Impact of Beta-lactam Allergy on Treatment of Outpatient Infections

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ABSTRACT

Purpose: The most commonly reported medication allergies in the United States involve beta-lactam antibiotics, creating an important consideration for prescribers when choosing optimal treatment of infections. Currently, few data exist on outpatient prescribing patterns in response to patients with a beta-lactam allergy. This study sought to evaluate the appropriateness of outpatient antibiotic therapy in patients with documented beta-lactam allergies within a Veterans Affairs health care system to evaluate areas of improvement in prescribing practices.

Methods: Patients receiving outpatient oral antibiotics were prospectively identified through real-time electronic alerts from June 2017 through February 2018. Prescriptions were then reviewed retrospectively to identify appropriateness of antibiotic, drug choice, dose, and duration based on current guideline recommendations. Data were compared between patients with a listed beta-lactam allergy and patients without a beta-lactam allergy to determine the impact on prescribing patterns and outcomes. Baseline characteristics were compared by using descriptive statistics. Significant risk factors for inappropriate prescribing were identified through a multivariable analysis.

Findings: The cohort included 1844 antibiotic prescriptions (documented beta-lactam allergy, 221; no beta-lactam allergy, 1623). Appropriate drug, dose, and duration for antibiotics prescribed in patients reporting a beta-lactam allergy versus nonallergic patients were 44.3% versus 53.0% ($P = 0.02$), 91.4% versus 86.2% ($P = 0.03$), and 75.1% versus 76.2% ($P = 0.83$), respectively. Patients with a reported beta-lactam allergy were 31% less likely to receive the correct drug for indication empirically (95% CI, 0.52−0.92) in the multivariable regression model when adjusted for fluoroquinolone use. In addition, patients reporting a beta-lactam allergy were 2.2 times (95% CI, 1.6−3.0) more likely to receive a fluoroquinolone antibiotic. Antibiotics were considered overall inappropriate based on at least one aspect of therapy in 79.6% of patients reporting a beta-lactam allergy and in 71% of nonallergic patients.

Implications: Antibiotic therapy in patients with a documented beta-lactam allergy was less likely to be appropriate overall, suggesting an area of improvement for prescribing habits. Future interventions should focus on prescriber education regarding first-line and alternative treatments for patients with beta-lactam allergies to ensure that optimal treatment is being provided. (*Clin Ther.* 2019;41:2529−2539) Published by Elsevier Inc.

Key words: allergy, beta-lactam, stewardship, antibiotic, drug utilization review, antimicrobial stewardship.

INTRODUCTION

Antibiotic allergy is an important factor for selection of appropriate antimicrobial therapy. The most commonly reported medication allergies in the United States are associated with beta-lactam antibiotics, with ~10% of the population reporting a penicillin allergy.[1]

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Oral beta-lactam antibiotics include penicillins with or without beta-lactamase inhibitors and cephalosporins. These antibiotics have a substantial role in the treatment of infectious diseases and are considered the first-line outpatient treatment for many common infections, including sinusitis, pharyngitis, and otitis media.[2–4] Alternative antibiotics used in patients with a beta-lactam allergy include fluoroquinolones, macrolides, and later generation cephalosporins, which are often broader spectrum than necessary. Later generation cephalosporins can be used depending on the risk of cross-reactivity.[5] Alternatively, agents that are less effective may be used in the presence of beta-lactam therapy. According to the Centers for Disease Control and Prevention, *Streptococcus pneumoniae* is resistant to at least 1 antibiotic in 30% of cases.[6] In the United States in 2005–2006, macrolide resistance increased to 35%.[7] Declining susceptibly is a worldwide problem; in Pakistan, for example, *S pneumoniae* resistance to macrolides was 34% in 2015, contrasting with amoxicillin, which has susceptibilities between 99.4% and 100%.[8] These agents are not always appropriately chosen and may increase costs, incidence of adverse drug events, and morbidity.[9] In particular, the prescribing of fluoroquinolones has become more of a concern due to their extensive adverse effect profile, including QT prolongation, cartilage damage, neurotoxicity, and aortic rupture.[10] The avoidance of broader spectrum therapy, or therapy that is less efficacious, in patients with a documented beta-lactam allergy could play an integral role in the prevention of antibiotic resistance.

Although inpatient practices are relatively well defined, few data exist on outpatient prescribing patterns in patients with reported allergies to beta-lactam antimicrobial agents. The goal of the present study was to evaluate the appropriateness of outpatient antibiotic selection in patients with a documented beta-lactam allergy and its impact on retreatment and readmission for infection. The effect of a reported beta-lactam allergy on rates of fluoroquinolone use was also examined.

PATIENTS AND METHODS

Study Design

This retrospective study was approved by the Research and Development Committee at the Veterans Affairs Western New York Health Care System as a quality assurance/quality improvement study, and as such, institutional review board approval was not required. During a study time frame of June 2017 to February 2018, the infectious disease pharmacy team received real-time computerized patient record system alerts regarding select outpatient oral antibiotics. Alerts were chosen based on frequency of antibiotic use in preparation for an outpatient antimicrobial stewardship program. These antibiotics included amoxicillin, amoxicillin/clavulanate, azithromycin, cefdinir, cefpodoxime, cephalexin, ciprofloxacin, levofloxacin, metronidazole, moxifloxacin, and trimethoprim/sulfamethoxazole. Clarithromycin and nitrofurantoin were excluded because clarithromycin is primarily used for *Helicobacter pylori* treatment, and nitrofurantoin is prescribed with lower frequency given the male-dominant population. Additional antibiotics were included if prescribed concomitantly with the aforementioned antibiotics.

Beta-lactams are often first-line treatment for many outpatient infections, and if a patient has a beta-lactam allergy, second-line drugs (which may be less familiar to providers) are often used. Thus, duration, dose, and overall need for antibiotics were also evaluated. Current guideline recommendations were referenced to evaluate the appropriateness of these targets. An infectious diseases physician was available to review any medical records when there was a question of appropriateness.

Patients were included if they were seen in the outpatient setting at the main campus or one of the seven community-based outpatient clinics. Using current literature recommendations, a retrospective chart review was conducted to determine appropriate choice of antibiotic in patients with and without a listed beta-lactam allergy. Patients included in the study were aged $\geq$18 years and were prescribed one or more of the selected outpatient antibiotics. Patients with inadequate chart documentation (ie, insufficient information regarding the patient's infection, unclear indication for antibiotic) were excluded. In addition, patients were excluded if they were seen at a facility or by a provider outside the Veterans Affairs Western New York Health Care System. Patients were also excluded if given an antibiotic for dental infections, prophylaxis, or orthopedic infections due to lack of standardized guidelines.

Baseline characteristics included age, body mass index, sex, race, temperature, serum creatinine, estimated creatinine clearance using actual body weight, and antibiotic allergies. Data on choice of drug, dose, and duration were collected. Also collected was information on diagnosis of infection per provider note; *International Classification of Diseases, Tenth Revision,* code for the encounter; the patient's clinical presentation (signs/symptoms); specific outpatient setting where the patient was seen; admission and/or retreatment within 30 days; and comorbid conditions. Furthermore, each patient's comorbid conditions were used to calculate their Charlson Comorbidity Index score.[11] If collected, cultures were also considered to assess antibiotic appropriateness. The nature of the reaction in patients with a documented beta-lactam allergy was also recorded.

Definitions

The need for an antibiotic and choice of drug, duration, and dose were evaluated by using current literature recommendations and compared between patients with and without a documented beta-lactam allergy. The Infectious Diseases Society of America guidelines were consulted for treatment of sinusitis, pharyngitis, community-acquired pneumonia, urinary tract infections, diabetic foot infections, infectious diarrhea, skin and soft tissue infections, and prostatitis.[2,3,12–18] The treatment of otitis media, bronchitis, epididymitis and orchitis, and sexually transmitted diseases was based on guidance from the Centers for Disease Control and Prevention.[4,19] Recommendations from the Surgical Infection Society and the Infectious Diseases Society of America were used for the treatment of diverticulitis.[20] Lastly, the Global Initiative for Chronic Obstructive Lung Disease guidance was consulted for treatment of chronic obstructive pulmonary disease (COPD) exacerbations.[21]

Aspects of the drug regimen were evaluated for appropriateness based on guidelines and patient-specific factors. Selection of the specific antibiotic was deemed appropriate if consistent with guideline-recommended first-line therapy, considering antibiotic allergies and culture data (Table I). In patients with contraindications or previous treatment failures, second-line therapy as outlined in the guidelines was also accepted as appropriate. Because empiric treatment is not frequently confirmed with cultures in the outpatient setting, previous treatment failure was classified as a lack of clinical response or symptom resolution with the first-line antibiotic. Antibiotic dose was considered appropriate if in accordance with literature recommendations, as well as any warranted dose adjustments based on the patient's renal function. Duration was accepted as appropriate if it was consistent with published literature. If antibiotic need, selection, dose, and duration were all correct, the patient's therapy was considered overall appropriate. Antibiotic usage was considered unnecessary if not indicated by guidelines or not warranted based on the patient's clinical presentation per chart review. Prescription of a beta-lactam antibiotic in patients who reported a beta-lactam allergy was still considered correct if the provider had valid documentation in the chart explaining the selection or cross-reactivity was known to be minimal. In the absence of a documented reaction, a reported beta-lactam allergy was considered to be valid.

Statistical Analysis

A bivariate analysis was used to compare baseline characteristics, severity of illness, and risk factors between patients with a documented beta-lactam allergy and patients without. A χ^2 test and Student's *t* test were used to analyze categorical and continuous data, respectively. Multivariable logistic regression was used to estimate odds ratios and 95% CIs and identify significant risk factors for appropriate treatment between the patient groups. All significant variables from the bivariate analysis were included initially, with the least significant variable eliminated in a stepwise fashion as a backward elimination. Significance was defined at $P < 0.05$. Analysis was performed by using JMP Pro version 14 (SAS Institute, Inc, Cary, North Carolina; 1989–2007).

RESULTS

The retrospective chart review was conducted on 1844 total antibiotic prescriptions (documented beta-lactam allergy, 221; no beta-lactam allergy, 1623). Patients without a beta-lactam allergy were more likely to be male. Patients with a reported beta-lactam allergy were more likely to have COPD or asthma, but other

comorbidities were balanced between the 2 groups (Table II).

Patients with a reported beta-lactam allergy were significantly less likely to receive the correct drug based on indication, with only 44% of patients reporting beta-lactam allergies receiving the appropriate antibiotic compared with 53% of non–beta-lactam allergic patients. Of patients who were beta-lactam allergic and received an incorrect drug, 29% were treated for ear, nose, and throat infections; 51% for respiratory tract infections; 10% for skin and skin structure infections; and 10% for urologic infections. Fifty-one percent of the overall population received the correct antibiotics. Based on guidelines and published recommendations, antibiotics were indicated in 54% of patients with a reported beta-lactam allergy compared with 60% of those without a beta-lactam allergy; this finding was not statistically different. Although the rates of correct duration did not differ significantly between groups, patients with a reported beta-lactam allergy were more likely to be given the correct dose (91% vs 86%; $P = 0.03$). Of significance, antibiotic prescribing for patients reporting a beta-lactam

Table I. Antibiotic selection for patients with and without beta-lactam allergy.

Outpatient Infection	First-Line Antibiotic	Alternative Antibiotic for Beta-Lactam Allergy
Bronchitis	Antibiotics not indicated	
CAP	Azithromycin or doxycycline ± beta-lactam*	Levofloxacin, moxifloxacin
COPD exacerbation	Azithromycin, doxycycline, or levofloxacin	NA
Epididymitis	Ciprofloxacin, Ceftriaxone + doxycycline	NA
Diverticulitis	Cefdinir + metronidazole	Ciprofloxacin + metronidazole
AOM	Amoxicillin	Azithromycin or clindamycin
Bacterial pharyngitis	Penicillin V potassium, Amoxicillin	Clindamycin or azithromycin
Prostatitis	Ciprofloxacin or TMP/SMX	NA
Bacterial rhinosinusitis	Amoxicillin/clavulanate	Doxycycline, levofloxacin, or moxifloxacin
SSTIs		
Cellulitis	Cephalexin	Clindamycin
Abscess	TMP/SMX, clindamycin, doxycycline	NA
Bite	Amoxicillin/clavulanate	Moxifloxacin, clindamycin
Diabetic foot	Amoxicillin/clavulanate	Moxifloxacin
STDs		
Chlamydia	Azithromycin or doxycycline	NA
Gonorrhea	Ceftriaxone + azithromycin	NA
UTIs		
Asymptomatic bacteriuria	Antibiotics not indicated	NA
Cystitis	TMP/SMX, ciprofloxacin, cefdinir	NA

AOM = acute otitis media; CAP = community-acquired pneumonia; COPD = chronic obstructive pulmonary disease; SSTI = skin and soft tissue infection; STD = sexually transmitted disease; UTI = urinary tract infection; TMP/SMX = trimethoprim/sulfamethoxazole; not applicable = NA.

* Depending on comorbidities.

Table II. Comparison of baseline characteristics between patients with and without beta-lactam allergy.

Baseline Characteristic	Beta-Lactam Allergy (n = 221)	No Beta-Lactam Allergy (n = 1623)	*P*
Age, mean (SD), y	61.7 (16.5)	62.5 (15.6)	0.45
Male sex	175 (79.2%)	1471 (90.6%)	<0.0001
Race			0.35
African American	25 (11.3%)	202 (12.5%)	
White	189 (85.5%)	1392 (85.8%)	
Other	7 (3.2%)	29 (1.8%)	
Body mass index, mean (SD), kg/m^2	31.1 (7.0)	30.9 (7.4)	0.66
Temperature, mean (SD), °F	97.8 (0.8)	97.8 (0.9)	0.71
Serum creatinine, mean (SD), mg/dL	1.0 (0.4)	1.1 (0.7)	0.25
Creatinine clearance, mean (SD), mL/min	106.6 (47.0)	107.5 (47.6)	0.79
COPD	64 (29.0%)	350 (21.6%)	0.01
Asthma	28 (12.7%)	108 (6.7%)	0.001
Myocardial infarction	13 (5.9%)	80 (4.9%)	0.54
Heart failure	9 (4.1%)	94 (5.8%)	0.30
PVD	34 (15.4%)	218 (13.4%)	0.43
CVA/TIA	21 (9.5%)	108 (6.7%)	0.12
Dementia	7 (3.2%)	34 (2.1%)	0.31
Connective tissue disease	6 (2.7%)	24 (1.5%)	0.17
PUD	1 (0.5%)	22 (1.4%)	0.26
Mild liver disease	12 (5.4%)	79 (4.9%)	0.72
Diabetes, no end-organ damage	38 (17.2%)	267 (16.5%)	0.78
Hemiplegia	1 (0.5%)	9 (0.6%)	0.85
Moderate to severe renal disease	13 (5.9%)	130 (8.0%)	0.27
Diabetes, with end-organ damage	23 (10.4%)	215 (13.3%)	0.24
Tumor without metastases	42 (19.0%)	276 (17.0%)	0.46
Leukemia	0	17 (1.1%)	0.13
Lymphoma	1 (0.5%)	6 (0.4%)	0.85
Moderate to severe liver disease	0	21 (1.3%)	0.09
Metastatic solid tumor	2 (0.9%)	15 (0.9%)	0.98
AIDS	0	3 (0.2%)	0.52
Charlson Comorbidity Index score			0.97
0–4	200 (90.5%)	1470 (90.6%)	
5–10	21 (9.5%)	153 (9.4%)	

COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident; PUD = peptic ulcer disease; PVD = peripheral vascular disease; TIA = transient ischemic attack.

allergy was less likely to be overall appropriate (determined by need for antibiotic, drug choice, dose, and duration) than patients without a beta-lactam allergy (20.4% vs 29.0%; $P = 0.007$). There was no statistically significant difference between rates of 30-day retreatment or readmission between the patient groups (Table III).

The most frequently used antibiotic in both groups of patients was azithromycin, with 40% of patients reporting a beta-lactam allergy and 27% of the

Table III. Antimicrobial stewardship practices and outcomes: patients with a beta-lactam allergy versus those without a beta-lactam allergy.

Variable	Beta-Lactam Allergy (n = 221)	No Beta-Lactam Allergy (n = 1623)	*P*
Correct drug for indication empirically	98 (44.3%)	860 (53.0%)	0.02
Correct dose	202 (91.4%)	1399 (86.2%)	0.03
Duration			0.83
Correct duration	166 (75.1%)	1236 (76.2%)	
Longer than indicated	42 (19.0%)	307 (18.9%)	
Shorter than indicated	13 (5.9%)	80 (4.9%)	
Antibiotic needed	119 (53.9%)	981 (60.4%)	0.06
Overall appropriateness of therapy (no change needed)	45 (20.4%)	471 (29.0%)	0.007
Indication			0.02
Bronchitis	40 (18.1%)	234 (14.4%)	
CAP	28 (12.7%)	125 (7.7%)	
COPD	18 (8.1%)	115 (7.1%)	
Epididymitis	3 (1.4%)	17 (1.1%)	
Gastrointestinal	4 (1.8%)	49 (3.0%)	
Otitis media	7 (3.2%)	80 (4.9%)	
Pharyngitis	8 (3.6%)	49 (3.0%)	
Prostatitis	5 (2.3%)	33 (2.0%)	
Sinusitis	43 (19.5%)	258 (15.9%)	
SSTI	28 (12.7%)	374 (23.0%)	
STD	1 (0.5%)	16 (1.0%)	
UTI	36 (16.3%)	273 (16.8%)	
Antibiotic			<0.0001
Amoxicillin/clavulanate	6 (2.7%)	297 (18.3%)	
Amoxicillin	2 (0.9%)	139 (8.6%)	
Amoxicillin + clarithromycin	0	6 (0.3%)	
Azithromycin	89 (40.3%)	432 (26.6%)	
Beta-lactam + TMP/SMX	0	28 (1.7%)	
Beta-lactam + atypical*	0	13 (0.8%)	
Cefdinir or cefpodoxime	8 (3.6%)	53 (3.3%)	
Cephalexin	8 (3.6%)	198 (12.2%)	
Ciprofloxacin	32 (14.5%)	189 (11.7%)	
Ciprofloxacin + metronidazole	1 (0.5%)	13 (0.8%)	
Clindamycin	0	3 (0.2%)	
Doxycycline	0	3 (0.2%)	
Fluoroquinolone + metronidazole	3 (1.4%)	12 (0.7%)	
Levofloxacin	20 (9.1%)	52 (3.2%)	
Moxifloxacin	19 (8.6%)	47 (2.9%)	
TMP/SMX	2 (0.9%)	7 (0.4%)	
Other	31 (14.0%)	131 (8.1%)	
Fluoroquinolone used (vs non-fluoroquinolone)	77 (34.8%)	316 (19.5%)	<0.0001

Table III. (*Continued*)

Variable	Beta-Lactam Allergy (n = 221)	No Beta-Lactam Allergy (n = 1623)	*P*
30-Day retreatment for infection	17 (7.7%)	154 (9.5%)	0.39
30-Day admission for infection	5 (2.3%)	37 (2.3%)	0.99

CAP = community-acquired pneumonia; COPD = chronic obstructive pulmonary disease; SSTI = skin and soft tissue infection; STD = sexually transmitted disease; UTI = urinary tract infection, TMP/SMX = trimethoprim/sulfamethoxazole.
* Atypical antibiotics included doxycycline and azithromycin.

patients without a beta-lactam allergy receiving this medication. Azithromycin was also the most commonly inappropriately prescribed antibiotic, regardless of allergy. This is likely related to a high rate of unnecessary antibiotic prescribing for bronchitis. Indications for antibiotics differed between the 2 groups. A higher proportion of patients with a reported beta-lactam allergy received antibiotics for bronchitis, community-acquired pneumonia, and sinusitis, whereas skin and soft tissue infections were more common in the patients without a reported beta-lactam allergy (Table III).

Patients with a reported beta-lactam allergy were significantly more likely to receive a fluoroquinolone antibiotic than those without the allergy (34.8% vs 19.5%; $P < 0.0001$). A fluoroquinolone was considered the incorrect drug for indication for 33 (42.9%) of the 77 patients reporting a beta-lactam allergy. In the beta-lactam allergy group, fluoroquinolone prescriptions were more likely to be appropriate than in the group with no beta-lactam allergy (68% vs 57%), but the difference was not statistically significant. Urologic indications were the most common area of usage of fluoroquinolones in both patient groups.

Of the 221 patients with a reported beta-lactam allergy, 24 (10.9%) received a beta-lactam antibiotic after evaluation from the provider on the nature of the allergy. Nine patients with a penicillin allergy received cefdinir, and 3 received cephalexin. Eight patients with a cephalosporin allergy received an aminopenicillin. One half of these patients were recorded as receiving the correct drug for indication empirically. None of these patients had an adverse reaction. The nature of the reactions was as follows: rash (29.9%), unknown (25.8%), hives (24.4%), anaphylaxis (14%), hypotension (2.7%), headache (1.8%), burning sensation (0.9%), and acute interstitial nephritis (0.5%).

In the multivariable logistic regression models, 2 variables predicted whether patients received the correct empiric antibiotic for infection. Patients with a reported beta-lactam allergy were 31% less likely to be prescribed the appropriate antibiotic based on indication, whereas patients with COPD were 1.3 times more likely to receive the correct drug for indication (Table IV). Patients with a reported beta-lactam allergy were more likely to be treated inappropriately and more often received fluoroquinolone antibiotics. The rate of an antibiotic being overall appropriate was 37% less likely if the patient had a reported beta-lactam allergy. In addition, patients reporting a beta-lactam allergy were 2.2 times more likely to receive a fluoroquinolone antibiotic.

DISCUSSION

Approximately 12% of our study population who were prescribed antibiotics had a documented beta-lactam allergy, slightly higher than previously established US population data for patients with a penicillin allergy.[1] Overall, antibiotic prescribing was suboptimal regardless of beta-lactam allergy status.[22] Patients with a documented beta-lactam allergy were less likely to receive the correct drug for their infection and have therapy that was considered overall appropriate (ie, antibiotic needed, correct drug, correct dose and duration). Although few data exist on outpatient antibiotic prescribing in response to a beta-lactam allergy, our findings were consistent with studies conducted in an inpatient setting. Trubiano et al[23] reported a higher rate of inappropriate antibiotic prescribing in patients with an antibiotic allergy (mostly to a beta-lactam)

Table IV. Multivariable logistic regression: odds of appropriate treatment. Variables included for each model have numeric odds ratios listed. Dashes (—) in the COPD row indicate that the variable was not significant and was therefore not included in the final multivariable model.

Variable	Odds for Correct Drug for Indication Empirically	Overall Appropriateness of Therapy (No Change Needed)	Use of Fluoroquinolone*
Beta-lactam allergy vs. no beta-lactam allergy	0.69; 95% CI (0.52—0.92)	0.63; 95% CI (0.44—0.90)	2.20; 95% CI (1.6—3.0)
COPD	1.27; 95% CI (1.02—1.60)	—	—

COPD = chronic obstructive pulmonary disease.
* Regimen included ciprofloxacin, moxifloxacin, or levofloxacin.

compared with those without the allergy (29% vs 23%, respectively). In another study, MacFadden et al[24] showed that 35% of patients with a beta-lactam allergy did not receive preferred therapy for their indication, even though more than one half of those patients reported a nonsevere reaction.

Patients with a documented beta-lactam allergy were significantly more likely to receive broader antibiotics such as a fluoroquinolone. These findings were similar to those of other studies, in which fluoroquinolones, macrolides, and clindamycin were used more frequently in patients with an antibiotic allergy.[25–27] Aside from promoting drug-resistant organisms, the use of broader spectrum therapy can have a variety of consequences. First, these therapies can be more expensive than a narrow-spectrum option. One study showed that the mean antibiotic cost for patients with a reported beta-lactam allergy was almost 37% higher than for patients without the allergy, while another analysis found an even more drastic cost increase of 63%.[28,25] In addition, broad-spectrum therapy has the potential for more significant adverse effects.[29] Fluoroquinolones and macrolides have cardiac considerations, including QT interval prolongation and risk of aortic rupture. These agents also have the potential to increase the frequency of *Clostridium difficile* infections.[30] In many cases, these broader agents can be avoided by selecting a more appropriate second-line agent in patients with a beta-lactam allergy, such as a later generation cephalosporin.

Azithromycin, which is less efficacious for organisms such as *S pneumoniae*, is often prescribed to patients with beta-lactam allergy. In the United States in 2005—2006, macrolide resistance increased to 35%.[7] Macrolide resistance to *S pneumoniae* is on the serious threat list for antimicrobial resistance from the Centers for Disease Control and Prevention.[6] Similarly, trimethoprim-sulfamethoxazole is 87% resistant and tetracycline is 57% resistant to *S pneumoniae*.[8]

A large contributor to the discrepancies found in antibiotic prescribing in patients with a beta-lactam allergy is the lack of understanding regarding cross-reactivity between pharmacologic classes. More recent studies show that structural similarities in the side chains are responsible for the allergy rather than solely the beta-lactam ring.[31,32] The reported incidence of cross-reactivity has been found to be <1%—5% for cephalosporins (with the highest rate of cross-reactivity in first-generation cephalosporins).[1,33–35] Many patients are labeled with a penicillin allergy early in life, and the uncertain nature of their allergy may result in hesitancy of providers to challenge with a beta-lactam from an alternate class. A study by Shah et al[36] found that rechallenge rates improved when the specific drug within the class was documented (ie, "amoxicillin" rather than "penicillins") and when the actual patient reaction was documented. During retrospective chart review in this study, 19% of patients with a documented beta-lactam allergy had no reaction recorded or it was marked "unknown." It is also important to make the distinction between a true allergy and a drug intolerance. Drug intolerances are unlikely to be immune mediated and may include gastrointestinal symptoms. These types of reactions do not preclude a patient from receiving the antibiotic.[37,38] Although nearly 10% of the

population reports a beta-lactam allergy, <1% are truly allergic when evaluated by using a skin test.[1] Although our study did not seek to verify the validity of a patient's allergy, a possible future direction for health care providers may involve hypersensitivity testing for patients to avoid unnecessarily precluding a first-line treatment.

There are limitations to the present study. The patients included were mostly male (89.3%) and of older age, from a single health care system of veterans. In addition, because data collection relied heavily on chart documentation by providers, there may have been inconsistencies in assessment of infection and evaluation of antibiotic selection. Antibiotics such as linezolid, doxycycline, clindamycin, fosfomycin, and nitrofurantoin were not collected because there were no alerts set up to the pharmacist at the time of this study. In addition, the design of the study relied on antibiotic prescriptions, and we were therefore unable to determine the likelihood of patients who were correctly not prescribed an antibiotic.

CONCLUSIONS

Patients with listed beta-lactam allergies often do not receive optimal therapy in the outpatient setting. It is essential for prescribers to be familiar with the guideline-recommended alternative treatments for patients with a beta-lactam allergy to avoid inadequate therapy. Providers may also benefit from additional education on beta-lactam cross-reactivity, strategies for rechallenging beta-lactam antibiotics, and criteria for adequate chart documentation of allergies. It is good practice to ask patients about their allergy and the nature of their reaction at each encounter, which can ensure up-to-date patient information and ideal treatment selection.

DISCLOSURES

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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