

Allergic Reactions in Hospitalized Patients With a Self-Reported Penicillin Allergy Who Receive a Cephalosporin or Meropenem

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Abstract

Background: Cefepime and meropenem are used frequently in hospitalized patients for broad-spectrum empiric coverage, however, practitioners are often reluctant to prescribe these antibiotics for patients with a self-reported nonsevere, nontype I allergic reaction to penicillin. **Methods:** Retrospective review of electronic medical records of adults with a self-reported allergy to penicillin who received at least 1 dose of cefepime, ceftriaxone, ceftazidime, cephalexin, or meropenem to assess incidence and type of allergic reactions. **Results:** Of 175 patients included, 10 (6%) patients experienced an allergic reaction. The incidence for individual study drugs were cefepime 6% (6 of 96), meropenem 5% (3 of 56), ceftazidime 8% (1 of 13), ceftriaxone 0% (0 of 69), and cephalexin 0% (0 of 8). The majority of patients experienced a rash with or without pruritus and fever. Patients with a concomitant "sulfa" allergy (odds ratio [OR] 5.4, 95% confidence interval [CI] 1.4-21, $P = .02$) or ≥ 3 other drug allergies (OR 6.4, 95% CI 1.3-32, $P = .025$) were more likely to have an allergic reaction. **Conclusions:** In one of the largest retrospective reviews of hospitalized patients who received full dose therapy with cefepime, ceftriaxone, and meropenem, the incidence of allergic reactions was low and reactions were mild. Cefepime, ceftriaxone, and meropenem can be considered for use in patients with a self-reported nontype I penicillin allergy.

Keywords

allergic reactions, penicillin allergy, cephalosporins, meropenem

Introduction

Beta-lactams are one of the most commonly prescribed antibiotics with a generally favorable safety profile. Broad-spectrum antibiotics such as cefepime and meropenem are frequently used in hospitalized patients for empiric coverage of *Pseudomonas aeruginosa* or multidrug resistant (MDR) organisms. Health care practitioners are often reluctant to prescribe these antibiotics in patients with a self-reported nonsevere penicillin allergy, choosing nonbeta-lactam alternatives such as fluoroquinolones, aztreonam, or aminoglycosides that may have reduced susceptibilities or greater risk of toxicity. Drug product shortages have recently become a factor that may also influence clinical decision making in antibiotic selection. In 2011, a national shortage of intravenous (IV) aztreonam, a frequently used alternative for treating nosocomial infections in patients with a penicillin allergy, challenged practitioners to find alternative options for empiric coverage. Prescribers were compelled to consider the use of drugs such as cefepime and meropenem

in patients with penicillin allergy histories based upon available evidence supporting their low risk of allergic reactions.

Allergic reactions to beta-lactam antibiotics may be classified based on immunologically mediated mechanism and timing. Immediate type I hypersensitivity reactions, which are immunoglobulin E (IgE) antibody mediated, are far less common but more clinically serious.^{1,2} They most frequently occur within 1 hour of antibiotic exposure but can occur up to 72 hours after and may include urticaria, angioedema,

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wheezing, hypotension, or anaphylaxis.¹ Delayed hypersensitivity reactions are not IgE mediated and usually occur more than 72 hours after drug exposure.¹ Delayed nontype I allergic reactions may present as serum sickness, drug fever, or most commonly a maculopapular or morbilliform rash.^{1,2}

The overall incidence of any hypersensitivity reaction to cephalosporins and carbapenems in the general population without a penicillin allergy is 1% to 3% and 0.3% to 2.3%, respectively.^{1,3} Cross-sensitivity reactions to cephalosporins in patients with a history of penicillin allergies have been shown to correlate with similarities between R-group side chains, while carbapenem cross-sensitivity reactions are believed to be mediated by the beta-lactam ring.²⁻⁴ Retrospective studies conducted in the 1960s and 1970s overestimated cross-reactivity rates between cephalosporins and penicillins between 8% and 18%, mainly due to the contamination of cephalosporins at that time with trace amounts of penicillin as well as the high similarity in side chains of first-generation cephalosporins.⁵⁻⁷ More recent studies have demonstrated much lower rates of allergic reactions for cephalosporins, ranging from 0% to 11%.⁸⁻¹⁰ A meta-analysis identified the rate of allergic reactions in patients with confirmed penicillin allergies is highest for first-generation cephalosporins but negligible for second- and third-generation cephalosporins.¹¹ Prospective skin test studies for carbapenems show a less than 1% rate of cross-reactivity in patients with penicillin allergy,¹²⁻¹⁴ while retrospective reviews observed a rate of allergic reactions between 9.2% and 11%.¹⁵⁻¹⁷

Management of patients with a history of penicillin allergy who require treatment with a cephalosporin or carbapenem would ideally include penicillin skin testing when available to rule out the presence of IgE penicillin-directed antibodies, since 90% of all patients tested will have a negative penicillin skin test response and can safely receive another beta-lactam antibiotic.¹⁸ However, penicillin skin testing may not always be available and not all patients will be candidates for skin testing if their self-reported penicillin allergy symptoms are not indicative of a severe type I reaction. Prior studies challenging patients with history of penicillin allergy with or without positive penicillin skin test results have had a very small sample size and many included only 1 time test doses of study drug, not therapeutic dose full course therapy.^{8,9,12-14,19} The objective of this study was to describe incidence of allergic reactions in hospitalized patients with a self-reported penicillin allergy who received full dose therapy with one of our formulary cephalosporins or meropenem.

Methods

An institutional review board-approved retrospective chart review of adult patients admitted between January 1, 2011, and January 1, 2012, was conducted. Patients were included if they were 18 years and older, had any severity self-reported penicillin or penicillin-derivative allergies documented in their medical record, and received at least 1 dose of one of our formulary cephalosporins cefepime ceftriaxone, cefoxitin, cephalixin, or

formulary carbapenem meropenem. This specific study period was chosen due to a national shortage of IV aztreonam. The choice of formulary cephalosporins to include was based on similarities among side chains to help support the finding that those with dissimilar side chains would be expected to have a low rate of allergic reaction in patients with a penicillin allergy.

Patients were excluded if they had a self-reported or previously witnessed allergy to any of the study cephalosporins or carbapenems or had received one of the study drugs during a prior admission and documentation in their medical record that they had tolerated it without any reaction. Patients with self-reported symptoms consistent with intolerance (nausea, diarrhea, and dry mouth) to penicillin rather than a true allergy were also excluded, as the objective of this study was to examine the incidence of allergic reactions that occurred in patients who reportedly experienced a prior allergic reaction to penicillin. In order to capture any delayed allergic reactions, patients were excluded if they were discharged less than 96 hours after receiving the first dose of study drug, knowing delayed hypersensitivity reactions usually occur more than 72 hours after drug exposure.¹

The overall incidence of allergic reactions, type of reaction, time to reaction, and a description of characteristics of patients who experienced an allergic reaction was evaluated. Patient's baseline characteristics and any concurrent immunosuppression (including recent or current corticosteroid or other immunosuppressant medication use or chemotherapy for active malignancy) that may confound the chance of an allergic reaction occurring were collected. All documentation of allergic reactions that occurred was extracted from the patients' electronic medical record. Additional data collected included the dose and frequency of study drug received, total days of therapy, indication for study drug, microbiologic culture results, and presence of MDR pathogens from positive cultures. Physician and nursing progress notes, medication administration records, and laboratory data were used to evaluate patients for allergic reactions. Chi-square and Fisher's exact test were used for categorical variables and Student's *t* test and Mann-Whitney *U* test for continuous variables. All statistical analyses were performed with SPSS version 20.

Results

Two hundred and sixteen patient medical records were initially identified for review. A total of 41 patients did not meet inclusion criteria; 7 patients had penicillin intolerances documented, 10 patients were discharged less than 96 hours after the first dose of study drug, and 24 patients had tolerated one of the study drugs during a prior admission. The remaining 175 patients were included in the final analysis. Baseline characteristics are presented in Table 1. The median age was 73 years and 65% of patients were female. The majority of patients had a self-reported allergy to penicillin (89%), followed by amoxicillin (7%), ampicillin (5%), and piperacillin/tazobactam (2%; Table 2). In 110 (63%) patients, a description of the penicillin allergy was "unknown," and in

Table 1. Characteristics of Study Group.^a

Characteristic	N = 175
Median age (range), years	73 (20-101)
Female sex	113 (65)
Race	
Caucasian	145 (83)
Asian	7 (4)
African American	5 (3)
Hispanic	6 (3)
Other/unknown	12 (7)
Median weight (range), kg	65 (33-156)
Median CrCl (range), mL/min	43 (4-179)
Underlying comorbidities	
Cardiovascular	110 (63)
Asthma/COPD	34 (19)
Diabetes mellitus	32 (18)
Chronic kidney disease	20 (11)
Autoimmune disease	9 (5)
Cirrhosis	4 (2)
Chronic steroid use	9 (5)
Recent steroid use	26 (15)
Immunosuppressive therapy	22 (13)

Abbreviations: COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance.

^aData are n (%), unless otherwise indicated. Recent steroid use defined as glucocorticoid use within 2 weeks of or during admission.

35 (20%) patients the description was a “rash.” The time frame for when the penicillin allergy occurred was not documented in 162 (93%) patients. The most common self-reported allergy other than penicillin was “sulfa” (13%), followed by other beta-lactams (9%) and fluoroquinolones (5%; Table 2).

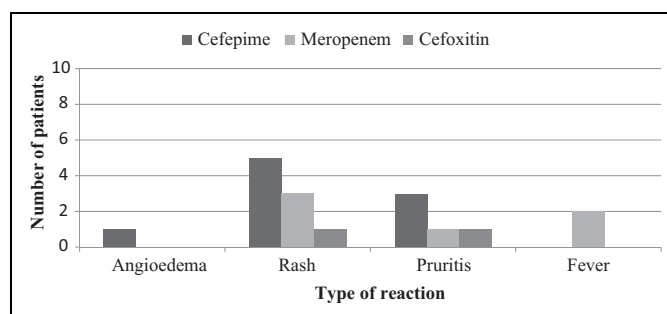
Of the 175 patients who received cefepime, ceftriaxone, cefoxitin, cephalixin, or meropenem, 10 (6%) developed an allergic reaction. The incidence of allergic reaction for patients who received at least 1 dose of each study drug was as follows: cefepime 6% (6 of 96), meropenem 5% (3 of 56), cefoxitin 8% (1 of 13), ceftriaxone 0% (0 of 69), and cephalixin 0% (0 of 8). Of the 10 patients who had an allergic reaction, 1 had a self-reported allergy to amoxicillin, 1 to piperacillin/tazobactam, and the remaining 8 to penicillin. The median time to allergic reaction was 20 hours, with a range of 0.75 to 336 hours (14 days). Three reactions occurred within 1 hour of drug administration per medical record documentation, one with symptoms described in the medical record consistent with an immediate type I hypersensitivity and the other two with symptoms described as a “rash” with patient complaints of pruritus. The remaining reactions all occurred 8 hours or more after the study drug was given. Among the 10 patients who had an allergic reaction to one of the study drugs, 1 patient had angioedema (immediate type I), while the remaining 9 experienced a rash with or without associated pruritus and fever (delayed nontype I; Figure 1). Six patients had a reaction that was treated with IV or oral diphenhydramine in addition to discontinuation of the antibiotic. The patient who had angioedema was concurrently on IV

Table 2. Penicillin (PCN) and Other Allergy Documentation.^a

	N = 175
Self-reported PCN or PCN derivative	
Original allergy documented	
Penicillin	155 (89)
Amoxicillin	12 (7)
Ampicillin	5 (3)
Piperacillin/tazobactam	3 (2)
Description of allergy	
Rash	35 (20)
Urticaria	14 (8)
Anaphylaxis/bronchospasm	4 (2)
Angioedema	4 (2)
Pruritus	2 (2)
Hypotension	1 (1)
Unknown	110 (63)
Time allergy occurred	
Childhood	3 (2)
Adolescence	1 (1)
More than 30 years ago	4 (2)
Within 15 years	1 (1)
Within 10 years	1 (1)
Within 1 year	1 (1)
Unknown	162 (93)
Other self-reported allergies ^a	
Sulfa	22 (13)
Other beta-lactam	15 (9)
Fluoroquinolone	9 (5)
Tetracycline	7 (4)
Macrolide	7 (4)
Vancomycin	5 (3)
Aminoglycoside	1 (1)
Contrast dye	13 (7)
ASA/NSAIDs	10 (6)
Opioid	11 (6)
Food	9 (5)
Other medications	24 (14)

Abbreviations: ASA, acetylsalicylic acid; NSAIDs, nonsteroidal anti-inflammatory drugs.

^aAll other reactions to antibiotics were self-reported to be allergic in nature, as opposed to intolerances, which were not included. Data are n (%) unless otherwise indicated.

**Figure 1.** Type of allergic reactions that occurred among 10 patients.

methylprednisolone therapy for an alternate indication, and the reaction resolved with the addition of an antihistamine. A summary of the 10 patients is provided in Table 3, along

Table 3. Summary of 10 Patients Who Experienced Allergic Reactions.

Patient	Age	Original PCN allergy (reaction)	Study drug reacted to (reaction)	Time to reaction, hours	Doses given prior to reaction	Baseline eosinophils, %	Eosinophils at reaction, %
1	55	Penicillin (unknown)	Cefepime (rash)	44	2	Not done	4
2	69	Penicillin (unknown)	Cefepime (rash)	1	1	2	2
3	20	Penicillin (unknown)	Cefepime (rash, pruritis)	53	4	1	23
4	64	Amoxicillin (unknown)	Cefepime (rash, pruritis)	16	2	2	Not done
5	82	Penicillin (unknown)	Cefepime (rash)	144	15	1	11
6	65	Penicillin (angioedema)	Cefepime (angioedema)	1	3	43	Not done
7	84	Piperacillin (Rash)	Meropenem (rash, pruritis)	24	1	Not done	Not done
8	85	Penicillin (unknown)	Meropenem (rash, fever)	336	44	1	5
9	44	Penicillin (unknown)	Meropenem (rash, fever)	8	1	2	1
10	27	Penicillin (unknown)	Cefoxitin (rash, pruritis)	0.75	1	1	1

Abbreviation: PCN, penicillin.

Table 4. Characteristics of Patients Who Experienced an Allergic Reaction.

Characteristic	Allergic reaction (n = 10)	No allergic reaction (n = 165)	Univariate analysis	
			OR (95% CI)	P Value
Asian race	2 (20)	5 (3)	8.0 (1.3-48)	.05
Other allergies				
Beta-lactam	2 (20)	7 (4)	5.7 (1-31)	.09
Sulfa	4 (40)	18 (11)	5.4 (1.4-21)	.02
Opioid	2 (20)	9 (5)	4.3 (0.8-23)	.12
Food	2 (20)	7 (4)	5.7 (1-31)	.09
Other med	3 (30)	21 (13)	2.9 (0.7-12)	.14
No other allergies	2 (20)	91 (55)	0.2 (0.04-0.9)	.05
≥3 drug allergies	3 (30)	11 (7)	5.9 (1.4-26)	.03

Abbreviations: CI, confidence interval; med, medications; OR, odds ratio. The bold values indicate statistically significant *p*-values (<.05).

with baseline eosinophils percentage and eosinophils at the time of reaction when available to help better characterize their reactions as being allergic.

The 10 patients who experienced an allergic reaction to any study drug were compared with the 165 patients who were able to tolerate all study drugs in order to determine whether there was a significant association with allergic reactions and baseline characteristics (Table 4). In a univariate analysis, 3 or more concomitant allergies (odds ratio [OR] 5.9, 95% confidence interval [CI] 1.4-26, *P* = .03), concomitant "sulfa" allergy (OR 5.4, 95% CI 1.4-21, *P* = .02), and Asian race (OR 8.0, 95% CI 1.3-48, *P* = .05) were associated with a higher likelihood of allergic reaction. Having no other documented allergies in addition to penicillin was associated with a decreased likelihood of allergic reaction (OR 0.2, 95% CI 0.04-0.9, *P* = .05). Because the incidence of allergic reactions was low, we did not perform a multivariate logistic regression analysis.

Discussion

This study describes the real-life clinical situation of the observed rate of allergic reactions when a cephalosporin or

meropenem is administered to a patient with a self-reported penicillin allergy. At our large academic medical center, health care practitioners were likely to find hospitalized patients with a penicillin allergy documented as "unknown" in their medical record with the time frame also unknown or not documented. A significant percentage of patients with a self-reported penicillin allergy may actually be reporting prior intolerance (such as gastric distress, headache, or dry mouth) rather than a true allergy, and the majority will have had a delayed type IV allergic reaction manifested by a maculopapular or morbilliform rash as opposed to a type I immediate hypersensitivity reaction such as angioedema, wheezing, urticaria, or anaphylaxis.¹ Only 10% of patients who report a penicillin allergy have a positive skin test indicating the presence of IgE antibodies.¹

Practitioners are often reluctant to consider broad-spectrum antibiotics such as cefepime or meropenem in individuals with a self-reported penicillin allergy and choose to prescribe an alternative nonbeta-lactam antibiotic such as a fluoroquinolone, aztreonam, or an aminoglycoside. These alternative classes may be associated with reduced susceptibilities against *P. aeruginosa* and other MDR pathogens (fluoroquinolones or aztreonam) or have increased risk of adverse effects such as QT interval prolongation, *Clostridium difficile* infection, nephrotoxicity, or ototoxicity (fluoroquinolones or aminoglycosides).²⁰⁻²⁷ In 2011, the sensitivities of nonintensive care unit isolates of *Escherichia coli* at our institution to ciprofloxacin and levofloxacin were 65% and 66%, respectively, compared to 87% for ceftriaxone and 89% for cefepime, making fluoroquinolones a poor choice for empiric coverage. Similarly, *P. aeruginosa* susceptibilities for ciprofloxacin and levofloxacin were lower (66% and 61%) compared to cefepime and imipenem (76% and 82%), respectively. Eleven percent of our study population had positive culture results for MDR pathogens, defined as drug resistance to 3 or more classes of antibiotics, which necessitated broad-spectrum coverage with cefepime or meropenem.²⁸

Prior studies have shown that cephalosporins with similar C6/7 side chains to penicillins are associated with higher rate of cross-reactivity in confirmed patients with penicillin allergy,

while the mediator of cross-reactivity for carbapenems is the beta-lactam core.²⁻⁴ A meta-analysis comparing allergic reactions to a cephalosporin in skin test confirmed penicillin allergic subjects concluded that a significant increase in allergic reaction exists for several first-generation cephalosporins, but no increase was observed for second- or third-generation cephalosporins.¹¹ We observed an allergic reaction rate of 6% for cefepime, which is consistent with published prospective and retrospective studies to date.⁷ Our study provides the largest number of patients with reported penicillin allergy who received IV therapy with cephalosporins or carbapenems in a clinical setting. None of the 69 patients who received ceftriaxone had an allergic reaction. Our findings for cross-reaction with ceftriaxone are consistent with 2 small prospective studies in which subjects who had positive skin tests for penicillin but subsequent negative skin tests for various cephalosporins were challenged with therapeutic intramuscular doses of ceftriaxone, and all patients in both studies were able to tolerate the dose without any allergic effect.^{8,9} However, our study is the first retrospective review to report no allergic reactions during IV administration of ceftriaxone (range 1-17 days of therapy) in patients with self-reported penicillin allergy. The inclusion of cefoxitin and cephalexin in this study was based on the assumption that due to similar side chains, patients who had a true penicillin allergy would be expected to have a higher rate of allergic reaction to these cephalosporins as opposed to cefepime or ceftriaxone, providing stronger evidence for use of the latter. None of the 8 patients who received cephalexin experienced an allergic reaction, yet all 8 had a self-reported allergy to penicillin, which does not share any similar side chains. Of 13 patients who received cefoxitin, 1 patient with a self-reported allergy to penicillin did experience an allergic reaction. Our observed allergic reaction rate of 5% for patients who received meropenem is lower than previous retrospective reports ranging from 9.2% to 11%, yet our study included the largest number of reported patients with penicillin allergy.¹⁵⁻¹⁷

Of the 10 allergic reactions that occurred, 9 manifested as a mild to moderate nonurticarial rash, with 4 patients also experiencing pruritus, and 2 patients who received meropenem developed a fever. The allergic reaction resolved in all 10 patients with the discontinuation of the offending agent and the addition of IV or oral diphenhydramine. The one patient who experienced angioedema after receiving a dose of cefepime presented to the hospital with a baseline eosinophilia of 43%, which peaked at 71% after cefepime was discontinued and later required bone marrow biopsy that revealed hypercellularity with 60% eosinophils. The original documented penicillin allergy was self-reported as angioedema, and the patient also experienced angioedema after receiving 1 dose of aztreonam and later on in the same admission she received cefepime, which given evidence there should be no cross-reactivity with monobactams provides evidence for a more complicated explanation for these multiple reactions.

A greater percentage of patients who had an allergic reaction in this study also had a concomitant "sulfa" allergy

documented in their chart when compared to those who did not have an allergic reaction (40% vs 11%, $P = .02$). In addition, a greater percentage of patients who were able to tolerate all study drugs had no other documented allergies except penicillin, compared to those who had an allergic reaction (55% vs 20%, $P = .05$). Having a history of other self-reported allergies may have increased the risk of cross-reactivity, and patients who had ≥ 3 other self-reported drug allergies in addition to penicillin were 6 times as likely to have an allergic reaction to cefepime, meropenem, or cefoxitin. Multiple drug allergy syndrome is a clinical condition that has been used to describe individuals who develop allergic reactions to more than 2 noncross-reacting medications and has been described in several studies.²⁹ A large retrospective cohort study of patients who had an allergic reaction event after receiving a penicillin and subsequently received a prescription for a cephalosporin found that the risk of an allergic reaction-like event was higher not only for cephalosporins (relative risk [RR] 10.1, 95% CI 7.4-13.8) but also for sulfonamides (RR 7.2, 95% CI 3.8-13.5).¹⁰ Similarly, in a study of penicillin skin test-positive patients, the allergic reaction rate was not significantly different between those who received oral cephalosporins and nonbeta-lactam antibiotics ($P = .12$) and was lower for cephalosporins versus nonbeta lactams in skin test-negative patients ($P = .005$).¹⁹ Multiple drug allergy syndrome can act as a confounder in studies trying to assess the cross-reactivity rates between beta-lactam antibiotics, although it may also explain the propensity of these individuals with multiple other drug allergies in addition to penicillin having a higher rate of allergic reaction to cephalosporins with dissimilar side chains. Interestingly, we found that Asian patients were more likely to have an allergic reaction to one of the study drugs. Of the 7 Asian patients in the study, 2 (29%) had an allergic reaction, 1 patient received cefepime and 1 patient received meropenem. The reason for this result is unclear, as no previous association between race and allergic reactions has been identified. Given the small number of Asian patients in our study population, no conclusions can be drawn from this finding, and the clinical implications are unknown.

Limitations of this study are that it was a single-center, retrospective review that was dependent on the quality and accuracy of documentation in the patient electronic medical record. However, this is one of the largest retrospective chart reviews examining the incidence of allergic reactions observed in patients with a self-reported penicillin allergy who receive therapy with a cephalosporin or carbapenem in a hospital setting. Although patient medical records were screened for documented discharge follow-up phone calls or readmissions within a few weeks after the admission during which the study drugs were received in order to capture any delayed allergic reactions that occurred, patients who may have experienced a delayed hypersensitivity reaction after discharge with no follow-up at our institution may not have been captured.

Although penicillin skin testing is ideal to guide cephalosporin or carbapenem administration to patients with a history

of IgE antibody-mediated penicillin allergy due to a high negative predictive value,¹⁸ only 13% of patients in our study would have been “candidates” for skin testing due to self-reported penicillin allergy histories of urticaria, angioedema, hypotension, and anaphylaxis (Table 2). The question still exists on how to address patients with self-reported penicillin allergies such a rash, pruritus, fever, or unknown reactions, which comprised 87% of our study population. Therefore, when penicillin skin testing is not indicated, it has been recommended that cephalosporins or carbapenems may be given in a full dose or graded challenge to patients with low risk of serious hypersensitivity reactions based on their documented allergy history.¹⁸ Drug desensitization can be considered in skin test-positive patients who require penicillin therapy, although it can be time consuming, require an elevated level of care, and is only temporary. Therefore, it does not provide a practical approach to managing all patients with reported penicillin allergies. Our study further confirms that the rate of mild allergic reactions observed in patients with a self-reported penicillin allergy who received full therapeutic dose IV cefepime, ceftriaxone, and meropenem is 0% to 6%, when compared to 0.3% to 3% among patients without penicillin allergy who will experience an allergic reaction to cephalosporins and carbapenems in general. Cefepime, ceftriaxone, and meropenem should be considered for use in the absence of any documented history of a serious type 1 hypersensitivity reaction.

Conclusion

Based on our review of our clinical experience during a national drug shortage of aztreonam, the observed incidence of allergic reactions in patients with self-reported penicillin allergy who received at least 1 dose of cefepime, ceftriaxone, cefoxitin, cephalixin, or meropenem is low. The allergic reactions that occurred were mild in nature. The majority of allergic reactions occurred as a rash with associated pruritus or fever and resolved with discontinuation of the antibiotic and the addition of diphenhydramine. Patients with a self-reported penicillin allergy who have a concomitant “sulfa” allergy or more than 3 other drug allergies documented in their chart may be more likely to have an allergic reaction to cephalosporins or meropenem, and greater caution may be warranted if prescribing these drugs. Cefepime, meropenem, and ceftriaxone can be considered for use in patients with a documented nontype I penicillin allergy in preference to nonbeta-lactam alternatives that may have decreased efficacy or potential increased risk of adverse effects.

Declaration of Conflicting Interests

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