

Consequences of avoiding β -lactams in patients with β -lactam allergies

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Background: The choice of empiric antibiotics for the treatment of gram-negative bacilli (GNB) bloodstream infections (BSIs) in patients presenting with a β -lactam (BL) allergy is often a difficult decision given that these agents are first-line treatment in many guidelines.

Objective: We sought to compare rates of clinical failure between patients with a history of BL allergy who received either a BL or a non- β -lactam (NBL).

Methods: Adult patients with a past medical history of BL allergy and receipt of antibiotics for treatment of a GNB BSI were included from 3 academic medical centers. Treatment groups were classified as BL or NBL groups based on the empiric antibiotics received. Clinical failure was assessed 72 to 96 hours after initiation of empiric antibiotics. Hypersensitivity reactions during receipt of antibiotic therapy for the index BSI were recorded.

Results: A total of 552 patients were included for analysis: 433 patients in the BL group and 119 patients in the NBL group. Clinical failure was higher in the NBL group compared with the BL group (38.7% vs 27.4%, $P = .030$). The most common cause of clinical failure was a temperature of greater than 38.0°C 72 to 96 hours after receipt of empiric antibiotics (NBL group: 22.7% vs BL group: 13.9%, $P = .016$). Hypersensitivity occurred in 16 (2.9%) of 552 patients. Thirteen (2.5%) of 552 patients experiencing hypersensitivity reactions were exposed to a BL during treatment for GNB BSI.

Conclusion: Among patients with a BL allergy, use of BL antibiotics is associated with a lower rate of clinical failure. The low rate of hypersensitivity provides further evidence about the risk of cross-reactivity between BL classes. These results support the practice of using a BL from an alternative class for patients in need of gram-negative antibiotic coverage. (*J Allergy Clin Immunol* 2015;■■■:■■■-■■■.)

Key words: β -Lactam allergy, penicillin allergy, empiric antibiotic, gram-negative, bloodstream infection

Abbreviations used

APACHE: Acute Physiology and Chronic Health Evaluation
BL: β -Lactam
BSI: Bloodstream infection
GNB: Gram-negative bacilli
NBL: Non- β -lactam
PMH: Past medical history

The reported incidence of β -lactam (BL) allergy for hospitalized patients is 17.3%. Penicillin allergy represents 15.6% of this population, and 1.7% are cephalosporin allergies.¹ In 2008, there were 1,141,000 hospitalizations in the United States with septicemia or sepsis as the first-listed, principal, or secondary diagnosis.² This results in approximately 200,000 hospitalizations annually in which the patient will have a reported allergy against first-line antibiotics.³ The choice of empiric antibiotics for the treatment of gram-negative infections in patients presenting with a BL allergy is a challenging clinical scenario. The Infectious Diseases Society of America recommends BL antibiotics as first-line empiric treatment when gram-negative coverage is needed for bacterial meningitis,⁴ sepsis,³ intra-abdominal infections,⁵ health care-associated pneumonia,⁶ diabetic foot infections,⁷ and skin and soft tissue infections.⁸ Absent from these guidelines are therapeutic recommendations for empiric treatment options in patients with a BL allergy.

"Drug allergy: an updated practice parameter" states that penicillin skin testing is the most reliable method for evaluating IgE-mediated penicillin allergy.⁹ Although this approach for noncritically ill patients could safely be done in the outpatient setting, the practice of penicillin skin testing before administration of empiric BL antibiotics would delay initiation for hospitalized patients. A delay in appropriate empiric therapy has been shown to increase mortality in multiple studies.¹⁰⁻¹²

Aztreonam, a monobactam, is widely accepted as a safe alternative in patients with a history of BL allergy when an antibiotic with gram-negative bacilli (GNB) coverage is needed.^{13,14} Aztreonam as empiric therapy is less desirable in comparison with other commonly used BLs because it might have limited coverage against many GNB.¹⁵ Other empiric non- β -lactam (NBL) treatment options include aminoglycosides, fluoroquinolones, tigecycline, or trimethoprim/sulfamethoxazole. However, a paucity of clinical outcomes data exists to support use of NBLs for patients who present with a suspected GNB bloodstream infection (BSI).

The purpose of this study was to compare clinical failure rates at 72 to 96 hours in patients with BL allergy who received NBL or BL antibiotics for the empiric treatment of a GNB BSI. Secondary outcomes included a description of the prevalence

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Disclosure of potential conflict of interest: M. N. Jeffres received payments for educational presentations at the Advances in Pharmacy Practice 2015 and Mid-Year Clinical Meeting. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication March 31, 2015; revised September 10, 2015; accepted for publication October 27, 2015.

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<http://dx.doi.org/10.1016/j.jaci.2015.10.026>

and severity of antibiotic hypersensitivity reactions, rate of appropriate empiric therapy, length of stay, and all-cause 28-day hospital mortality.

METHODS

Study population

This was a multicenter, retrospective cohort analysis that examined clinical, microbiologic, and laboratory parameters in patients with a BL allergy and a documented GNB BSI receiving empiric BL or NBL antibiotics. Enrolled patients were admitted to one of 3 academic medical centers (Mayo Clinic Hospital–Rochester, Barnes-Jewish Hospital, or University of Medical Center of Southern Nevada) from 2010–2013. To be included in the study, patients were 18 years or older, had a documented GNB BSI and a BL allergy reported in the past medical history (PMH), and received intravenous antibiotics with intrinsic GNB activity. Exclusion criteria included patients with a polymicrobial BSI. This study was approved by each site's institutional review board, and consent was waived because of the retrospective nature of the study.

Definitions

The BL group included patients who received any BL antibiotic (penicillin, cephalosporin, and/or carbapenem) with GNB coverage or a combination of BL and NBL antibiotics for at least the first 24 hours of empiric therapy. The NBL cohort exclusively received NBL antibiotics with GNB coverage within this time period. Aztreonam was categorized as an NBL for the purpose of this study. The primary end point of clinical failure was assessed at 72 to 96 hours after receipt of empiric antibiotics and represented a composite of 1 or more of the following: temperature of 38.0°C or greater, need for new mechanical ventilation, increased or new need for vasopressor support, new admission to an intensive care unit, or death.

Secondary outcomes evaluated were antibiotic hypersensitivity reactions, appropriate empiric therapy, length of stay, and all-cause 28-day hospital mortality. Hypersensitivity was defined as documentation of an allergic or hypersensitivity reaction in the medical record temporally related to receipt of any antibiotic for the treatment of the index GNB BSI. Hypersensitivity was categorized as rash, hives and/or edema, anaphylaxis, or organ toxicity. The more severe hypersensitivity description was used for patients with more than 1 reaction. For example, if a patient experienced edema and anaphylaxis, the reaction was recorded as anaphylaxis. To meet the definition of anaphylaxis, a patient had to experience at least 2 of the following symptoms after receipt of an antibiotic: involvement of the skin, respiratory compromise, reduced blood pressure, or gastrointestinal symptoms. Appropriate empiric therapy was defined as receipt of an antibiotic with *in vitro* coverage of the cultured pathogen within 24 hours of blood culture draw.^{16–18} Modified Acute Physiology and Chronic Health Evaluation (APACHE) II scores, excluding the Glasgow Coma Scale, were calculated based on laboratory and clinical data from the day of antibiotic start.¹⁹ The source of infection was categorized as primary BSI unless the same genus and species of pathogen was cultured from a different site within 24 hours of the index blood culture. Sources included respiratory, urine, intra-abdominal, and other.

PMH allergy data collected from the electronic health record included BL class (penicillin, cephalosporin, or carbapenem), of which patients could belong to more than 1. PMH BL allergy reaction descriptions were collected and labeled as rash, hives and/or edema, gastrointestinal intolerance, anaphylaxis, other, or unknown/undocumented. The more severe allergy description was used for patients with more than 1 reaction.

Statistical analysis

A sample size of 400 was calculated by using the assumptions of a 75% use rate of BL antibiotics and a 25% use rate of NBL antibiotics, a 15% difference in clinical failure, and a 2-tailed α value of .05. These assumptions resulted in a power of 86%. Baseline categorical variables were compared by using the χ^2 or 2-tailed Fisher exact test, when appropriate. Continuous variables were compared by using the *t* test. Variables that were statistically different between

treatment groups were manually entered into a logistic regression model. Variables that confounded the relationship between treatment and the primary outcome were retained in the final multivariable model. The primary outcome of clinical failure at 72 to 96 hours between patients receiving a BL or an NBL empirically was analyzed by using the χ^2 test. Frequencies and percentages were used to describe hypersensitivity reactions. For all tests of statistical significance, a 2-tailed α value was set at .05. SPSS software (version 22.0; IBM, Armonk, NY) was used for analysis.

RESULTS

Patients

During the study period, 552 episodes of GNB BSI occurred in patients with a PMH of BL allergy. Of these, 433 (78.4%) patients received a BL and 119 (21.6%) received an NBL as empiric therapy.

BL allergy was further categorized based on PMH, with 67 incidences of more than 1 BL allergy at baseline. The incidence of penicillin, cephalosporin, and carbapenem allergy was 418 (75.7%), 167 (30.3%), and 34 (6.3%), respectively. PMH allergy descriptions were rash ($n = 236$, 42.8%), hives and/or edema ($n = 105$, 19%), unknown or undocumented ($n = 103$, 18.7%), anaphylaxis ($n = 50$, 9.1%), gastrointestinal intolerance ($n = 19$, 3.4%), and other reactions ($n = 39$, 7.1%). Allergy to NBL antibiotics was documented for 214 (38.8%) patients. Allergy to medications other than antibiotics was documented for 245 (44.4%) patients.

The distribution of gram-negative isolates was as follows: *Escherichia coli*, 188 (34.1%); *Klebsiella* species, 128 (23.2%); *Pseudomonas aeruginosa*, 96 (17.4%); *Enterobacter* species, 60 (10.9%); *Acinetobacter* species, 33 (6.0%); *Proteus* species, 17 (3.1%); *Serratia* species, 14 (2.5%); *Citrobacter* species, 13 (2.4%); and other GNB isolates, 53 (9.6%). The distribution of infection source was as follows: primary BSI, 293 (53.1%); urine, 131 (23.7%); respiratory, 61 (11.1%); intra-abdominal, 24 (4.3%); and other, 43 (7.8%).

BL versus NBL group

Patient characteristics between the BL and NBL groups are listed in Table I. Members of the BL group had significantly greater APACHE II scores, received more immunosuppressive medications and vasopressors at antibiotic start, and were more commonly infected with *Escherichia coli*. Members of the NBL group had a significantly higher proportion of male subjects, used more mechanical ventilation at the time of antibiotic start, and were infected with different GNB pathogens.

Outcomes

The primary outcome of clinical failure at 72 to 96 hours occurred at a greater frequency in the NBL group compared with the BL group (37.7% vs 27.4%, $P = .030$; Table II). The most common cause of clinical failure was a temperature of 38.0°C or greater. The NBL group had a lower rate of appropriate empiric therapy (74.8%) when compared with the BL group (91.7%, $P < .001$), which included receipt of antibiotics with *in vitro* coverage against the infecting pathogen within 24 hours of blood culture. Length of stay and mortality were similar between the BL and NBL groups.

Variables that were selected for the logistic regression model for clinical failure included NBL treatment, male sex,

TABLE I. Characteristics of patients with GNB BSIs treated with BLs compared with those treated with NBLs

	BL group (n = 433)	NBL group (n = 119)	P value
Male sex, no. (%)	221 (51.0)	72 (60.5)	.042
Age (y), mean $\pm$ SD	57.8 $\pm$ 14.6	59.6 $\pm$ 16.0	.240
BMI (kg/m ²), mean $\pm$ SD	29.6 $\pm$ 9.3	31.2 $\pm$ 12.0	.277
White race, no. (%)	310 (71.6)	84 (70.6)	.512
PMH BL allergy, no. (%)			
Penicillin	323 (74.6)	95 (79.8)	.144
Cephalosporin	129 (29.8)	38 (31.9)	.365
Carbapenem	28 (6.5)	6 (5.0)	.373
NBL allergy	165 (38.1)	49 (41.2)	.306
PMH BL allergy description, no. (%)			.089
Rash	187 (43.2)	49 (41.2)	
Hives/edema	82 (18.9)	23 (19.3)	
Unknown/undocumented	83 (19.2)	20 (16.8)	
Anaphylaxis	32 (7.4)	18 (15.1)	
Other	31 (7.2)	8 (6.7)	
GI intolerance	18 (4.2)	1 (0.8)	
Comorbid diseases, no. (%)			
Active malignancy	148 (34.3)	36 (30.3)	.245
Diabetes	111 (25.6)	38 (31.9)	.106
Chronic kidney disease	38 (8.8)	12 (10.1)	.387
Cirrhosis	29 (6.7)	6 (5.0)	.340
Immunosuppressive medications	178 (41.1)	32 (26.9)	.003
Severity of illness			
APACHE II score, mean $\pm$ SD	18.4 $\pm$ 6.9	16.8 $\pm$ 6.6	.030
ICU at antibiotic start, no. (%)	196 (45.3)	53 (44.5)	.486
Vasopressor use at antibiotic start, no. (%)	104 (24.0)	15 (12.6)	.004
Mechanical ventilation at antibiotic start, no. (%)	93 (21.5)	36 (30.3)	.032
Infecting pathogen, no. (%)			
<i>Escherichia coli</i>	158 (36.5)	30 (25.2)	.013
<i>Klebsiella</i> species	100 (23.1)	28 (23.5)	.504
<i>Pseudomonas aeruginosa</i>	78 (18.0)	18 (15.1)	.278
<i>Enterobacter</i> species	45 (10.4)	15 (12.6)	.295
<i>Acinetobacter</i> species	24 (5.5)	9 (7.9)	.265
<i>Proteus</i> species	16 (3.7)	1 (0.8)	.088
<i>Serratia</i> species	11 (2.5)	3 (2.5)	.644
<i>Citrobacter</i> species	10 (2.3)	3 (2.5)	.556
Other GNB	34 (7.9)	19 (16.0)	.009
Source of infection, no. (%)			.228
Primary BSI or unknown	225 (52.0)	68 (57.1)	
Urine	108 (24.9)	23 (19.3)	
Respiratory	44 (10.2)	17 (14.3)	
Intra-abdominal	22 (5.1)	2 (1.7)	
Other	34 (7.9)	9 (7.6)	

BMI, Body mass index; GI, gastrointestinal; ICU, intensive care unit.

immunosuppression, APACHE II score, vasopressor receipt, mechanical ventilation requirement, and infecting pathogens of *E coli* and other GNB. APACHE II scores, receipt of vasopressors, and receipt of mechanical ventilation were statistically significant and retained in the final multivariable regression model. Higher risk of clinical failure remained for patients treated with an NBL after adjusting for these factors (adjusted odds ratio, 1.9; 95% CI, 1.1-3.0; $P = .012$).

Sixteen (2.9%) of 522 patients experienced a hypersensitivity reaction during the BSI index admission (Table III). Patients with hypersensitivity reactions were exposed to both BLs and NBLs during empiric and directed antibiotic treatment. The following reactions were documented: rash ($n = 5$), itching ($n = 1$),

TABLE II. Outcomes of patients with GNB BSIs treated with BLs compared with those treated with NBLs

	BL group (n = 433)	NBL group (n = 119)	P value
Clinical failure at 72-96 h, no. (%)	115 (27.4)	36 (38.7)	.030
Fever	60 (13.9)	27 (22.7)	.016
Vasopressor initiation	12 (2.8)	4 (3.4)	.465
Mechanical ventilation initiation	21 (4.8)	5 (4.2)	.497
Intensive care unit admission	9 (2.1)	4 (3.4)	.301
Death	36 (8.3)	11 (9.2)	.434
Appropriate empiric antibiotics, no. (%)	396 (91.7)	89 (74.8)	<.001
Length of stay (d), mean $\pm$ SD	21.5 $\pm$ 30.0	30.9 $\pm$ 52.4	.065
28-d Mortality, no. (%)	71 (16.4)	19 (16.0)	.518

shortness of breath ($n = 2$), cell line toxicity ($n = 4$), anaphylaxis ($n = 2$), and unknown/undocumented ($n = 2$). Thirteen of these 16 patients received a BL for the treatment of the GNB BSI, including empiric and/or directed therapy. Three patients were exposed to the same BL class as their prior allergy. Two patients with penicillin allergy received piperacillin/tazobactam (rash and anaphylaxis), and 1 patient with a cephalosporin allergy received cefepime (rash).

Baseline characteristics and outcomes were different for patients who experienced a hypersensitivity reaction while being treated for the index GNB BSI in comparison with patients who did not (Table IV). Differences between groups include the frequency of PMH allergy description of anaphylaxis. Patients with a history of anaphylaxis were more likely to experience a hypersensitivity reaction during treatment of the index GNB BSI. One (0.9%) of 103 patients with an unknown/undocumented PMH BL allergy experienced a hypersensitivity reaction during treatment for the index BSI. Rates of vasopressor initiation, mechanical ventilation initiation, and intensive care admission were similar for patients experiencing a hypersensitivity reaction in comparison with those who did not. No patients in this group died and hospital length of stay was similar.

DISCUSSION

Currently, clinicians have the undesirable decision to expose a patient with a BL allergy to a BL antibiotic and subsequently risk an allergic reaction or, treat the patient with an NBL antibiotic for which clinical BSI outcomes data are lacking. In our study patients empirically treated with an NBL had a higher rate of clinical failure at 72 to 96 hours compared with those treated with a BL. This outcome is likely due to the lower rate of appropriate empiric therapy in the NBL group.

Our results are similar to those of the few studies comparing efficacy of NBLs with that of BLs. Only 1 randomized control trial has been published comparing imipenem/cilastatin with levofloxacin for the treatment of BSI-related sepsis.²⁰ As with a majority of antimicrobial studies, the trial was designed to prove noninferiority and provided a Δ value of 15%. This study demonstrated that levofloxacin was not inferior to imipenem/cilastatin at test of cure assessed 28 days after the last antibiotic dose. Additionally, a meta-analysis of secondary GNB BSI compared tigecycline with multiple antibiotic comparators (aztreonam included) and reported a clinical cure rate of 81% versus 91% in the tigecycline and comparator arms, respectively.²¹ This was

TABLE III. Antibiotic exposure and hypersensitivity description

Patient	PMH antibiotic allergy history	Chronologic antibiotic exposure	Hypersensitivity reaction
1	Penicillin: rash	Ciprofloxacin, cefepime	Rash
2	Penicillin: hives	Meropenem, ciprofloxacin	Rash
3	Penicillin and meropenem: rash	Cefepime	Rash
4	Amoxicillin/clavulanate: cholestatic hepatitis	Piperacillin/tazobactam, meropenem, gentamicin	Rash
5	Cephalosporins: rash	Cefepime, gentamicin, ciprofloxacin	Rash
6	Penicillin: hives	Cefepime, ciprofloxacin	Itching
7	Penicillins: rash	Ciprofloxacin, metronidazole	Shortness of breath
8	Penicillin: rash	Aztreonam, cefepime, aztreonam, gentamicin	Shortness of breath
9	Penicillin: unknown	Piperacillin/tazobactam, aztreonam, meropenem, ciprofloxacin	Anaphylaxis
10	Penicillin: unknown	Moxifloxacin, azithromycin, cefepime, aztreonam	Anaphylaxis
11	Penicillin and vancomycin: anaphylaxis; cephalosporins: rash and itching	Cefepime, sulfamethoxazole	Leukopenia
12	Cefepime: rash	Vancomycin, meropenem, daptomycin, metronidazole, levofloxacin, piperacillin/tazobactam	Leukopenia
13	Penicillin: unknown	Cefepime, piperacillin/tazobactam, linezolid, meropenem, ciprofloxacin	Pancytopenia
14	Penicillin and sulfa: swelling and anaphylaxis	Aztreonam	Thrombocytopenia
15	Penicillin: unknown	Meropenem, vancomycin	Undocumented
16	Penicillin: rash, swelling	Levofloxacin, vancomycin, metronidazole	Undocumented

TABLE IV. Characteristics of patients who experienced a hypersensitivity reaction during treatment of index gram-negative BSI compared with patients who did not experience a hypersensitivity reaction

	Reaction (n = 16)	No reaction (n = 536)	P value
PMH BL allergy, no. (%)			
Penicillin	12 (75.0)	406 (75.7)	.571
Cephalosporin	7 (43.8)	160 (29.9)	.178
Carbapenem	1 (6.3)	33 (6.2)	.644
NBL antibiotic allergy	9 (56.3)	205 (38.2)	.117
PMH BL allergy description, no. (%)			.034
Rash	6 (37.5)	230 (42.9)	
Hives/edema	2 (12.5)	103 (19.2)	
Unknown/undocumented	1 (6.3)	102 (19.0)	
Anaphylaxis	5 (31.3)	45 (8.4)	
Other	2 (12.5)	37 (6.9)	
GI intolerance	0 (0)	19 (3.5)	
Clinical failure at 72-96 h, no. (%)	7 (43.8)	157 (29.3)	.165
Fever	2 (12.5)	85 (15.9)	.525
Vasopressor initiation	2 (12.5)	14 (2.6)	.075
Mechanical ventilation initiation	2 (12.5)	24 (4.5)	.171
Intensive care unit admission	2 (12.5)	11 (2.1)	.051
Death	0 (0)	47 (8.8)	.236
Hospital length of stay (d), mean $\pm$ SD	23.7 $\pm$ 18.1	23.5 $\pm$ 36.5	.986
Postculture length of stay (d), mean $\pm$ SD	13.3 $\pm$ 17.2	13.3 $\pm$ 17.1	.698
28-d Mortality, no. (%)	0	84 (16.9)	.087

GI, Gastrointestinal.

a subset *post hoc* analysis and did not show statistical difference. Studies comparing the efficacy of BLs versus NBLs for pulmonary and intra-abdominal infections have cure rates that range from 77% to 81% for NBLs to 89% to 91% for BLs.²²⁻²⁷ Even though cure rates for BL treatment arms were numerically higher than for their NBL counterparts, all studies were designed as noninferiority trials, and cure rates were not directly compared.

Another design limitation of these trials pertaining to the empiric treatment of patients with GNB infections is the definition chosen for clinical cure. In all studies patients were assessed for clinical cure after completion of the assigned antibiotic course, in many cases up to 28 days after completion of therapy. This type of outcome does not mirror clinical practice because it is routine to evaluate a patient's clinical response to antibiotic treatment much earlier after initiation of treatment, commonly within 72 to 96 hours.

Recent studies have found poor outcomes for patients labeled as having a BL allergy. Macy and Contreras²⁸ performed a matched cohort study of more than 100,000 Kaiser Permanente Health plan patients. They found that patients with penicillin allergies had higher rates of *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant *Enterococcus* species infections and longer lengths of stay compared with those without penicillin allergies. In addition to worse clinical outcomes, potentially unnecessary avoidance of BL antibiotics has been shown to increase health care costs for the patient and hospital. A study by Picard et al²⁹ found that patients identified as having a penicillin allergy carried an additional cost of more than \$15,000 because of the use of alternative NBL antibiotics. As evidenced by Li et al,³⁰ NBL costs can be 1.82- to 2.58-fold higher compared with first-line antibiotics when used in patients with a penicillin allergy.

We report a hypersensitivity rate of 2.9% in our study population of 552 patients with a documented BL allergy. The low rate of hypersensitivity is likely a result of a combination of factors. A recent study in children found only 6.8% of patients with a penicillin allergy had a reproducible reaction after medication rechallenge.³¹ It has been established that penicillin-specific antibodies rapidly wane over time.⁹ The patients included in our analysis were adults and might have lost sensitivity to penicillin with time. This suggests that the risk of causing a true IgE-mediated allergic reaction with the use of BLs in an adult GNB BSI population might be low.

Additionally, most patients in this study received a BL outside of the allergy class listed in the PMH. For example, patients with a

penicillin allergy received either a cephalosporin or a carbapenem. Large database evaluations investigating cross-reactivity or the likelihood of experiencing a hypersensitivity reaction to another class of BLs in the presence of a penicillin allergy are varied.^{32,33} *In vivo* research indicates that in patients with an IgE-mediated allergic reaction to penicillin, the rate of cross-reactivity to other BLs, such as cephalosporins, is approximately 10%³⁴ and as low as 1% for carbapenems.^{35,36} Although the risk of anaphylaxis or an IgE-mediated reaction is worrisome, it is rarely fatal.³⁷

One of the limitations of our study is the possibility of underreporting of hypersensitivity reactions. Not all patients received an allergy consult, and it is difficult to confirm details of the reaction with respect to timing and type of hypersensitivity based on reliance of documentation in patients' charts. Another limitation was use of empiric antibiotics in the BL group, which might have consisted of a combination of BL and NBL antibiotics. It is possible that the use of multiple antimicrobials could favor the BL group to achieve better outcomes. Additionally, the severity of illness measures was different between the groups. APACHE II scores and vasopressor use were significantly higher in the BL group; however, there were more patients receiving mechanical ventilation in the NBL group. Despite the aforementioned limitations, the likelihood of a prospective study that enrolls patients with a BL allergy to receive a BL antibiotic is unlikely because of the liability risk.

In conclusion, despite potential concern of inducing an antibiotic hypersensitivity reaction in a patient with a documented BL allergy, nearly 80% of this GNB BSI patient cohort received a BL as empiric therapy. The use of BL antibiotics in patients with a BL allergy was associated with a significantly lower rate of clinical failure at 72 to 96 hours. Additionally, the rate of hypersensitivity in this cohort provides further evidence that the risk of cross-reactivity between BL classes is quite low. These results do not support the practice of avoiding all BL antibiotics in the scenario of an allergy to a single class of BL. Use of an antibiotic in the same class of allergy should continue to be avoided. Clinicians can use these data to improve clinical outcomes by providing the most appropriate empiric antimicrobial regimens for adult patients with suspected GNB BSI.

Clinical implications: Patients with a history of BL allergies are more likely to experience treatment failure when treated with an NBL and no less likely to experience a hypersensitivity reaction.

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