Safety of Beta-Lactam Administration in Persons with a Documented Beta-Lactam Allergy

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BACKGROUND

- Approximately 10% of United States patients report having an allergy to a penicillin antibiotic, however < 1% of patients are truly allergic[1]
- Beta-lactam antimicrobials are common first-line antimicrobial agents for management of bacterial infections[1]
- Individuals with a history of beta-lactam allergy are more likely to receive alternative broad-spectrum antibiotics which may be less efficacious or lead to an increased risk of adverse events[2]
- Penicillin skin testing (PST) is labor and time intensive, and cannot be performed in acute situations
- The R1 side chain is the major proponent for cross-reactivity between beta lactam antibiotics due to antibody recognition[3]
- To avoid delays in therapy, patients can be prescribed full doses of structurally non-related beta-lactam antibiotics due to the low similarity of side chains between these medications and penicillin[3]
- There is a lack of data regarding safety outcomes in patients who are treated with a beta-lactam that have a documented allergy

OBJECTIVES

- To evaluate safety outcomes in patients with a documented beta-lactam allergy in the electronic medical record (EMR) who received at least one full dose of a beta-lactam antibiotic

METHODS

Study Design	Single-center, retrospective, observational study of patients at SUNY Downstate Health Sciences University from January 2015 – October 2021

Inclusion Criteria	Exclusion Criteria
1. Documented beta-lactam allergy in the electronic medical record (EMR) 2. Receipt of at least one dose of any beta-lactam antimicrobial, excluding aztreonam	1. No documented allergy 2. Documented allergy to aztreonam 3. No beta-lactam antimicrobial administered

OUTCOMES

Primary (Safety Outcomes)	Secondary Outcomes
1. Incidence of allergic reaction 2. Days to onset of reaction 3. Type of reaction that occurred 4. Pharmacological therapy required to manage reaction 5. Adverse drug events other than allergic reaction that occur while on therapy (*Clostridoides difficile* infection)	1. Number of patients who received allergy consult / penicillin skin testing

RESULTS

Table 1. Baseline characteristics

Baseline Characteristics	N = 121
Age, median (IQR)	64 (53 – 77)
Female Gender, n (%)	90 (73.8)
Infectious Diseases consult, n (%)	38 (31)
Beta-lactam duration days, median (IQR)	4 (3 – 7)
Reaction description in Electronic Medical Record	
Unknown, n (%)	28 (23)
Anaphylaxis, n (%)	7 (5..8)
Angioedema, n (%)	10 (8.2)
Hives, n (%)	38 (31.4)
Rash, n (%)	24 (19.8)

Figure 1. Antimicrobials administered

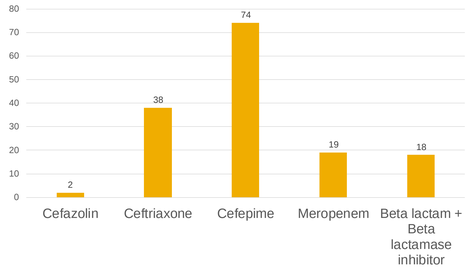

Table 2. Antimicrobial indications

Indication for use	N = 121
Bacteremia, n (%)	6 (4.9)
Intra-abdominal infection, n (%)	5 (4.1)
Pneumonia, n (%)	51 (42.1)
Urinary Tract Infection, n (%)	29 (23.9)
Skin & Soft Tissue Infection, n (%)	10 (12.1)

Table 3. Outcomes

Outcome	N = 121
Incidence of allergic reaction, n (%)	2 (1.6)
C. difficile test performed, n (%)	13 (11)
C. difficile infection, n (%)	3 (2.4)
Allergy consult / penicillin skin testing, n (%)	4 (3.3)

Table 4. Patients with Documented Anaphylaxis Prior to Antimicrobial Administration

Patients with documented anaphylaxis reaction prior to administration (N = 7)	
Offending agent • Penicillin (5/7) • Cephalexin (1/7) • Piperacillin-tazobactam (1/7)	Antimicrobials administered • Cefepime (6/7) • Piperacillin-tazobactam (3/7) • Ceftriaxone (2/7)
• Piperacillin-tazobactam not administered to patient with reported anaphylaxis • No documented allergic reactions or adverse drug events following beta-lactam administration	

Figure 2. Documented Reactions After Antimicrobial Administration

Patient 1
- Baseline allergy in Electronic Medical Record: Penicillin (hives)
- Offending antimicrobial: Cefepime
- Reaction that occurred: Serum sickness suspected by ID consult service on day 7
- Intervention: Cefepime switched to levofloxacin to complete course of therapy

Patient 2
- Baseline allergy in Electronic Medical Record: Penicillin (unknown)
- Offending antimicrobial: Cefepime
- Reaction that occurred: Perianal rash, suspected drug rash vs. HSV vesicles on day 3 of cefepime administration
- Intervention: Cefepime switched to aztreonam to complete course of therapy

DISCUSSION

- Administering alternative beta-lactam agents in patients with a documented allergy was safe with no anaphylactic reactions or need for rescue agents
- Included patients were re-challenged based on history documented in electronic medical record
- All antimicrobials were administered as full-doses, with no test-doses or desensitization protocols
- Although small sample size (n = 7), no patients with documented anaphylactic reaction experienced an allergic reaction
- 23% of patients had an unknown allergy documented in the electronic medical record, emphasis should be placed on re-challenging patients with documented allergies when feasible
- Few patients in the analysis received allergy consult or allergy de-labeling via penicillin skin testing
- *C. difficile* incidence collected as an objective adverse drug event endpoint confirmable by chart review
- Although small sample size, the incidence of allergic reaction is consistent with previously reported literature

LIMITATIONS

- Retrospective chart review, may not have captured all eligible patients during time-period
- Predominate antimicrobials administered were 3rd and 4th generation cephalosporins
- Large number of documented unknown allergies

CONCLUSION

- Administration of beta-lactams with dissimilar R1 side chains is generally safe and effective in patients with documented beta-lactam allergies

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