicillin tolerance demonstrated, four with a negative penicillin DPT and one through community exposure. One patient with a positive skin test moved to another country and was lost to follow up. The full details of penicillin skin testing results for
these patients are contained in Appendix 1. There were no positive penicillin DPTs or reports of reactions to penicillin in the community.

Nine patients did not have penicillin skin testing done. Seven of these had tolerated penicillins in the community in the interval between their reaction to cefazolin and being seen in the anaesthetic allergy clinic. The other two patients have been lost to follow up.

In summary, from the 83 patients with an allergic hypersensitivity reaction to cefazolin, one was excluded because of an atypical delay of ten hours. Six patients who had grade one reactions; tryptases that were either negative, not done or unable to be interpreted due to poor timing and who only tested positive at the highest IDT concentration (20 mg.ml$^{-1}$) were excluded due to the risk of a false positive skin test. Eight of the 82 patients had a history of penicillin allergy and the results of their investigations are described separately. Among the remaining 68 patients, 64 had evidence of penicillin tolerance—negative DPT (36), community exposure to penicillin (18) and negative penicillin skin testing (10)—and four were lost to follow-up (two had not had penicillin skin testing, one had equivocal penicillin skin test results and one had positive penicillin skin test results).

The best-case scenario is that there are no cases of penicillin allergy in this group of 68 patients. This assumes that all four patients lost to follow-up are not allergic to penicillin. In this scenario we expect the true number of positives to be in the range of 0-4 cases (calculated 95% CI -0.7–4.4%, Agresti-Coull).

The worst-case scenario is that all four patients lost to follow-up are allergic to penicillin. In this scenario we expect 1–10 cases with ‘true’ allergy (calculated 95% CI, 1.3–9.9%, Agresti-Coull). This is highly unlikely given that we did not have any positive DPTs or reports of reactions to penicillin in the community and we had a high rate of false positive penicillin skin tests (at least five of the six).

**Patients with a history of penicillin allergy**

Eight of the 82 patients had a history of penicillin allergy. Seven of the eight had a rash with penicillin in childhood. One patient had a red rash with penicillin within the previous year. All these patients had penicillin skin testing done. Seven of the eight (including the patient with the rash within the last year) had negative penicillin skin testing. One patient had a negative challenge. The other six patients with negative skin tests were offered challenges but either declined or were lost to follow-up. One patient with a childhood rash had a positive penicillin skin test and was not offered a challenge. Supplementary table (S3) contains details of investigations for each of these patients.

**Discussion**

Cross-sensitivity to penicillin is uncommon in patients with confirmed hypersensitivity to cefazolin and no history of penicillin allergy. This is likely because hypersensitivity to penicillins and cephalosporins is mainly determined not by the beta lactam ring, but by side chains. We did not have any positive penicillin DPTs or reports of reactions to penicillin prescribed in the community among the 68 patients in our study.

One of the limitations of our study is that not all patients completed investigations into penicillin cross sensitivity. Ten of our patients with negative penicillin skin testing did not have either a penicillin DPT or community exposure to penicillin. In addition, one patient with a positive penicillin skin test and two patients with no penicillin skin testing were also lost to follow-up. One patient with an equivocal penicillin skin test died of unrelated causes before investigations could be completed.

One of the strengths of our study is that it illustrates the real-world difficulties of implementing the current recommendations for the investigation of these patients and the resultant unintended negative consequences for patients. Despite our best efforts, 13 of our 68 patients (19%) are now, almost certainly inappropriately, labelled as penicillin allergic.

Penicillin skin testing in this cohort of patients is time consuming, costly, and unreliable with a significant rate of false positives that may lead to patients being inappropriately labelled as penicillin allergic. Penicillin DPT, the gold standard to confirm tolerance, adds further delay and expense to the process and many
patients are lost to follow-up. This finding has significant implications for the practical management of antibiotic prophylaxis and treatment in patients with confirmed hypersensitivity to cefazolin.

In their recent meta-analysis Sousa-Pinto et al\textsuperscript{27} assess the accuracy of penicillin skin testing in the diagnostic evaluation of patients reporting a penicillin/beta lactam allergy. Skin tests had a summary sensitivity of 30.7\% (95\% CI, 18.9\%-45.9\%) and a specificity of 96.8\% (95\% CI, 94.2\%-98.3\%). Predictive value depends on the underlying prevalence of penicillin allergy i.e., it declines as the underlying prevalence falls. It is likely that the accuracy of penicillin skin testing in our population with cefazolin hypersensitivity, but no history of penicillin allergy would be worse than in a population reporting a penicillin allergy. This is illustrated by the high rate of false positive skin tests in our cohort of 68 (five of the six penicillin skin test positive patients subsequently tolerated penicillin, one was lost to follow-up).

In view of the results of our study and our review of the literature, we have changed our approach to patients with perioperative allergic hypersensitivity reactions to cefazolin and no history of penicillin allergy. We no longer routinely do penicillin skin testing or a penicillin DPT. Our advice is that these patients are at low risk of reacting to penicillins and should be given these drugs if required. The risk is never zero, but this is outweighed by the benefits of access to an important group of antibiotics.

Patients with perioperative hypersensitivity reactions to cefazolin and a history of penicillin allergy have their penicillin allergy assessed separately and are either confirmed as penicillin allergic, de-labelled on history alone or offered penicillin skin testing and/or penicillin DPT as appropriate.

Patients can have allergic hypersensitivity reactions to more than one drug. In the case of cefazolin and penicillin this is most likely due to dual allergy or co-reactivity rather than to cross-sensitivity\textsuperscript{12}.

A more conservative approach with a combination of penicillin and/or alternate cephalosporin skin testing and DPT as part of the investigation of patients with confirmed allergic hypersensitivity reactions to cefazolin is still widely recommended\textsuperscript{28,29}. These patients are often advised to avoid all penicillins and cephalosporins until investigations are completed. Investigation usually takes place at a specialist unit in a major hospital. Skin testing can often be completed in a single visit but a DPT will almost always require a second appointment. The median waiting time for a penicillin DPT at our institution during the study period was 83.5 days.

A significant proportion of these patients are lost to follow up and never have a DPT (10 of the 52 patients in our cohort with negative penicillin skin testing). This means that they are labelled as potentially allergic to penicillins and other cephalosporins with all the attendant disadvantages. In addition, patients who have a positive or equivocal penicillin skin test would be considered too high risk for a DPT in many centres (seven patients in our cohort).

Many patients have their surgery postponed at the time of their perioperative hypersensitivity reaction. If the surgery is elective, it is usually postponed until such time as investigations have been completed (a minimum of 4–6 weeks). If the surgery is urgent and this delay is to the detriment of the patient, surgery is rescheduled to take place before investigations have been completed. If cefazolin was given before the reaction, the conservative approach is to recommend avoidance of all penicillins and cephalosporins and to use other, less effective, antibiotics such as clindamycin and vancomycin for surgical antimicrobial prophylaxis. Our advice in this situation is to avoid cefazolin but that any other cephalosporin and any penicillin can be used.

References


15. Farinha SM, Cardoso BK, Tomaz EM, Inácio FF. Cefazolin allergy-different sensitization profiles [conference abstract]. *Clinical and Translational Allergy* 2018; 8(suppl 3): P110


**Table 1** Demographics, clinical features during reaction, time to onset and grade of reaction. Values are number (proportion) or median (IQR [range])

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients, n</strong></td>
<td>68</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>36 (53%)</td>
</tr>
<tr>
<td>Male</td>
<td>32 (47%)</td>
</tr>
<tr>
<td><strong>Age; years</strong></td>
<td>47 (31-58 [17-83])</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Māori</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Pacific</td>
<td>7 (10%)</td>
</tr>
<tr>
<td>Asian</td>
<td>12 (18%)</td>
</tr>
<tr>
<td>European</td>
<td>41 (60%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (3%)</td>
</tr>
<tr>
<td><strong>Clinical features during the reaction</strong></td>
<td></td>
</tr>
<tr>
<td>Mucocutaneous only</td>
<td>7 (10%)</td>
</tr>
<tr>
<td>Cardiovascular only</td>
<td>1 (%)</td>
</tr>
<tr>
<td>Respiratory only</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Mucocutaneous and Cardiovascular</td>
<td>39 (57%)</td>
</tr>
<tr>
<td>Mucocutaneous and Respiratory</td>
<td>8 (12%)</td>
</tr>
<tr>
<td>Mucocutaneous, Cardiovascular and Respiratory</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Cardiovascular and Respiratory</td>
<td>4 (6%)</td>
</tr>
<tr>
<td><strong>Time to onset of reaction</strong></td>
<td>3 (2-5 [1-20])</td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td></td>
</tr>
<tr>
<td>1 (Mild)</td>
<td>7 (10%)</td>
</tr>
<tr>
<td>2 (Moderate)</td>
<td>19 (28%)</td>
</tr>
<tr>
<td>3 (Life threatening)</td>
<td>38 (56%)</td>
</tr>
<tr>
<td>4 (Cardiac arrest)</td>
<td>4 (6%)</td>
</tr>
</tbody>
</table>

+ An estimated time in minutes between administration of cefazolin and onset of symptoms was available for 61 of the 68 patients. The time to onset of symptoms was uncertain in seven of the 68 patients, mostly because a rash was only noted at the end of a short operation (all less than 30 minutes) when the drapes were removed.

**Table 2** Details of investigations to diagnose an allergic hypersensitivity reaction to cefazolin. Values are number (proportion) or median (IQR [range])

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time from reaction until seen in clinic; days</strong></td>
<td>84.5 (60.5-117.2 [2-538])</td>
</tr>
<tr>
<td>Tryptase</td>
<td></td>
</tr>
<tr>
<td>Not done/unable to be interpreted</td>
<td>54 (79%)</td>
</tr>
<tr>
<td>Positive</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Cefazolin skin testing results</td>
<td></td>
</tr>
<tr>
<td>++ Positive SPT at 20 mg.ml⁻¹</td>
<td>0</td>
</tr>
<tr>
<td>Positive IDT at 0.2 mg.ml⁻¹</td>
<td>1</td>
</tr>
<tr>
<td>Positive IDT at 1 mg.ml⁻¹</td>
<td>2</td>
</tr>
<tr>
<td>Positive IDT at 2 mg.ml⁻¹</td>
<td>3</td>
</tr>
<tr>
<td>Positive IDT at 20 mg.ml⁻¹</td>
<td>4</td>
</tr>
</tbody>
</table>

+ Standard practice is to wait four to six weeks (28-42 days) after a reaction before performing skin testing in order to avoid false negative results. One patient in our cohort is an outlier and was skin tested in hospital two days after the reaction.

++ Skin testing was done for 66 of the 68 patients. One patient was given only one drug (cefazolin) and skin testing was not done. One patient had already had two previous episodes of rash with cefazolin and skin testing was not done. SPT = skin prick test. IDT = intradermal test.

**Table 3** Results of investigations into cross sensitivity with penicillin

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative DPT⁺</strong></td>
<td>32</td>
</tr>
<tr>
<td><strong>Positive DPT</strong></td>
<td>0</td>
</tr>
<tr>
<td><strong>Community penicillin exposure</strong></td>
<td>10</td>
</tr>
<tr>
<td><strong>No DPT</strong></td>
<td></td>
</tr>
</tbody>
</table>

+ DPT = drug provocation test

++ these patients were lost to follow up

§ this patient died of an unrelated cause before penicillin DPT could be performed
Diagram 1. Summary of best available evidence of penicillin tolerance for each patient with an allergic hypersensitivity reaction to cefazolin

68 patients with allergic hypersensitivity reactions to cefazolin
- 36 negative DPTs
- 18 community exposure to penicillin
- 10 negative penicillin skin testing
- 4 lost to follow up
- 2 no penicillin skin testing
- 1 positive penicillin skin testing†
- 1 equivocal penicillin skin testing‡

† this patient moved to another country and was lost to follow up
‡ this patient died of an unrelated cause before penicillin DPT could be performed

Hosted file

Allergy Supplementary table S3 Details of eight patients with a history of penicillin allergy.docx available at https://authorea.com/users/666446/articles/667299-retrospective-observational-study-of-penicillin-cross-sensitivity-in-patients-with-confirmed-perioperative-allergic-hypersensitivity-reactions-to-cefazolin

Hosted file

Allergy Supplementary table S1 Details of excluded patients with grade 1 reactions and positive cefazolin IDT at 20 mcg/ml.docx available at https://authorea.com/users/666446/articles/667299-retrospective-observational-study-of-penicillin-cross-sensitivity-in-patients-with-confirmed-perioperative-allergic-hypersensitivity-reactions-to-cefazolin
Hosted file

Allergy Supplementary table S2 Details of individual patients arranged according to severity of reaction available at https://authorea.com/users/666446/articles/667299-retrospective-observational-study-of-penicillin-cross-sensitivity-in-patients-with-confirmed-perioperative-allergic-hypersensitivity-reactions-to-cefazolin