Impact of Penicillin Allergy on Time to First Dose of Antimicrobial Therapy and Clinical Outcomes

Erin L. Conway, PharmD[1]; Ken Lin, PharmD[1]; John A. Sellick, DO[1,2];
Kari Kurtzhalts, PharmD[1]; James Carbo, PharmD[1]; Michael C. Ott, PharmD, BCPS[3]; and
Kari A. Mergenhagen, PharmD, BCPS AQ-ID[1]

[1]Veterans Affairs Western New York Healthcare System, Buffalo, New York; [2]Division of Infectious
Diseases, University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, New York; and
[3]Erie County Medical Center, Buffalo, New York

ABSTRACT

Purpose: The objective of this study was to evaluate the impact of a listed penicillin allergy on the time to first dose of antibiotic in a Veterans Affairs hospital. Additional clinical outcomes of patients with penicillin allergies were compared with those of patients without a penicillin allergy.

Methods: A retrospective chart review of veterans admitted through the emergency department with a diagnosis of pneumonia, urinary tract infection, bacteremia, and sepsis from January 2006 to December 2015 was conducted. The primary outcome was time to first dose of antibiotic treatment, defined as the time from when the patient presented to the emergency department to the medication administration time. Secondary outcomes included total antibiotic therapy duration and treatment outcomes, including mortality, length of stay, and 30-day readmission rate.

Findings: A total of 403 patients were included in the final analysis; 57 patients (14.1%) had a listed penicillin allergy. The average age of the population was 75 years and 99% of the population was male. The mean time to first dose of antibiotic treatment for patients with a penicillin allergy was prolonged compared with those without a penicillin allergy (236.1 vs 186.6 minutes; $P = 0.03$), resulting in an approximately 50-minute delay. Penicillin-allergic patients were more likely to receive a carbapenem or fluoroquinolone antibiotic ($P < 0.0001$).

Implications: Patients with a penicillin allergy had a prolonged time to first dose of antibiotic therapy. No significant differences were found in total antibiotic duration, length of stay, or 30-day readmission rate. The small sample size, older population, and single-center nature of this study may limit the generalizability of the present findings to other populations. (Clin Ther. 2017;▮:▮▮▮–▮▮▮) © 2017 Published by Elsevier HS Journals, Inc.

Key words: allergy, emergency department, penicillin.

INTRODUCTION

Penicillin allergies account for one of the most common medication-related allergies reported in the United States. Previous studies estimate that ~10% to 15% of the population has reported allergies to this commonly used antimicrobial class.[1–3] The incidence of allergies validated with penicillin skin testing ranges between 7% and 28% of patients reporting a penicillin allergy.[4–7] Many patients lack a detailed history of their allergy, including antibiotic agent and nature of allergic reaction. These incomplete patient data lead to suboptimal treatment options[8].

For patients with a listed penicillin allergy, there are substantial consequences of using second-line therapies and associated adverse outcomes. In these patients, increased use of fluoroquinolones, vancomycin, clindamycin, and macrolides has been observed.[9,10] A Canadian study found that patients with penicillin allergies were associated with increased cost of hospitalization, up to $15,672.[3] Similarly, an additional study found a 63% higher mean antibiotic cost for penicillin-allergic patients.[11]

Unfortunately, the presence of a penicillin allergy may prevent the use of other β-lactam antibiotics, despite the low rate of cross-reactivity. Among health

care providers, there is a lack of knowledge regarding the safe use of alternative β-lactams in penicillin-allergic patients. Fear of a cross-reaction among β-lactams leads to broader or suboptimal antibiotic use, increased health care costs, adverse patient outcomes, and the development of bacterial resistance.[12]

The Surviving Sepsis Campaign guideline includes specific recommendations regarding the timing of antibiotic therapies.[13] This guideline recommends the administration of effective IV antimicrobial agents within the first hour of recognition of septic shock or severe sepsis without septic shock and the administration of broad-spectrum antibiotics within 3 hours from emergency department (ED) triage. In 2006, Kumar et al[14] reported a 7.6% increase in mortality in patients with sepsis for every hour of delay of antibiotics after the onset of shock. Subsequent studies, however, have failed to duplicate these findings with similar results.[15–17]

Time to first dose is not a new concept. Kahn et al[18] retrospectively evaluated Medicare patients with pneumonia to launch the concept that antibiotic administration within 4 hours of arrival was associated with a 30-day reduction in mortality. In a 2002 study of ventilator-associated pneumonia, patients given appropriate antibiotics >24 hours after diagnosis were found to die 8 times more than those treated earlier.[19] There are no such data for urinary tract infections (UTIs) with regard to time to first dose. However, there is biologic plausibility, and if the patient is ill enough, mortality can occur if the patient's physiologic reserves are exhausted.[20]

There are limited data that address the impact of penicillin allergy on time to first dose of antibiotic administration in the ED. The goal of the present study was to examine the differences in time to first dose of antibiotic and clinical outcomes between patients with a documented penicillin allergy versus those without such an allergy.

PATIENTS AND METHODS
Design
This study was a single-center, retrospective chart review conducted among patients who were seen in the ED and admitted to the Veterans Affairs Western New York Healthcare System with a diagnosis of pneumonia, UTI, sepsis, or bacteremia between January 1, 2006, and December 1, 2015. Patient charts

were identified by using the following *International Classification of Diseases, Ninth Revision,* codes: pneumonia, 481, 482, 486, 507, 518; UTI, 599, 599.8, and 599.9; sepsis, 785.52, 995.90, 995.91, 995.92, 995.93, and 995.95; and bacteremia, 790.7.

Study Population
Patients were included in the study if they presented to the ED and were treated for one the aforementioned infections. The time that the patient presented to the ED and the time of first antibiotic administration must be documented in the Veterans Affairs computerized patient record system. Only the first admission of serial admissions was included in the study.

Patients were excluded if they initially presented at non–Veterans Affairs Western New York Healthcare System institutions (eg, ED, civilian hospital, other health care clinic), or if the time of first antibiotic administration could not be determined. Immunosuppressed patients (defined according to those with active and systemic cancer receiving chemotherapy within 28 days before admission, a diagnosis of HIV with AIDS, solid organ and/or bone marrow transplantation, or absolute neutrophil count <1500 cells/μL within 28 days before admission), comfort measure care, and any patients who left against medical advice were excluded from the study. To ensure a diagnosis of complicated UTI, female subjects were excluded from the study. Exclusion criteria also included lung abscess, empyema, prostatitis, renal abscess, urinary stents or nephrostomy tubes, genitourinary fistula, and a concurrent infection.

Outcome Measures
The primary objective of the present study was to evaluate the time to first dose of antibiotic for penicillin-allergic patients versus those not allergic to penicillin. The time to first dose was defined as the time between patient presentation to the ED and the time of antibiotic administration according to the administration medication note in the computerized patient record system. Secondary objectives were to evaluate total duration of antibiotics, total duration of IV antibiotics, length of stay (LOS), and readmission rates within 30 days.

Baseline demographic characteristics collected included age, sex, race, weight, height, body mass index, serum creatinine level, creatinine clearance, type of listed reaction to penicillin, Charlson comorbidity