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Research Article

Addressing Pediatric Penicillin Allergies through Use of an Inpatient Algorithm

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Abstract

Background: The impact of labeling patients penicillin-allergic include increased hospital length-of-stay and use of broad-spectrum antibiotics. Despite these undesirable consequences, few studies have addressed solutions and no protocol existed at our institution to address penicillin allergies in the pediatric population.

Objective: In our quality improvement project, we assessed the impact of implementing an algorithm among penicillin-allergic pediatric inpatients on increasing outpatient referrals for drug allergy evaluation and reducing use of penicillin alternatives.

Methods: Retrospective chart review was conducted to identify penicillin-allergic pediatric inpatients admitted from April 2018 to May 2019 (pre-intervention), and August 2019 to August 2020 (post-intervention, after implementation of the algorithm). The aims of our study were to increase de-labeling, decrease use of penicillin alternatives, and increase allergy referrals.

Results: β-lactam antibiotics were the preferred drug in 26/36 (72.2%) vs 39/48 (81.3%) in the post-intervention group. Among these patients, there were 10/26 (38.5%) vs 28/39 (71.2%) that received cephalosporins during admission (p = .008). Outpatient referrals for penicillin allergy evaluation were 3/94 (3.2%) in the pre-intervention group and 19/99 (19.2%) in the post intervention group.

Conclusion: Our study suggests that implementation of a penicillin allergy algorithm in a pediatric hospital may be associated with increased outpatient allergy referrals, increased use of cephalosporins, and decreased use of alternative antibiotics.

Clinical Implications: Implementing penicillin allergy algorithms in pediatric hospitals should be considered to address the burden of pediatric penicillin allergy labels.

INTRODUCTION

Antibiotic allergy is a growing public health concern in the pediatric population. Up to 10% of children are labeled beta-lactam allergic [1], yet the majority can tolerate beta-lactams after being evaluated by an allergist, with more than 90% able to pass a challenge to amoxicillin with no reaction [2]. Penicillin and its derivatives remain the preferred treatment for many childhood infections. Prior studies in children and adults have demonstrated adverse outcomes with a penicillin allergy label including increased hospital length-of-stay and use of broad-spectrum antibiotics [3,4]. Penicillin allergy management algorithms for adults have been used to improve antibiotic stewardship [4]. At the time of inception of this project, there was a paucity of data on the effect of applying a penicillin allergy de-labeling algorithm to pediatric inpatients and there was no protocol in place at our institution to address penicillin allergies in pediatric inpatients. We implemented an algorithm to optimize the approach to penicillin allergic patients as part of a long-term quality improvement (QI) project to improve antibiotic stewardship.

A retrospective chart review of pediatric inpatients with a penicillin allergy admitted to a tertiary care center in New York City 4/2018-5/2019 was conducted (approved by the institution QI committee and safety team). Patients with a listed allergy to penicillin or one of its derivatives were identified using a reporting tool in the electronic health record (EHR) system (Epic Slicer Dicer). An inpatient penicillin allergy algorithm (Figure 1), was designed using information published by Shenoy and colleagues [5].This algorithm was disseminated over a 3-month-period via paper copies displayed in workrooms, e-mail, and educational sessions to residents and faculty emphasizing the importance of addressing penicillin allergy in children. The primary outcome measure was efficacy of the algorithm, which was measured as percentage of inpatients with penicillin allergy labels that were de-labeled during their admission. Secondary outcome measures included the percent change in type of inpatient antibiotic used and the number of allergy referrals upon discharge. Data from the pre-/post-intervention periods were summarized as proportions and percentages. Chi-square test or Fisher's exact test was used to compare the frequency of selected antibiotics prescribed during admission for patients in which beta-lactam antibiotics were preferred to treat their infection. Post-intervention data collection was performed 8/2019 to 8/2020 to assess the algorithm's impact.

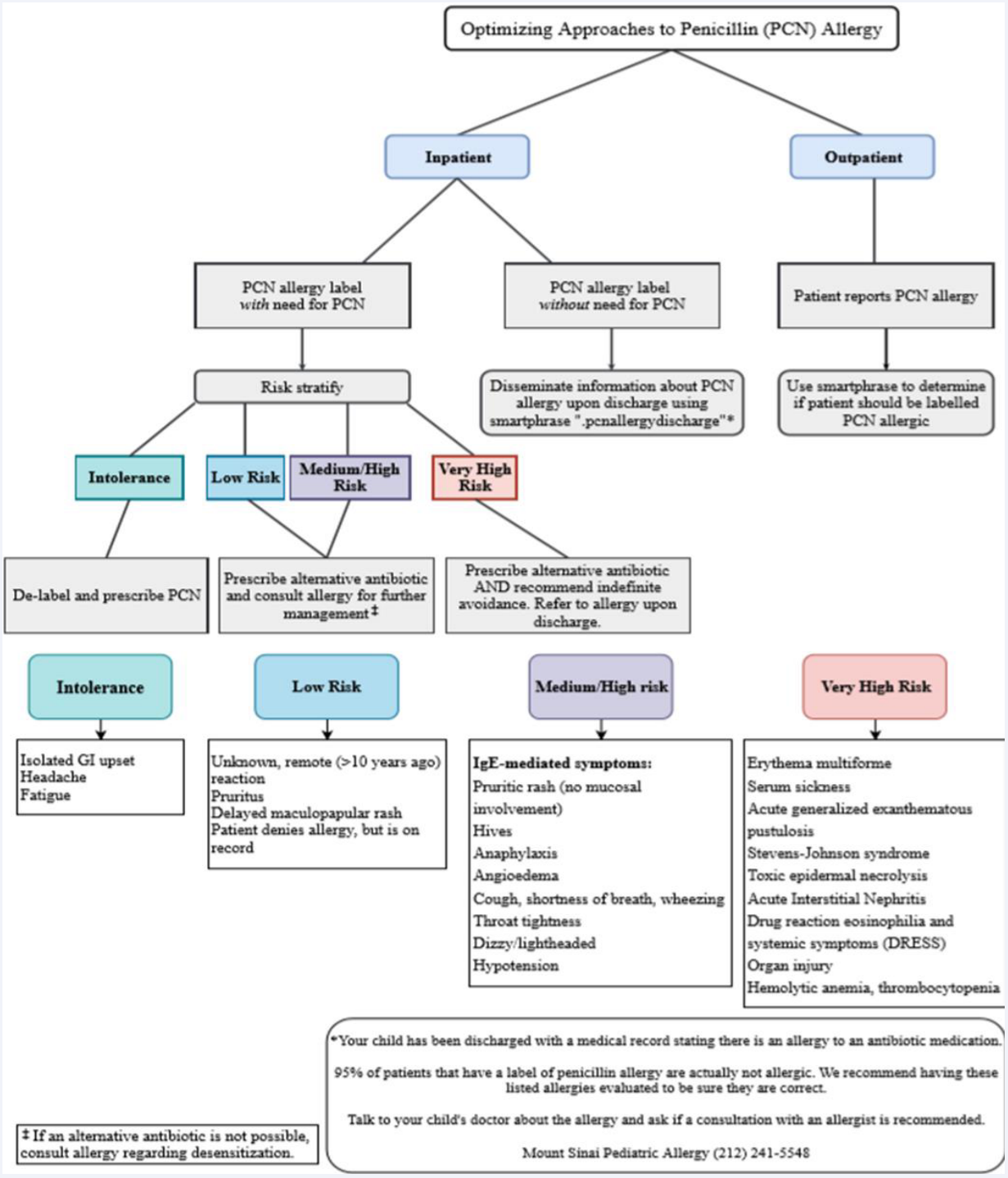

Figure 1 Optimizing Approaches to Penicillin (PCN) Allergy: An Algorithm.

RESULTS AND DISCUSSION

Ninety-four of 2810 (3.3%) carried a penicillin allergy label in the pre-intervention group and 99 of 2227 (4.4%) patients in the post-intervention group. Table 1 lists additional information gathered for each patient who had been labelled as allergic to penicillin. In the post-intervention group, there were no patients that had an intolerance history. As such, none were de-labeled inpatient.

Based on the type of infection, β-lactam antibiotics were the preferred treatment in 72.2% of patients in the pre-intervention group and 81.3% in the post-intervention group. Due to the listed penicillin allergy, some of these patients received alternative antibiotics such as clindamycin and fluoroquinolones. Table 2 presents the frequency of selected antibiotics prescribed during admission for patients in which beta-lactam antibiotics would be the antibiotic of choice to treat their infection.

Table 1: Patient Characteristics Pre- and Post-Intervention.

Patient Characteristics	Pre-Intervention, All patients (n = 94)	Post-Intervention, All patients (n = 99)
% Male (n)	55.3% (52)	56.6% (56)
% Female (n)	44.7% (42)	43.4% (43)
Beta-lactam Reaction Details*		
Anaphylaxis	2.1% (2)	4.0% (4)
Rash	57.4% (54)	61.6% (61)
Urticaria	38.3% (36)	22.2% (22)
GI upset	1.1% (1)	2.0% (2)
Respiratory	2.1% (2)	1.0% (1)
Hypotension	0% (0)	1.0% (1)
Serum Sickness	1.1% (1)	0% (0)
SJS	1.1% (1)	0% (0)
Angioedema	1.1% (1)	0% (0)
Other	5.3% (5)	2.0% (2)
Unknown	5.3% (5)	8.1% (8)
% Need for Any Antibiotic (n)	38.3% (36)	48.4% (48)
% B-lactam as preferred Antibiotic to Treat Infection (n)[D]	72.2% (26)	81.3% (39)
% Presumed or Confirmed Infection (n)	n = 36	n = 48
Peri-operative Prophylaxis	11.1% (4)	43.8% (21)
Skin	19.4% (7)	6.3% (3)
GU/Renal	5.6% (2)	10.4% (5)
Respiratory	22.2% (8)	6.3% (3)
Bacteremia	16.7% (6)	6.3% (3)
GI/Liver	19.4% (7)	16.7% (8)
Joint/Bone	2.8% (1)	0% (0)
Neurologic	0% (0)	4.2% (2)
Other	2.8% (1)	6.3% (3)

*More than one reaction may have been listed for an individual patient

[D]Preferred treatment for an infection was determined by first-line standard of care antibiotic choices for a type of infection (eg pneumonia) as well as cultures/sensitivities data, if available

Three of 94 children (3.2%) were referred for outpatient penicillin allergy evaluation in the pre-intervention group and 19/99 (19.2%) in the post-intervention group. Five of the 19 referred presented to the allergy clinic. Testing was not indicated in two of those five patients due to history of anaphylaxis to beta-lactam antibiotics, and instead complete avoidance was recommended.

Broad-spectrum antibiotic use contributes to antibiotic resistance, increased hospital costs, and overall undermines antibiotic stewardship initiatives. Our intervention showed a decrease in clindamycin and fluoroquinolone use, each by approximately 10% and an increase in cephalosporin use in those that were labeled penicillin-allergic. There was a statistically significant increase in use of cephalosporins between the pre- and post-intervention groups, 38% vs. 71%, respectively (p=.008). After being introduced to the algorithm and to the other educational materials emphasizing the importance of addressing penicillin allergy, providers appear to have chosen cephalosporins more often. It should be noted, however, that use of penicillins between the pre-/post-intervention groups was unchanged and our primary outcome of de-labeling patients of their penicillin allergy was not achieved since none were de-labeled post-intervention.

Introduction of the algorithm was associated with an increase in the percentage of patients referred to outpatient allergy (3.2% vs. 19.2%) in the pre- and post-intervention groups, respectively. Although there was a marked increase in the number of outpatient allergy referrals, few of these patients had an appointment scheduled. At the time of data analysis, 5 of 19 patients had an allergy consultation. If each of these referrals led to a penicillin allergy evaluation, this could lead to significant potential benefit by increasing de-labeling and preventing further use of alternative/broad-spectrum antibiotics. Importance of addressing the penicillin allergy label as an outpatient may not have been emphasized upon discharge, which may explain the small proportion of patients that made appointments. While

Table 2: Antibiotic Prescribed During Admission for Patients in which B-lactam was the Antibiotic of Choice to Treat Infection.

Antibiotic Prescribed During Admission	Pre-Intervention, n = 26	Post-Intervention, n = 39	P value*
Cephalosporins	38.5% (10)	71.8% (28)	**0.008**
Clindamycin	15.4% (4)	5.1% (2)	0.21
Fluoroquinolones	23.1% (6)	10.3% (4)	0.18
Penicillins	11.5% (3)	10.3% (4)	1.00
Other	11.5% (3)	2.6% (1)	

* The Chi-square test or Fisher's exact test was used.

[D] The alternative antibiotics reported most often were included in the analysis (fluoroquinolones and clindamycin). Vancomycin was excluded from our analysis as our pediatric hospital policy is to use this antibiotic for any patient that has a central line infection or other severe illness (eg sepsis-like clinical picture) and does not necessarily follow the conventions of choosing an antibiotic based on presumed organism.

a short statement of the importance of addressing a child's penicillin allergy and clinic contact information was included in the template entered into discharge instructions as part of our intervention, families were responsible for scheduling. This may be an area of focus for the next iteration of the project.

There were limitations to our study. The algorithm was only available in paper format, which could be overlooked or forgotten when not integrated into the workflow within the EHR. Attempts to incorporate our algorithm into the EHR or to make changes to the EHR's allergy section were unsuccessful, largely due to inflexibility of certain features of the EHR. Severity of infection may be a confounding variable that was not examined in this study, as "sicker" patients may have more use of broad-spectrum antibiotics before an organism was identified. The post-intervention timeline included some of the COVID-19 pandemic, with the pandemic's peak during March-May 2020 in New York City. The pandemic may have affected assessment of penicillin allergies, as many specialties limited visits in the outpatient setting and inpatient consultation was reserved for urgent need.

Our study suggests that implementation of a penicillin allergy algorithm in a pediatric hospital may be associated with increases in outpatient allergy referrals, an increase in use of cephalosporins, and a decrease in use of alternative antibiotics. Future directions include working with the hospital antibiotic stewardship team to incorporate an electronic version of the algorithm into the EHR, which may increase ease of access and utilization. A recent study implemented an electronic algorithm to identify low-risk penicillin-allergic pediatric patients and showed that the electronic algorithm was superior to the paper version at identifying these patients [6]. Increasing outpatient allergy referrals has also been accomplished through targeting pediatric primary care physicians [7], which is also a next step in our study. More education should be provided to those taking care of pediatric inpatients, as front-line providers are crucial in reconciling and addressing listed allergies during the admission process. A recent study conducted among penicillin-allergic pediatric inpatients has demonstrated success in de-labeling patients using a clinical care pathway that equips these front-line providers with the protocol to proceed directly to drug challenge for low-risk patients, without the need for Allergy consultation [8,9]. In addition, increased collaboration with the infectious disease team may further promote antibiotic stewardship and lead to the goal of increased penicillin allergy de-labeling.

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