Tackling inpatient penicillin allergies: Assessing tools for antimicrobial stewardship

Kimberly G. Blumenthal, MD, MSc,[a,b,c,d]* Paige G. Wickner, MD, MPH,[d,e]* Shelley Hurwitz, PhD,[d,f] Nicholas Pricco, BS,[g] Alexandra E. Nee, BA,[h] Karl Laskowski, MD, MBA,[d,f] Erica S. Shenoy, MD, PhD,[b,d,i,j] and Rochelle P. Walensky, MD, MPH[b,d,i]

Boston, Mass, Minneapolis, Minn, and Valhalla, NY

Background: Reported penicillin allergy rarely reflects penicillin intolerance. Failure to address inpatient penicillin allergies results in more broad-spectrum antibiotic use, treatment failures, and adverse drug events.

Objective: We aimed to determine the optimal approach to penicillin allergies among medical inpatients.

Methods: We evaluated internal medicine inpatients reporting penicillin allergy in 3 periods: (1) standard of care (SOC), (2) penicillin skin testing (ST), and (3) computerized guideline application with decision support (APP). The primary outcome was use of a penicillin or cephalosporin, comparing interventions to SOC using multivariable logistic regression.

Results: There were 625 patients: SOC, 148; ST, 278; and APP, 199. Of 278 ST patients, 179 (64%) were skin test eligible; 43 (24%) received testing and none were allergic. In the APP period, there were 292 unique Web site views; 112 users (38%) completed clinical decision support. Although ST period patients did not have increased odds of penicillin or cephalosporin use overall (adjusted odds ratio [aOR] 1.3; 95% CI, 0.8-2.0), we observed significant increased odds of penicillin or cephalosporin use overall in the APP period (aOR, 1.8; 95% CI, 1.1-2.9) and in a per-protocol analysis of the skin tested subset (aOR, 5.7; 95% CI, 2.6-12.5).

Conclusions: Both APP and ST—when completed—increased the use of penicillin and cephalosporin antibiotics among inpatients reporting penicillin allergy. While the skin tested subset showed an almost 6-fold impact, the computerized guideline significantly increased penicillin or cephalosporin use overall nearly 2-fold and was readily implemented. (J Allergy Clin Immunol 2017;140:154-61.)

Key words: *Stewardship, skin test, test dose, decision support, computerized guideline*

Penicillin allergy is reported in up to 15% of inpatients and is associated with increased use of alternative antibiotics, including vancomycin, clindamycin, aminoglycosides, and aztreonam.[1-4] Compared with beta-lactam antibiotics, these drugs are less effective in some clinical circumstances,[5-8] more toxic,[4,9] more costly,[10,11] and generally cover a broader antimicrobial spectrum. When a beta-lactam antibiotic is the preferred inpatient antibiotic, but not administered because of alleged allergy, patients experience more treatment failures and adverse events.[4,8] Patients reporting penicillin allergy have increased odds of antibiotic-resistant organisms, such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*.[12]

Despite a reported penicillin allergy, more than 95% of patients evaluated for such allergy are found penicillin and cephalosporin tolerant.[10,12-16] Therefore, active attention to clarifying old and inaccurate penicillin allergies is supported by various US guidelines and agencies as an important feature of antimicrobial stewardship.[17-20] Because the optimal approach to the evaluation and management of inpatient penicillin allergy is unknown, yet impacts a substantial number of patients per year, we

From [a]the Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, [b]Medical Practice Evaluation Center, Massachusetts General Hospital, [c]Edward P. Lawrence Center for Quality and Safety, Massachusetts General Hospital and the Massachusetts General Professional Organization, [d]Harvard Medical School, [e]the Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Brigham and Women's Hospital, and [f]the Department of Medicine, Brigham and Women's Hospital, Boston; [g]the University of Minnesota Medical School, Minneapolis; [h]the New York Medical College, Valhalla; [i]the Division of Infectious Disease, Department of Medicine, and [j]the Infection Control Unit, Massachusetts General Hospital, Boston.

*These authors contributed equally to this work.

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Corresponding author: Kimberly G. Blumenthal, MD, MSc, Massachusetts General Hospital, Medical Practice Evaluation Center, 50 Staniford St, 9th Fl, Boston, MA 02114. E-mail: kblumenthal1@partners.org.

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Abbreviations used
APP: Computerized guideline application with decision support
BWH: Brigham and Women's Hospital
OR: Odds ratio
SOC: Standard of care
ST: Penicillin skin testing
ST-PP: Skin test per-protocol

implemented and assessed 2 health care delivery system innovations to improve antibiotic choice among medical inpatients reporting a history of penicillin allergy.

METHODS

Design overview

We conducted a quasi-experimental study evaluating prospectively identified cohorts of internal medicine inpatients at the Brigham and Women's Hospital (BWH). We sequentially evaluated 3 strategies: (1) BWH standard of care (SOC); (2) history-appropriate penicillin skin testing (ST), a process-based innovation; and (3) a computerized guideline application with clinical decision support (APP), a technology-based innovation. We compared antibiotic use in the intervention periods to the SOC period. This study was approved by the Partners Human Research Committee.

Study population

A daily electronic tracker identified medical inpatients with a history of penicillin allergy prescribed 1 or more doses of any antimicrobial in all periods (Fig 1). Patient readmissions and patients not meriting treatment of a presumed infection were excluded. The latter exclusion comprised patients who did not receive therapeutic antibiotics in the first 7 days of hospitalization, and those who received less than 48 hours of antibiotic therapy, accounting for both discharge antibiotics and amended dosing frequency associated with renal dosing.[21]

Study periods

BWH standard of care. SOC was the comparison period when no active intervention was performed. SOC patient data were collected from June 9, 2014, through November 5, 2014. As an academic, tertiary care facility, BWH has an antibiotic stewardship program that restricts some broad-spectrum and costly antibiotics (eg, linezolid and daptomycin). BWH also has a drug allergy program with inpatient Allergy/Immunology consultation and 24-hour on-call services. During SOC, all skin testing and test dose challenge[22] procedures were performed only when referred by the primary team and deemed appropriate after Allergy/Immunology consultation (see this article's Standard procedure for skin testing and test doses in all periods section and Fig E1, *A*, in the Online Repository at www.jacionline.org).

Penicillin skin testing. The ST period began November 12, 2014, and continued through June 30, 2015. During the ST period, all tracker-identified patients were screened by the care redesign team for skin test eligibility. Patients ineligible for skin testing included patients with penicillin intolerances (eg, gastrointestinal upset), patients taking medications that interfered with skin testing (eg, antihistamines), and patients with multiple beta-lactam allergies, penicillin anaphylaxis in the last 5 years, or a type II to IV hypersensitivity reaction[23] to penicillin. Skin testing was routinely intended for all skin test eligible patients, but required permission from the primary team, coordination of skin testing using a moonlighting pool of allergy trainees and nurses, and patient consent (see this article's Standard procedure for skin testing and test doses in all periods section and Fig E1, *B*). Patients with both negative skin testing and tolerance of an oral amoxicillin test dose were deemed not allergic. The primary medical team and the patients were updated regarding changes in allergy status.

Computerized guideline application with clinical decision support. After a 5-month study break due to a hospital-wide electronic health record conversion,[24] the APP period ran from November 20, 2015, through June 13, 2016 (Fig E1, *C*). A clinical pathway that guided beta-lactam antibiotic use in patients with listed penicillin allergy was previously developed, implemented, and assessed at an academic hospital affiliate (see this article's Evidence supporting the structure of the clinical pathway/guideline section in the Online Repository at www.jacionline.org).[5,25-27] The guideline empowered inpatient providers to group allergic reactions into hypersensitivity type, then recommended if and how specific beta-lactam antibiotics be used (ie, very low risk, full doses; low risk, test doses; medium to high risk, Allergy/Immunology consultation; serious type II-IV hypersensitivity reactions, avoidance).

The previously studied pathway was adapted into a computerized guideline,[28,29] a mobile-friendly Web site with optional clinical decision support, functionally similar to a smartphone application (see this article's Development and testing of computerized guideline/app section in the Online Repository at www.jacionline.org). Because of the coincident electronic health record conversion at the BWH, the computerized guideline was not integrated into the electronic health record, but remained a distinct clinical workflow. The guideline was accessible at any BWH desktop computer or mobile device on the secure intranet. Providers could access the pathway figures directly from the Web site and/or login to use clinical decision support. After decision support computed the patient's likely allergic reaction type, it stratified the reaction into a risk category and displayed recommendations for further action (see Fig E2 in this article's Online Repository at www.jacionline.org). The Web site housed additional educational information and provider videos.

Data collection

All patient data were collected from the electronic health record, with duplicative entry, initially by research assistants (N.P. and A.E.N.), followed by internal medicine housestaff. Data were entered and maintained using Research Electronic Data Capture hosted at Partners HealthCare.[30]

Demographic characteristics

Collected patient data included age, sex, race, admission date, discharge date, admission diagnosis, allergy history, intensive care unit stay and duration time, Infectious Diseases consultation, Allergy/Immunology consultation, history of colonization or infection with methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant *Enterococcus*, renal disease, and overall length of stay. Two board-certified internists and allergists/immunologists (K.G.B. and P.G.W.) determined which admission diagnoses were related to an infection as well as which penicillin allergies were intolerances.

Intervention uptake

In the ST period, we determined the frequency with which eligible patients completed skin testing. In the APP period, we tracked usage through reports from Google Analytics Solutions (Web site views) and clinical decision support responses.

Outcomes

The primary outcome was use of formulary unrestricted penicillins or cephalosporins (see Table E1 in this article's Online Repository at www.jacionline.org). Penicillin and cephalosporin use was identified through inpatient antibiotic administrations. Secondary outcomes included the proportion of patients discharged on a penicillin or cephalosporin antibiotic, inpatient use of alternative antibiotics, and resultant adverse drug reactions.

Penicillins and cephalosporins on BWH formulary were included; cephalosporins were grouped by generation for analysis. Because of the intent to improve antibiotic choice, we excluded penicillins and cephalosporins historically restricted by BWH's antibiotic stewardship program, including piperacillin-tazobactam, ceftaroline, ceftolozane-