Implementation of a Pharmacist-Driven Penicillin and Cephalosporin Allergy Assessment Tool: A Pilot Evaluation

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OBJECTIVE Penicillin is the most commonly reported drug allergy despite the low incidence of true immune-mediated reactions. Penicillin allergy labels have been shown to lead to significant patient, institutional, and public health care consequences. This project's purpose was to improve quality of care for patients with penicillin and cephalosporin allergies, admitted to a pediatric institution, by implementation of a pharmacist-driven allergy assessment tool.

METHODS A group of physicians, pharmacists, and a nurse collaborated for process development. The process was standardized, and a tool was created to assist with assessments. Pharmacists were educated on the importance of this quality improvement project and trained on the process and tool used. Implementation occurred on March 2, 2020.

RESULTS During the 3-month implementation period, 40 patients were admitted with a documented penicillin or cephalosporin allergy. Of these, 11 patients (27.5%) received an allergy assessment. Most were identified as having low or moderate risk of recurrent reaction with future use of a penicillin or cephalosporin agent (81.8%), and 2 patients (18.2%) were de-labeled from their documented allergy.

CONCLUSIONS Penicillin and cephalosporin allergy assessment implementation at a pediatric hospital was successfully implemented and allowed for identification and initiation of future quality improvement projects including implementation of penicillin skin testing and direct oral amoxicillin challenges.

ABBREVIATIONS AAAAI, American Academy of Allergy, Asthma, and Immunology; CDC, Centers for Disease Control and Prevention; EHR, electronic health record; IgE, immunoglobulin E; QI, quality improvement

KEYWORDS adverse drug reaction; cephalosporin; drug hypersensitivity; interprofessional; penicillin; pharmacists; quality of health care

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Introduction

Penicillin allergy is the most commonly reported drug allergy. Per the CDC, about 10% of patients have a documented penicillin allergy in their medical records.¹ Although reported frequently, less than 1% of the population has a true immunoglobulin E (IgE)-mediated allergy and about 80% of these patients will lose their reactivity after 10 years.¹ Therefore, a large proportion of patients labeled with a penicillin allergy are either inappropriately labeled or have lost reactivity and can safely receive penicillin agents. A 2013 study showed that 98% of hospitalized patients with a history of penicillin allergy would have negative allergy test results.²

Any labeled beta-lactam allergy can lead to avoidance of other beta-lactams given the concern for cross-reactivity. Previous literature suggested cross-reactivity rates up to 10%; however, more recent literature suggests this risk is less than 2%.³ Avoidance of beta-lactam agents due to a labeled allergy may result in unnecessary exposure to

broader-spectrum antibiotics; such exposure has been associated with higher health care costs, increased risk of antibiotic resistance, suboptimal antibiotic therapy, higher rates of *Clostridioides difficile* infections, and increased length of hospital stay.^{1,3,4} Thoroughly assessing documented penicillin or cephalosporin allergies to identify patients without a true IgE-mediated allergy may help decrease use of broad-spectrum antibiotics, reduce antimicrobial resistance and adverse events, and allow use of more appropriate therapies, thereby improving antimicrobial stewardship practices.

Owing to these potential benefits, many organizations support the development of avenues for assessing penicillin allergies. The Society for Healthcare Epidemiology of America, Infectious Diseases Society of America, and American Academy of Allergy, Asthma, and Immunology (AAAAI) have joined forces to provide toolkits, videos, and other resources to help with the evaluation and management of penicillin allergies. Specifically, the AAAAI stated that “encouraging verification of patient-reported

penicillin allergy as a means of combatting antimicrobial resistance” is one of their advocacy priorities.⁴ In addition, the CDC has included assessing penicillin allergies as a priority intervention to improve antibiotic use in their “Core Elements of Hospital Antimicrobial Stewardship Programs” report from 2019.⁵ Given the overwhelming organizational support and guidance, many health care systems across the country developed and implemented penicillin allergy assessment processes and allergy testing programs. However, most of the published material depicts the development and efficacy of penicillin allergy testing strategies and fails to include the core material of allergy assessment process development and implementation.

Similar to the reported documented penicillin allergy rates defined in the general population, about 7.2% of patients admitted to our pediatric institution have a labeled penicillin or cephalosporin allergy. There currently is not a standardized process for assessing these documented allergies. The purpose of this project is to improve quality of care for patients admitted to our pediatric institution with a documented penicillin or cephalosporin allergy. Over a 3-month period, we aim to: 1) complete allergy assessments in 80% of patients admitted with a penicillin or cephalosporin allergy, using a developed allergy assessment tool; 2) complete allergy assessment in conjunction with medication histories 100% of the time; and 3) de-label 30% of patients with a penicillin or cephalosporin documented allergy.

Methods

Study Design and Setting. This single center, quality improvement (QI) project took place at a pediatric hospital located within an adult academic health center. Our multidisciplinary team consisted of a pediatric infectious diseases physician, a pediatric hospital medicine fellow, an allergist, pediatric-trained pharmacists, infectious disease certified pharmacists, and an advanced practice registered nurse. Development and implementation took place over a 10-month period, August 2019 through May 2020. The development phase consisted of 3 steps: process standardization, allergy assessment tool creation, and staff training. The implementation phase spanned a 3-month period, March through May 2020. All patients admitted to all medical units, including critical care units, at the pediatric hospital were included for evaluation. Only patients admitted with a documented penicillin or cephalosporin allergy were deemed appropriate for assessment. The penicillin and cephalosporin drug classes were chosen for this project because of the quantity and quality of literature available regarding allergies to these specific drug classes. In addition, our adult hospital counterpart reviews penicillin and cephalosporin allergies in adult patients.

Process Standardization. Prior to this project, there was no developed process for assessing patient allergies at our pediatric hospital. A few years prior, the

Table. Summary of Allergy Assessment Patient Interview Fields in Electronic Health Record Navigator

Interview source
Documented allergy
Indication for medication
Years since reaction occurred
Medication route
Reaction symptoms
Onset of symptoms (timing)
Experienced same reaction in the past
Management of reaction
Medication given again without reaction recurrence
Similar medication given again without reaction recurrence
Tolerated antibiotics with dates administered

antimicrobial stewardship pharmacists at our adult hospital counterpart implemented penicillin and cephalosporin allergy assessments in adult patients. However, this process was only performed by a handful of pharmacists and could not be easily replicated to improve standard of care on a large scale. Therefore, a standardized process was created to ensure all clinical pediatric pharmacists would have adequate support to conduct penicillin and cephalosporin allergy assessments in our pediatric hospital. Patient interview questions were formulated (Table). A patient's allergy history, deemed by answers to the interview questions, allowed stratification into a risk category that depicted the risk associated with future use of a penicillin or cephalosporin agent: no risk, low risk, moderate risk, and high risk. Each risk category was linked to an appropriate clinical recommendation: de-label penicillin or cephalosporin allergy (i.e., remove documented allergy from patient's medical record), seek alternative testing strategies, and avoid use of beta-lactam agents. The process was detailed in a standard operating procedure and a flowchart algorithm (Figure). Alternative testing strategies were not yet available to patients admitted to the pediatric hospital, so referral for outpatient evaluation was recommended.

Electronic Allergy Assessment Tool Creation. To improve efficiency, an electronic tool was created to assist with allergy assessments. This institution uses Epic as an EHR. An Epic navigator already in use in the adult population was enhanced to allow for more automated capabilities. The patient interview questions and answer selections were contained in a flowsheet within this navigator. Background rules were coded into the electronic navigator to auto-populate a patient's risk

Figure. Allergy assessment algorithm.

HSR, hypersensitivity reaction; IgE, immunoglobulin E; OP, outpatient; PAST, penicillin allergy skin testing

* Test doses and skin testing not available inpatient for cephalosporin allergies

category as based on answer selections to the patient interview questions. This was done to alleviate clinical judgement for risk stratification and eliminate human error. A documentation template was also developed to minimize pharmacist work time. This template carried over the answers to patient interview questions, patient's stratified risk category, and associated clinical recommendation into a note accessible in the patient's EHR.

Personnel Education. With the goal to improve standard of care and assess all penicillin and cephalosporin allergies in patients admitted to our pediatric

institution, we needed to train our frontline personnel. All decentralized clinical pediatric pharmacists received education and training that consisted of an overview presentation on penicillin and cephalosporin allergies and a scheduled 1-on-1 to practice real-time in-person patient cases.

Implementation and Study Measures. Formal implementation occurred from March 2, 2020, to May 31, 2020. Outcome measures include total number of assessments completed over the 3-month implementation period and number of patients with an allergy de-labeled post assessment. Process measures are

proportion of allergy assessments completed and proportion completed by a pharmacist during initial medication history. Balancing measure is the average time taken to complete an allergy assessment with the developed tool. Implementation evolved over time as a result of constant evaluation of the process, balancing measures, and challenges with the novel SARS-CoV-2 pandemic. In-person patient interviews shifted to patient phone interviews, personnel conducting assessments expanded, and a double check system was created to help capture a larger proportion of patients receiving assessments.

Data Collection and Analysis. A single study team member collected clinically relevant data, using an automated electronic report daily. The report included patients who were admitted to the pediatric institution from the day prior with a documented penicillin or cephalosporin allergy. The following data were collected for each patient: age, assessment completion status, date of assessment, time to complete assessment, concurrent completion of admission medication history, documented allergy and reaction, stratified risk of recurrent reaction, associated clinical management recommendation, whether the patient was receiving antibiotics at time of assessment, which antibiotics and for what indication.

Results

From March 2, 2020, to May 31, 2020, forty individual patients with a documented penicillin or cephalosporin allergy were admitted to a medical unit at the pediatric hospital. During the first 6 weeks of implementation, allergy assessments were performed in 4 of 24 eligible patients (16.7%). After process improvements were used, allergy assessments were performed in 7 of 16 eligible patients (43.8%) in the remaining 7 weeks. Over the entire 3-month implementation phase, a total of 11 patients received an allergy assessment (27.5%). Most patients with a completed allergy assessment also received an admission medication history ($n = 9$). Of the 40 patients with a documented penicillin or cephalosporin allergy on admission, only 14 received a pharmacist-completed medication history (35%), which is below the institution's standard pharmacist completion rate. Of note, completion of admission medication histories is a shared responsibility at our institution. Four patients with a documented penicillin or cephalosporin allergy had a medication history performed without an allergy assessment, while 25 patients received neither a medication history nor an allergy assessment.

Of the 11 allergy assessments completed, amoxicillin was the most commonly reported medication allergy ($n = 7$), followed by amoxicillin-clavulanate ($n = 2$), cefdinir ($n = 2$), ceftriaxone ($n = 2$), and penicillin G ($n = 1$). Two patients had multiple beta-lactam allergies documented. Rash was the most commonly reported reaction type in those who received an allergy assess-

ment ($n = 7$), followed by hives ($n = 2$) and swelling of lips, hands, or feet ($n = 2$). Shortness of breath and diarrhea were each reported in 1 patient. There was 1 instance in which the patient did not have a reaction to the documented medication allergy; however, the patient was inaccurately labeled owing to confusion with a sibling's allergy to the documented medication.

Moderate risk was the most common risk stratification category ($n = 7$; 64%) in patients who received an allergy assessment, followed by low risk ($n = 2$; 18%) and no risk ($n = 2$; 18%). There were no patients deemed at high risk of recurrent reaction with future use of a penicillin or cephalosporin agent. From these identified risk categories, most patients were recommended to receive alternative allergy testing ($n = 9$). As mentioned previously, these services were not available inpatient at the time of implementation. Patients were advised to follow up with an outpatient allergist to complete testing. The 2 patients with documented allergies that were stratified into the no risk category had their penicillin and/or cephalosporin allergy removed from their medical record.

To further qualify the clinical course of the patients who had an allergy assessment completed, 5 received antibiotics during the current admission for various indications (febrile neutropenia, *Pneumocystis jirovecii* pneumonia prophylaxis, perioperative prophylaxis, bacteremia, and cystic fibrosis exacerbation). Of those who received an antibiotic while admitted, 2 received a cephalosporin prior to completion of an allergy assessment despite having a documented amoxicillin allergy. Another 2 patients received a cephalosporin after their allergy assessment was completed. It is unknown if the choice of antibiotic was a result of the completed allergy assessment. There was 1 patient who did not receive a first-line antibiotic for perioperative prophylaxis according to evidence-based guidelines. However, it is unknown if the documented amoxicillin allergy was directly correlated with the inappropriate antibiotic selection. As our balancing measure, it was noted that all assessments performed by our pharmacists took 10 minutes or less.

Case Report

A pharmacist-driven penicillin and cephalosporin allergy assessment process and tool was successfully implemented in a single center, pediatric institution. Of patients with a documented penicillin or cephalosporin allergy, admitted to the medical units at the pediatric hospital, 27.5% received an allergy assessment by a pharmacist. Of the assessments completed, 82% were in conjunction with admission medication history. Of the assessments completed, most patients (81.8%) were deemed at low or moderate risk of recurrent reaction with future use of a penicillin and/or cephalosporin agent and were considered candidates for further allergy testing strategies (e.g., penicillin skin testing

and/or direct oral dose challenges). The remaining patients (18.2%) were deemed to be at no risk of recurrent reaction and were recommended to have their allergies de-labeled, or removed from their EHR, by the assessing pharmacist.

Although the specific aims of this QI project were not met, the allergy assessment process was effectively created and used by our frontline clinical pediatric pharmacists. Given the large proportion of our patients recommended for alternative allergy testing strategies, it is crucial to develop methods to perform this testing while patients are admitted to the hospital. The described allergy assessment process developed during this QI project and results obtained helped lay the foundation for a subsequent implementation project led by members of our QI team set to begin August 2020: implementation of penicillin allergy skin testing and direct oral amoxicillin dose challenges.

The description and results of this project were intended to improve local standard of care. Future initiatives include expansion of this standardized allergy assessment process to other populations across our health system. Sharing our experience with the implementation of a pharmacist-driven penicillin and cephalosporin allergy assessment tool provides other pediatric and adult institutions with the background information needed to develop similar processes in the future.

The potential rationale for the low completion of allergy assessments is multifactorial. Given this was a local QI project designed to implement a new standard of care, our goal was for our frontline staff to adopt the new process. However, the allergy assessment process was an added responsibility to the pharmacists' daily tasks without adding any additional resources. This was particularly challenging for evening and weekend admissions. In addition, the allergy assessment was expected to take place at the time of medication history, but medication history rates at our institution are not yet 100%. This project was also greatly affected by the novel SARS-CoV-2 global pandemic. As experienced all over the country, our institution was challenged with a decreased census, limited visitor policies, changes in pharmacy operations to incorporate social distancing as well as preservation of personal protective equipment, and overall pharmacy staffing shortages. These factors significantly affected the pharmacists' ability to incorporate a new process into their workflow and prompted the necessity to change our in-person medication history and allergy assessment process to phone interviews.

To accommodate for these barriers, our QI team met 6 weeks into the implementation phase to discuss process adjustments that would help improve the proportion of allergy assessments completed. We provided guidance to our frontline pharmacists to address barriers associated with completing al-

lergy assessment interviews via telephone. Another adjustment made was the expansion of personnel completing allergy assessments to include other QI team members to supplement the work of our frontline pediatric pharmacists. Lastly, we developed a double check system to help ensure that all patients admitted with a documented penicillin or cephalosporin allergy received an allergy assessment. A designated member of our QI team reviewed all patients admitted the day prior with a penicillin or cephalosporin allergy to identify which patients still needed an allergy assessment. The QI team member contacted the frontline pharmacist caring for the patient with the allergy to encourage the completion of an allergy assessment. If time did not allow the frontline staff to complete, one of the QI team members completed the allergy assessment. After the incorporation of these process improvements, more allergy assessments were captured in the remaining 7 weeks of implementation as compared with the first 6 weeks (43.8% vs 16%, respectively).

It is our hope that implementation of allergy assessments helped to educate patients, caregivers, and other health care personnel on the incidence and impact of penicillin and cephalosporin allergy labels. By de-labeling documented penicillin or cephalosporin allergies in patients without an IgE-mediated reaction, we hope to indirectly enhance local antimicrobial stewardship practices by decreasing the use of unnecessary broad-spectrum antibiotics and using optimal antibiotics for a patient's condition. Owing to the nature of this implementation project, the authors did not assess clinical outcomes associated with implementation. Opportunities for future research include a retrospective chart review to evaluate the clinical effects caused by de-labeling a pediatric patient's penicillin or cephalosporin allergy (e.g., reduced broad-spectrum antimicrobial exposure, decreased antimicrobial-related adverse events) pre- and post-implementation of allergy assessments.

Article Information

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