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BETA-LACTAM ALLERGY DE-LABELING IN A PEDIATRIC POPULATION

Dr Mohit Aggarwal[1*] , Dr Niraj Kumar [2]

[1]*Assistant professor , department of paediatrics , VIMS , gajraula
[2]Assistant professor, department of paediatrics , VIMS , gajraula

***Corresponding author :** Dr Mohit Aggarwal
*Assistant professor , department of paediatrics , VIMS , gajraula

Abstract :

OBJECTIVE

To assess the ability to de-label pediatric patients of their beta-lactam allergy by using a newly implemented institutional protocol and to identify potential barriers to the de-labeling process.

METHODS

All patients with reported allergies to prespecified beta-lactam antibiotics were eligible for a beta-lactam allergy interview. Following the interview, patients were grouped into 4 risk categories—no risk, low risk, moderate risk, and high risk—and assessed for intervention eligibility. Potential interventions included de-labeling based on the interview alone or proceeding to an oral amoxicillin challenge with or without penicillin allergy skin testing.

RESULTS

Of the 62 patients eligible for beta-lactam allergy interviews, 40% (n = 25) were de-labeled. Among de-labeled patients, 60% (n = 15) were de-labeled on the basis of the interview alone. Additionally, no failures were documented in patients who underwent an oral amoxicillin challenge or penicillin skin testing. Barriers to performing oral amoxicillin challenges or penicillin skin testing included concomitant systemic steroid or antihistamine use, refusal of intervention, and insufficient resources to perform penicillin skin testing.

CONCLUSIONS

There was a high frequency of patients de-labeled of their beta-lactam allergies in this study. Increased education to patients, parents, and providers on the de-labeling process, as well as increased personnel available to coordinate and perform de-labeling interventions, may result in more beta-lactam allergy de-labeling.

Keywords : de-labeling, oral amoxicillin challenge, pediatrics, penicillin allergy, penicillin skin testing

Introduction :

Approximately 10% of patients worldwide report allergies to the penicillin class of antibiotics.[1–5] Within this cohort, clinically significant immunoglobulin E (IgE) or T-lymphocyte–mediated reactions occur in less than 5% to 10%.[1–5] IgE-mediated reactions occur relatively quickly after introduction of the offending agent (1–6 hours) and include symptoms such as urticaria, bronchospasm, and anaphylaxis, whereas T-lymphocyte–mediated reactions typically have a delayed onset (days to weeks) and include symptoms such as maculopapular rash or severe

dermatologic reactions.[6] In comparison, reactions not representing a true immunologic response include isolated gastrointestinal symptoms or benign rashes and can develop at varying time points subsequent to contact with the offending agent.[6] In addition, IgE-mediated penicillin allergies are known to decrease over time, with 80% of patients with a reported allergy gaining tolerability after 10 years.[1] An actively listed penicillin allergy in the patient's electronic health record (EHR) can also affect major decisions regarding antibiotic therapy, including avoidance of cephalosporins and other first-line agents.[6,7] Owing to the spectrum of activity, tolerability, cost, and supporting data for use of penicillin and other beta-lactam antibiotics, guidelines commonly recommend these agents as first-line therapies for many infectious conditions.[8] Additionally, avoidance of these antibiotics in the setting of a documented allergy has been shown to carry negative consequences.[8] Use of alternative antibiotics can result in increased antimicrobial resistance, increased incidence of adverse events, and increased health care costs.[1,3,6]

Avoidance of the penicillin class and other beta-lactam antibiotics is particularly concerning in the - pediatric population. Numerous childhood infections including community-acquired pneumonia, acute otitis media, and streptococcal pharyngitis have recommendations to use these agents as first-line therapy.[6] Additionally, with no deliberate intervention, these documented allergies will persist in the child's EHR and lead to future avoidance of beta-lactam antibiotics as the child ages.[9] Allergy de-labeling, or the removal of potentially inappropriately listed allergies from a patient's medical record via patient interview and often drug challenge, has emerged as a solution to this problem. An increasing body of literature has consistently shown the utility and safety of penicillin skin testing and oral amoxicillin challenge as methods to facilitate allergy de-labeling in patients with documented non-severe allergies to the penicillin class of antibiotics.[1–9] The success of these de-labeling interventions has made them an important part of antimicrobial stewardship efforts globally, because they align with key antimicrobial stewardship program (ASP) goals including reduced antimicrobial resistance and increased antimicrobial appropriateness.[10] Although the benefits to de-labeling are highly supported throughout literature and recommended in ASP guidelines worldwide, the ideal way to implement de-labeling in clinical practice remains undetermined.[10] Therefore, the goal of this study was to assess the effect of a newly implemented beta-lactam allergy de-labeling protocol at a pediatric community hospital and identify barriers to the de-labeling process. The institutional beta-lactam de-labeling protocol created was primarily pharmacy driven and reviewed by multiple health care disciplines prior to implementation.

Material and method :

This was a prospective, observational study. Patients eligible for the de-labeling process were identified via daily chart review of all hospitalized patients admitted with antibiotic allergies as identified in the EHR (Epic), and intervention eligibility was determined after the initial de-labeling interview. Documented allergies to penicillin, amoxicillin, ampicillin, amoxicillin-clavulanic acid, ampicillin-sulbactam, nafcillin, oxacillin, dicloxacillin, piperacillin-tazobactam, aztreonam, all cephalosporins, and all carbapenems qualified for the initial interview. Allergens eligible for an oral amoxicillin challenge with or without penicillin skin testing included penicillin, amoxicillin, ampicillin, amoxicillin-clavulanic acid, ampicillin-sulbactam, nafcillin, oxacillin, dicloxacillin, and piperacillin-tazobactam. Cephalosporin and carbapenem allergies were not eligible for de-labeling via an oral amoxicillin challenge/penicillin skin testing owing to lack of cross-reactivity between penicillins and these other beta-lactam subgroups, as well as lack of data supporting use of oral amoxicillin challenge/penicillin skin testing in this setting.[11,12] Exclusions to the patient/caregiver interview process included critically ill patients receiving vasopressors and/or high-level sedation (i.e., requiring continuous infusion sedative agents) and/or mechanical ventilation. Exclusions to an oral amoxicillin challenge and/or penicillin skin testing included receipt of systemic antihistamine or corticosteroid agents within the last 48 hours, those with "nothing by mouth" status, and patients with current symptoms similar to an IgE or IgE-like reaction.

Allergy interviews were conducted by clinical pharmacists, which included both EHR review prior to the interview followed by patient/caregiver questioning.. Based on the information gathered

during chart review and the interview process, the patient's reported allergy was stratified into a risk category of no risk, low risk, moderate risk, or high risk. For patients categorized as "no risk," de-labeling of their allergy could occur on the basis of their interview alone. Patients with low-risk reactions qualified for a nongraded oral amoxicillin challenge. This challenge consisted of a single dose of amoxicillin 250 mg with the patient being monitored by nursing staff over a 1-hour timeframe post dose for development of an IgE-mediated reaction. Patients with moderate-risk reactions were recommended to undergo penicillin skin testing, followed by an oral amoxicillin challenge if skin testing results were negative. Penicillin skin testing was performed by licensed physicians, physician extenders, and/or nurses, who have completed mandatory training and demonstrated competency in penicillin allergy skin testing procedures, per institutional protocol. Penicillin skin testing included an initial skin prick test followed by intradermal testing upon a negative result for skin prick testing. Both Pre-Pen (AllerQuest LLC, Plainville, CT) and penicillin G (diluted to 10,000 units/mL) were used in both the skin prick and intradermal testing. Those patients with high-risk reactions were advised to avoid penicillin and were referred to an outpatient allergy specialist. Allergy interviews and interventions, if applicable, were documented in the patient's EHR upon completion. If a patient was able to be de-labeled of their beta-lactam allergy, education was provided to the patients, caregivers, and providers by pharmacy staff on the removal of this allergy label and its implications on the patient's ability to safely receive beta-lactam antibiotics. Documentation of allergy label removal and the education stated above was also recorded in the patient's EHR

Results

Sixty-two patients were eligible for beta-lactam de-labeling interviews during the study period. The median age of patients evaluated was 11.0 years (6.0–14.5) and 34 patients (55%) were female. Twenty-four patients evaluated (39%) were currently admitted for an infectious process requiring antibiotic therapy. Among allergens listed in the EHR, penicillin-containing (24%) and amoxicillin-containing (68%) agents were the most common. Reactions most commonly reported to the listed allergens were urticarial (45%) and non-urticarial (31%) rashes. Of the study participants, 25 patients (40%) were successfully de-labeled of their beta-lactam allergy . Most de-labeled study participants (60%) were de-labeled with the beta-lactam allergy interview alone, while the other 40% underwent the oral amoxicillin challenge and/or penicillin skin testing. Among patients interviewed, 25 patients (40%) were not eligible for interventions beyond the de-labeling interview, based on the approved institutional protocol. Of patients ineligible for oral amoxicillin challenge and/or penicillin skin testing, primary reasons included concomitant use of systemic antihistamines or steroid agents within the previous 48 hours (60%), patients with current IgE or IgE-like symptoms (16%), and documented allergy to a cephalosporin agent (12%) (Table 3). In certain patients, de-labeling was stopped owing to various reasons, including preferences of caregivers/providers/patients and logistical problems associated with managing penicillin skin testing. None of the patients who received the oral amoxicillin challenge and/or skin test had an allergic reaction. Of note, only 1 patient in this study was classified as having a high-risk reaction and referred to an outpatient allergist for evaluation. Among patients with barriers to intervention and for those who were not eligible for intervention, outpatient allergist evaluation was recommended. Five study patients (21%) who were de-labeled had antibiotic therapy further streamlined with a beta-lactam.

Discussion

This study supports the implementation of a beta-lactam allergy de-labeling program as an effective means to remove incorrectly reported allergic reactions. The de-labeling interview alone was impactful, which was consistent with previously reported data.[2] Those challenged with oral amoxicillin, with or without prior penicillin skin testing, had no reported IgE-mediated reaction, which is also consistent with current data.[3–5,8,13] This allergy de-labeling may later result in appropriate selection of beta-lactams in cases where they are considered first-line therapies.

Comparatively, a study by Steenvoorden et al[13] showed a higher rate of change in current antibiotic treatment subsequent to de-labeling (42% versus 21%). Although the frequency of change was greater, this can be influenced by many factors such as local prescribing patterns, the infection or organism being targeted, and other unique patient factors.[13] This study not only demonstrated active antimicrobial modifications, but also suggests these interventions may have lasting effects on future antimicrobial selection. Despite adult patients having a greater prevalence of documented antibiotic allergy, these labels are most often applied during childhood, a period when febrile respiratory illnesses are increasingly common and antibiotic usage is heightened.[14] Viral illnesses during childhood also occur at an increased rate and literature has shown the development of rashes during the infectious process, with Epstein-Barr virus being an example of a possible causative vector.[1] Because antibiotics are commonly overprescribed during viral illnesses, viral rashes have the potential to be inaccurately documented as antibiotic allergies. Furthermore, patients may have an allergy added to their medical record for things such as family history of an allergy to the offending agent or a non–IgE-mediated adverse effect of the agent. Jones and colleagues[14] concluded that with patients most often receiving these beta-lactam allergy labels in childhood, allergy overdiagnosis and lack of de-labeling interventions are major contributors to the harms associated with avoiding beta-lactam antibiotics in adulthood.

Conclusion

Our study demonstrated successful implementation of a beta-lactam de-labeling protocol at a community pediatric children's hospital. Our study was also able to add to the current body of literature supporting de-labeling initiatives by providing a more detailed investigation into possible barriers to implementation, an aspect where the most ideal approach still seems uncertain.[10] Future revisions may include adjusting risk stratification, including alternatives to penicillin skin testing, earlier identification (prior to antihistamine or corticosteroid use), increasing pharmacist presence in critical areas such as the emergency department, and expanding the breadth of beta-lactam antibiotics included in our institutional protocol. All of these changes may allow for increased opportunity for beta-lactam allergy de-labeling and further insight into the ideal implementation strategy for institutions seeking to create de-labeling services.

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