

Impact of a Standardized Beta-Lactam Allergy Questionnaire on Aztreonam Use

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Abstract

Methods: This quasi-experimental study compared the aztreonam utilization in patients with self-reported beta-lactam allergies admitted to an inpatient service between two study periods (pre- and post-implementation). Post-implementation followed the initiation of a standardized beta-lactam allergy questionnaire, a student pharmacist-driven performance improvement project for beta-lactam allergy documentation. Interviews clarified the allergy, reaction history, and any previous tolerance of beta-lactams. If receiving aztreonam at the time of the questionnaire, recommendations were made for changes in therapy if deemed appropriate by the pharmacist. **Results:** A total of 95 patients were included in the pre-implementation group versus 65 patients in the post-implementation group. Baseline characteristics were similar. The average number of aztreonam doses per 1000 patient-days in the post-implementation group was decreased (21.23 vs 9.05, $P = .003$). The average number of days of therapy per 1000 patient-days in the post-implementation group was decreased (8.79-4.24, $P = .016$). An increase in the number of aztreonam de-escalations was observed post-implementation ($P = .003$). A total of 122 questionnaires were completed with 114 allergy documentation updates. There were no reported instances of adverse events. **Conclusion:** Utilization of a standardized beta-lactam allergy questionnaire as a pharmacy education tool resulted in a statistically significant decrease in aztreonam utilization, based on doses, days of therapy, and de-escalations.

Keywords

aztreonam, pharmacy education, allergy, beta-lactam

Introduction

Inappropriate allergy documentation and reporting can provide a barrier to antimicrobial stewardship programs as up to 25% of patients self-report an allergy to at least one antimicrobial agent, the most common agent being penicillin.¹ Allergies may not be investigated further by providers, potentially resulting in use of non-preferred antimicrobials, prolonged length of stay, and increased health-care costs.² Patients may recollect a minimal history of the allergy or list intolerances, such as gastrointestinal events, which are not truly immunologic reactions. Approximately 2% to 4% of patients with penicillin allergies will have a positive skin test, with true anaphylactic reactions to penicillin occurring in only 0.01% to 0.04% of patients.³ Cephalosporins should be recognized as potential alternative treatment in many cases as they present less than a 1% risk of cross-reactivity of penicillin allergies, with that risk nearly eliminated if later generations are utilized.⁴

Addressing patient self-reported penicillin and beta-lactam allergies has the ability to limit unnecessary utilization of non-preferred antimicrobials and help decrease the chance of developing resistance.^{4,5} It has been estimated that up to 30% of patients with self-reported penicillin allergies will receive antimicrobial therapy that deviates from standard of care.⁶ Non-

preferred agents can also result in an increased economic burden on a health-care system.

Aztreonam, a monobactam antimicrobial agent, is commonly reserved for patients with severe beta-lactam allergies, such as angioedema or anaphylaxis, requiring broad-spectrum Gram-negative coverage, including *Pseudomonas aeruginosa*. However, due to increased resistance in *P aeruginosa* isolates, national best practice guidelines for both uncomplicated cystitis and pyelonephritis and complicated intra-abdominal infections have deemed aztreonam an unreliable agent for empiric Gram-negative coverage.⁷⁻⁹ Antimicrobial stewardship programs have begun to target aztreonam use in patient self-reported allergies. Implementation of prescribing guidelines for patients reporting penicillin or cephalosporin

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allergies has been shown to promote a 7-fold increase in test doses of beta-lactam agents and a significant decrease in the number of doses of alternative agents.¹⁰ Pharmacist-led interventions have resulted in decreased aztreonam utilization, discontinuation of unnecessary antimicrobial therapy, and cost savings.^{11,12}

The purpose of this study was to determine whether implementation of a standardized beta-lactam allergy questionnaire will result in decreased utilization of aztreonam based on the number of aztreonam doses per 1000 patient-days.

Methods

This quasi-experimental study was conducted at Baptist Medical Center Jacksonville, a 489-bed tertiary care referral community facility in Jacksonville, Florida. The study compared aztreonam utilization in patients with self-reported beta-lactam allergies admitted to an inpatient service between two study periods (pre-implementation: May 6, 2016, through September 5, 2016; post-implementation: September 6, 2016, and December 31, 2016). The post-implementation period followed the initiation of a standardized beta-lactam allergy questionnaire, which was a student pharmacist-driven performance improvement project with a goal of improving beta-lactam allergy documentation for physician order entry and pharmacist verification. The questionnaire was designed to collect information regarding previous tolerance of beta-lactam agents, the history of the allergic reaction (time frame, reaction, reaction severity), and any antimicrobial therapy the patient may be receiving during the current admission (Table 1). Questionnaire development was guided by both literature reviews of similar initiatives and input from the institution's Infectious Disease pharmacist and the Antimicrobial Stewardship Committee.^{2,11} Their involvement was essential in ensuring appropriate and qualitative information was obtained from interviews to guide potential antimicrobial transitions. Student pharmacists underwent an hour-long training session on how to appropriately obtain questionnaire answers. This study was approved by institutional review board of Baptist Health.

Patients with self-reported beta-lactam allergies, as well as patients with aztreonam orders, were identified daily via the electronic medical record (EMR). Student pharmacists were assigned identified patients for interviews to clarify the reported allergy, the reaction history, and any previous tolerance of a beta-lactam agent. The EMR history was also reviewed to determine whether the patient had previously tolerated a beta-lactam agent during an earlier hospital admission. Allergy documentation in the EMR was updated to reflect information gathered from the questionnaire, with an emphasis on reactions and previous tolerance. If the patient had an aztreonam order at the time of the questionnaire, recommendations were made to the prescriber regarding changes in therapy if deemed appropriate by the supervising pharmacist. Patients were evaluated for potential changes in therapy regardless of allergy type, including

Table 1. Beta-Lactam Allergy Questionnaire/Assessment Sheet.

Patient Profile Assessment	
What antimicrobial the patient take?	
What was the reaction?	
When was the allergy added?	
Patient has documented penicillin/cephalosporin/carbapenem administered during previous hospitalization?	
Patient Interview	
What antibiotic (beta-lactam) do you remember taking?	
How long ago was it? Greater than 10 years?	
What was the reaction?	
Localized or full body?	
Were you taking any other new medications at this time?	
Was the reaction immediate or greater than 24 hours later?	
What other antibiotics have you taken? Ask about common brand/generics (Keflex/cephalexin, amoxicillin, Augmentin, Omnicef/cefdinir)	
Have you had any reactions to other antibiotics?	
What pharmacy do you currently use	
Current Hospitalization	
Is the patient admitted for an infection?	
Is the patient currently on antibiotics?	
Is the patient currently receiving aztreonam?	
Current antibiotics (if applicable)	
Current antibiotics and # of days/doses	
Prescribing physician	
Was the allergy documentation updated in the MAR?	
Has desensitization been attempted?	

“severe allergic reactions,” which would include anaphylaxis, angioedema, shortness of breath, or swelling. These patients were included as they may be candidates for a non-beta-lactam agent, be eligible de-escalation of Gram-negative coverage, or have documentation of previous tolerance to a beta-lactam agent. Patients were excluded from questionnaires if they were experiencing/had altered mental status (delirium, Alzheimer's disease), were mechanically ventilated, or were exhibiting agitation/hostility.

The primary outcome measurement was doses of aztreonam per 1000 patient-days. A sample size of 64 patients in each group was calculated to determine a 20% effect size with a power of 80% ($\alpha = 0.05$). Secondary outcomes included days of therapy per 1000 patient-days, aztreonam cost, number of patients transitioned from aztreonam to guideline-recommended agents, adverse reactions in patients transitioned from aztreonam, and the number of allergy documentation updates. Adverse reaction data were collected via documentation in the EMR. The primary end point was analyzed using Student's *t* test. The secondary end points were evaluated utilizing Student's *t* test for continuous data and Fisher's exact test for categorical/nominal data.

Results

A total of 95 patients were included in the pre-implementation group and 65 patients in the post-implementation group. All baseline characteristics were similar between the 2 groups (Table 2). Less than half of patients had reactions

Table 2. Baseline Characteristics.

Variable	Preimplementation (n = 95)	Postimplementation (n = 65)	P Value
Age, mean	63.9	64.4	.896
Male, n (%)	33 (35)	14 (22)	.072
Ethnicity, n (%)			.417
White	72 (76)	44 (68)	
Black	22 (23)	19 (29)	
Other	1 (1)	2 (2)	
Beta-lactam allergy documentation, n (%)	92 (97)	63 (97)	.977
Reaction type documentation, n (%)			.371
Yes	32 (34)	29 (45)	
No	60 (63)	34 (52)	
No allergy	3 (3)	2 (2)	
Listed reaction, n (%) ^a			
Unspecified	61 (64)	34 (52)	
Itching	2 (2)	1 (2)	
Rash	7 (7)	5 (8)	
Anaphylaxis	6 (6)	5 (8)	
Hives	8 (8)	11 (17)	
Swelling	6 (6)	7 (11)	
Miscellaneous	5 (5)	2 (3)	
Severe allergic reaction, n (%) ^b			.370
Yes	19 (21)	12 (19)	
No	13 (14)	34 (54)	
Unspecified	60 (65)	17 (27)	
Previously tolerated beta-lactam agent, n (%)	31 (33)	23 (35)	.718
ICU admission, n (%)	25 (26)	17 (26)	.982
Mechanically ventilated patients, n (%)	13 (14)	6 (9)	.392
Infectious disease consult, n (%)	56 (59)	43 (66)	.357
Indication for use, n (%)			
Empiric	18 (19)	8 (12)	
Pneumonia	22 (23)	20 (31)	
Urinary tract infection	14 (15)	10 (15)	
Gastrointestinal infection	11 (12)	7 (11)	
Skin/soft tissue infection	14 (15)	5 (8)	
Sepsis	7 (7)	10 (15)	
Other	9 (9)	5 (8)	

Abbreviation: ICU, intensive care unit.

^aPatients may report more than 1 reaction.^bPatients were considered to have a "severe allergic reaction" if anaphylaxis, angioedema, shortness of breath, or swelling were stated as a reaction.

documented for their beta-lactam allergy in both the pre- and post-implementation groups (34% and 45%, respectively). Reactions listed were commonly dermatological in nature (itching, rash, hives, etc). Severe reactions, defined as anaphylaxis, angioedema, shortness of breath, or swelling, were documented in approximately 20% of patients in both groups. The most common documented indication for use was pneumonia.

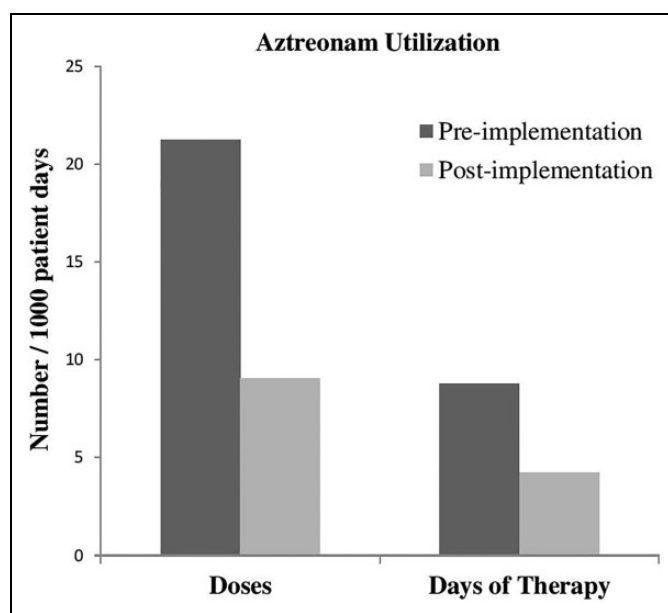


Figure 1. Comparison between pre- and post-implementation periods for number of doses of aztreonam per 1000 patient days and days of therapy per 1000 patient days. Both outcomes demonstrated a statistically significant decrease in aztreonam utilization.

The average number of aztreonam doses per 1000 patient-days in the post-implementation group was lower when compared to the pre-implementation group (21.23 vs 9.05, $P = .003$), as was the average number of days of therapy per 1000 patient-days in the post-implementation group (8.79-4.24, $P = .016$; Figure 1). There was an increase in the number of aztreonam de-escalations to guideline-recommended antimicrobial agent in the post-implementation group when compared to the pre-implementation group (86% vs 65%, $P = .003$; Table 3). The number of transitions to beta-lactam agents increased, while the number of transitions to fluoroquinolones decreased. In comparison with the pre-implementation period, a US\$12 889 cost savings over the 4-month post-implementation period was observed, correlating with an estimated annual savings of US\$37 857. A total of 122 beta-lactam allergy questionnaires were completed during the post-implementation period (Table 4). Of these questionnaires, 114 patients had allergy documentation updates to reflect patient-stated reactions and/or previous tolerance of beta-lactam agents. The most commonly reported beta-lactam allergy was to penicillin, with the most common reaction being hives. Forty-eight percent of patients had a reaction listed for the documented beta-lactam allergy prior to the interview. Forty-nine percent of interviewed patients had previously tolerated a beta-lactam agent on a previous admission and 4% of patients stated they had experienced a known reaction to a second beta-lactam agent following the initial allergic reaction. Of the 24 patients receiving aztreonam at the time of their questionnaire, 22 were de-escalated to alternative therapies, most commonly a beta-lactam agent (59%). If a patient was transitioned to a beta-lactam agent during their hospitalization following results of the questionnaire,

Table 3. Aztreonam De-Escalations.

Variable	Preimplementation (n = 95)	Postimplementation (n = 65)	P Value
Number of de-escalations, n (%)	62 (65)	56 (86)	.003
Transition agents, n (%)			
Beta-lactams	12 (19)	28 (50)	
Fluoroquinolones	24 (39)	7 (13)	
Other	15 (24)	10 (18)	
Discontinued	11 (18)	8 (14)	
Patient expired	–	3 (5)	

additional documentation of the well-tolerated agent was also added to the allergy profile. There were no reported adverse events in either group throughout the study period.

Discussion

Incomplete documentation of beta-lactam allergies is a common and challenging obstacle to antimicrobial stewardship initiatives. This study demonstrates the positive impact of a standardized beta-lactam allergy questionnaire and student pharmacist involvement on improvement of beta-lactam allergy documentation and aztreonam antimicrobial stewardship.

Pharmacist-led initiatives can play an essential role in optimizing antimicrobial stewardship. Estep et al evaluated the clinical and economic impact of an antimicrobial stewardship quality initiative focusing on allergy assessment with prospective pharmacist review of aztreonam orders in patients with documented beta-lactam allergies.¹¹ A higher number of patients were able to be transitioned to beta-lactam therapy with no adverse reactions and an annual cost savings of US\$28 134. Swearingen et al¹² evaluated the effect of pharmacist-led interventions on aztreonam utilization following newly implemented criteria for use in an academic medical center. Aztreonam was restricted to patients with anaphylactic reactions to beta-lactams. Communication with prescribers regarding antibiotic modification decisions was initiated by pharmacists. Following interventions, allergy profiles were updated and the patient was monitored for any adverse events. Statistically significant reductions in aztreonam orders were seen and complete discontinuation of unnecessary antimicrobial therapy was achieved in one-third of patients.

This study was unique in its ability to utilize student pharmacists to conduct patient interviews to improve beta-lactam allergy documentation. Student pharmacists possess the knowledge regarding medication allergies and guideline-recommended therapies to aid in streamlining the transition from aztreonam to more preferred antimicrobial agents via their supervising pharmacist. While not all patients were transitioned to beta-lactam agents from aztreonam, information obtained from the questionnaires and updated allergy documentation allowed for a decrease in the number of patients transitioned to fluoroquinolones. Reduction in fluoroquinolone use has potential to lower

Table 4. Beta-lactam Allergy Questionnaire Results (n=122).

Agent stated by patient, n (%)	
Penicillin	78 (64)
Cephalexin	6 (5)
Ceftriaxone	4 (3)
Amoxicillin or amoxicillin/clavulanate	11 (10)
Ampicillin	5 (4)
Unknown	9 (7)
Reaction documented, n (%)	58 (48)
History of beta-lactam tolerance on previous admission, n (%)	60 (49)
Stated reaction, n (%)	
Rash/hives	48 (39)
Severe ^a	36 (30)
Nausea/vomiting	4 (4)
Itching	3 (3)
Syncope	3 (2)
Unknown	16 (13)
Miscellaneous	8 (7)
No allergy	5 (4)
Reactions to other beta-lactam agents, n (%)	
Yes	5 (4)
No	50 (41)
Unknown	61 (51)
No allergy	5 (4)
Receiving aztreonam, n (%)	24 (20)
Aztreonam de-escalated, n = 24, n (%)	22 (92)
De-escalation agent, n = 22, n (%)	
Beta-lactam	13 (59)
Fluoroquinolone	3 (13)
Linezolid	1 (5)
Clindamycin	1 (5)
Vancomycin	2 (9)
Discontinued	2 (9)
Allergy documentation update, n (%)	114 (94)

^aPatients were considered to have a "severe allergic reaction" if anaphylaxis, angioedema, shortness of breath, or swelling were stated as a reaction.

risks for collateral infections, adverse effects, and drug interactions. While antimicrobial stewardship was the primary focus of this study, a cost benefit from decreased aztreonam utilization was observed. Student pharmacists may represent a cost-effective strategy for allergy documentation updates and other antimicrobial stewardship efforts.

Several limitations were present throughout this study. This was a retrospective chart review conducted at a single tertiary care institution. A total of 8 student pharmacists were utilized across the 4-month post-implementation period. While each received a standardized training session on utilization of the beta-lactam allergy questionnaire, there were inconsistencies in the caliber of interviews that were conducted between the students. Recommendations to prescribers were also based on information the student pharmacist was able to obtain from the patient. The beta-lactam allergy questionnaire was vetted by the Antimicrobial Stewardship Committee; however, there were also inconsistencies in the acceptance of prescribers regarding pharmacist involvement in making recommendations regarding aztreonam transitions following allergy documentation updates. Finally, as the majority of aztreonam orders were

placed on evening or weekend shifts, there were periods of time that patients received multiple days or doses before student pharmacists could be assigned patients to interview.

Conclusion

Overall, the utilization of a standardized beta-lactam allergy questionnaire resulted in a statistically significant decrease in the number of aztreonam doses per 1000 patient-days and the number of days of therapy per 1000 patient-days. This decrease in use resulted in approximately a US\$13 000 cost savings over a 4-month period. Utilization of student pharmacists to interview patients with self-reported beta-lactam allergies showed an increased number of aztreonam de-escalations via updated allergy documentation. As the establishment of an antimicrobial stewardship program in hospitals is now a requirement by The Joint Commission, this project may be easily implemented in institutions that have availability of student pharmacists to aid in improvement of beta-lactam allergy documentation and decrease aztreonam use.

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Declaration of Conflicting Interests

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