Brief report

Penicillin or cephalosporin antibiotic allergy label: Influence on length of stay and hospital readmission

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Background: A penicillin or cephalosporin antibiotic (PCA) allergy label (PCAAL) has negative implications for both the patient and health care alike.

Objective: A retrospective study was undertaken to evaluate the influence of a PCAAL on length of stay (LOS) and hospital readmissions.

Methods: Over 4 weeks, inpatients with a PCAAL who were referred to the allergy service or opportunistically reviewed were grouped in the categories delabeled (group 1a) or advice not followed (ie, label carriage) (group 1b). Comparator groups without a PCAAL were identified, those either on a PCA (the PCA group [group 2]) or on a non-PCA (the non-PCA group [group 3]).

Results: The study population comprised 77 patients as follows: group 1a (n = 19), group 1b (n = 6), group 2 (n = 36), and group 3 (n = 16). Those in group 1a were significantly older (median age 78 years) than those in group 1b (median age 53 years [*P* = .013]) or group 3 (median age 59 years [*P* = .013]). There was a trend toward lower LOS in group 1a (10 days) than in group 1b (11.5 days [*P* = not significant]). Group 2 had a significantly lower LOS (6 days) than either both group 1a (10 days [*P* = .043]) or group 3 (15 days [*P* = .002]). Group 3 had the highest rate of patients readmitted within 30 days (n = 5 [71.4%]).

Conclusion: A PCAAL carries influence on both LOS and readmissions, thus identifying the prompt need for allergy review to provide specific recommendations: delabeling and transition to an appropriate antibiotic. The significantly older group of those with a PCAAL who received a PCA after delabeling (ie, a 20-year age difference) may also be a signal that more elderly and comorbid patients benefit from this intervention the most. (J Allergy Clin Immunol Global 2024;3:100272.)

Key words: *Allergy label, inpatient, antibiotic stewardship, delabeling, length of stay*

INTRODUCTION

An allergy label to penicillin or cephalosporin antibiotic (PCA) is common; however, there is increasing recognition that a majority of those with such a label can be safely delabeled. For hospitalized patients specifically, as such a label can be present in up to 16% of patients,[1] a continued emphasis on such a label needs to be encouraged. This is of importance, as the label has significant negative implications for both the patient and health care alike.

From a patient perspective, such a label is often present in older individuals with more comorbidities than in those without a label.[2,3] Such patients also have an increased likelihood of adverse reactions and higher likelihood of treatment failure.[3-5] The use of alternate, less targeted treatments often leads to multiple antibiotic prescriptions, raising health care costs[6] as well as occurrence of complications such as *Clostridium difficile*.[7] Furthermore, the label is also attributed to a longer length of stay (LOS), which in turn affects the overall demands on the health care system.[2,7-9]

Given these implications, active inpatient delabeling in routine clinical practice is required. Globally, although antimicrobial stewardship (AMS) programs have been instituted in many facilities, in our experience, the limited number of practicing allergists, lack of dedicated time, and underrecognition by clinicians remain significant barriers to such delabeling. Studies have demonstrated encouraging results through risk stratification and delabeling by nonallergists (ie, trained nursing and pharmacists) in the first instance, which should evolve into routine clinical practice to address such barriers.[10,11] Therefore, a paradigm shift is urgently required, as there is now growing evidence supporting the importance of both inpatient and outpatient drug allergy delabeling.

A retrospective clinical audit was undertaken to evaluate both LOS and hospital readmission in patients with or without a PCA allergy label (PCAAL) at a 593-bed tertiary hospital. Patients were screened either through the electronic medical record or if they had been actively referred from an inpatient department (excluding the emergency department, short stay medical and surgical units, and psychiatry unit). Over a 4-week period in

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Abbreviations used
AMS: Antimicrobial stewardship
LOS: Length of stay
PCA: Penicillin or cephalosporin antibiotic
PCAAL: PCA allergy label

February 2023, patient groups were identified as follows: patients with a PCAAL in whom allergy consultation was performed and advice was followed (ie, delabeling was performed) [group 1a] or not followed (ie, the patient continued to carry the label [group 1b]), patients without a PCAAL who were taking a PCA (group 2), and patients without a PCAAL who were not taking a PCA (group 3).

Demographic (age and sex) and admitting clinical unit data were collected. Total LOS from date of allergy consult (in days calculated as the difference between dates of admission or review and discharge) was recorded. The electronic medical record was reviewed in June 2023 to record readmission of patients (in days calculated as the difference between dates of discharge and readmission).

The study was approved by the Southern Adelaide Local Health Network (SALHN) Quality Register (reference no. 4753). Statistical analyses with the Mann-Whitney *U* test were performed using GraphPad Prism software, version 9.5.1 (GraphPad Software, Inc, San Diego, Calif).

RESULTS AND DISCUSSION

A total of 77 patients were identified and grouped as follows: group 1a (n = 19), group 1b (n = 6), group 2 (n = 36) and group 3 (n = 16). Their median age was 65 years. Patients in group 1a were significantly older (median age 78 years) than both group 1b (53 years [P = .013]) and group 3 (59 years [P = .013]). There were more males (n = 47 [61%]) than females (Table I).

Surgical specialties (n = 41 [53.2%]) and general medicine (n = 20 [26%]) had the highest numbers of patients, followed by medical specialties (n = 14 [18.2%]), the intensive care unit (n = 5 [6.5%]). and general surgery teams (n = 2 [2.6%]).

In group 1a, the antibiotic prescriptions were as follows: vancomycin (n = 8), clindamycin (n = 5), clindamycin and ciprofloxacin (n = 1), clindamycin and ceftriaxone (n = 1), vancomycin and metronidazole (n = 1), vancomycin and cefazolin (n = 1), vancomycin and ciprofloxacin (n = 1), and meropenem (n = 1). After delabeling, 14 of these patients (73.7%) were changed to a PCA: amoxicillin and clavulanic acid (n = 11), flucloxacillin (n = 2), or ceftriaxone (n = 1). In group 1b, the antibiotic prescriptions included clindamycin (n = 4), clindamycin and azithromycin (n = 1), and vancomycin (n = 1).

In group 2, antibiotic prescriptions were piperacillin and tazobactam (n = 11); amoxicillin and clavulanic acid (n = 8); cefazolin (n = 5); ceftriaxone and metronidazole (n = 2); amoxicillin and gentamicin (n = 1); benzyl penicillin and metronidazole (n = 1); cefazolin and metronidazole (n = 1); ceftriaxone (n = 1); ceftriaxone and azithromycin (n = 1); ceftriaxone and gentamicin (n = 1); ceftriaxone and doxycycline (n = 1); cephalexin (n = 1); flucloxacillin (n = 1); flucloxacillin, ciprofloxacin, and gentamicin (n = 1); and piperacillin, tazobactam, and vancomycin (n = 1). In this group, 1 patient (2.8%) had an antibiotic allergy label (vancomycin).

In group 3, the antibiotics included vancomycin (n = 12), vancomycin and anidulafungin (n = 1), vancomycin and ciprofloxacin (n = 1), and clindamycin (n = 2). One patient (6.3%) had an antibiotic allergy label (ceftriaxone).

Overall, the median LOS was 9 days, being highest in group 3 (at 15 days). Although total LOS and days to discharge after allergy consultation were lower in group 1a (10 days and 4 days, respectively) than in group 1b (11.5 days and 5 days, respectively), neither reached statistical significance. Group 2 had a significantly lower LOS (6 days) than either group 1a (10 days [P = .043]) or group 3 (15 days [P = .002]) (Fig 1). Collectively, no patients experienced any adverse reactions during their hospitalization with the respective antibiotics.

Readmissions were present in around half of the cohort (n = 39 [50.6%]). Group 3 had the highest proportion of patients readmitted within 30 days (n = 5 [71.4%]), followed by group 1b (n = 2 [66.6%]). In group 1a, readmission was observed most within 30 days (n = 6 [46.2%]) and at 60 to 120 days (n = 4 [30.8%]). There were no readmissions for the same person more than once across the data set.

This study demonstrates that an inpatient PCAAL has implications for both LOS and readmissions. Specifically, active and prompt allergy consult for a patient with a PCAAL to enable delabeling results in a lower LOS. Patients without a PCAAL who are taking a PCA had a significantly lower LOS, which highlights the fact that addressing these labels during inpatient admission must be prioritized. Despite our study's small numbers, the LOS figures are comparable to those for other larger cohorts. For example, in a study evaluating more than 102,000 patients, the difference in LOS was 1 day (8 days vs 7 days [P < .001]).[12] In another study specifically evaluating those with hematologic malignancy, this difference was 3.7 days ($P \leq .001$), suggesting that disease-specific factors contribute further to such LOS.[8] The significantly older group of those with a PCAAL who received a PCA after delabeling (ie, a 20-year age difference) may also be a signal that more elderly and comorbid patients benefit from this intervention the most. Future studies with more patients matched for age and/or comorbidities will address this proposition.

The increased LOS translates into higher financial implications for health care, the elevation of which has been reported to be up to 10-fold.[13] An explanation may include utility of a non-PCA, as was also observed in group 3 of our cohort, which had a significantly higher overall LOS. Other considerations include the cost of alternate medications, not only for acute hospitalization but also after discharge, the latter of which can result in higher-cost medication prescriptions in 38% of patients.[14] The fact that many of our patients with a PCAAL were admitted under surgical specialty groups emphasizes the fact that unit-specific active delabeling may be provided, as the label is also associated with increased surgical complications, further contributing to longer LOS.[15]

Earlier assessment of allergy labels may result in prompt recommendations, which include delabeling and transition to an appropriate antibiotic, as represented by the patients in group 1a. Although the notion of AMS is present in our institution, further work on inpatient delabeling is required, given that 6 patients (group 1b) did not have a recommendation actioned. These

TABLE I. Demographics for the groups, admitting unit, LOS, and readmission

Characteristic	Group 1a (n = 19)	Group 1b (n = 6)	Group 2 (n = 36)	Group 3 (n = 16)	Total (n = 77)
Age (y), median (IQR)	78 (61-83)	53 (29-71)	65.5 (49.8-80.3)	59 (48-72)	65 (50-79)
Sex	11 M (57.9%) and 8 F	3 M (50%) and 3 F	23 M (63.9%) and 13 F	10 M (62.5%) and 6 F	47 M (61%) and 30 F
Admitting unit, no. (%)					
General medicine	5 (26.3%)	3 (50%)	9 (25%)	3 (18.8%)	20 (26%)
Medical specialty	5 (26.3%)	—	6 (16.7%)	2 (12.3%)	14 (18.2%)
General surgery	1 (5.3%)	—	1 (2.8%)	—	2 (2.6%)
Surgical specialty	8 (42.1%)	3 (50%)	17 (47.2%)	11 (68.8%)	41 (53.2%)
ICU	—	—	3 (8.3%)	2 (12.3%)	5 (6.5%)
Overall LOS (d), median (IQR)	10 (6-18)	11.5 (4-23)	6 (3.3-12)	15 (8.5-29.8)	9 (5-17)
LOS following drug allergy review (d), median (IQR)	4 (1-10)	5 (0.75-11)	N/A	N/A	N/A
Total readmissions (d), no. (%)	13 (68.4%)	3 (50%)	16 (44.4%)	7 (41.2%)	39 (50.6%)
<30	6 (46.2%)	2 (66.6%)	4 (25%)	5 (71.4%)	17 (21.3%)
30-60	2 (15.4%)	1 (33.3%)	6 (37.5%)	1 (14.3%)	10 (25.6%)
60-120	4 (30.8%)	—	3 (18.8%)	1 (14.3)	8 (11.6%)
>120	1 (7.7%)	—	3 (18.8%)	—	4 (10.3%)

Statistical analyses for age differences: group 1a versus group 3, $P = .013$; group 1a versus group 1b, $P = .013$; and LOS, group 1a versus group 2, $P = .042$; group 1a versus group 3, $P = .010$; and group 2 versus group 3, $P = .002$.
ICU, Intensive care unit; *IQR*, interquartile range; *N/A*, not available.

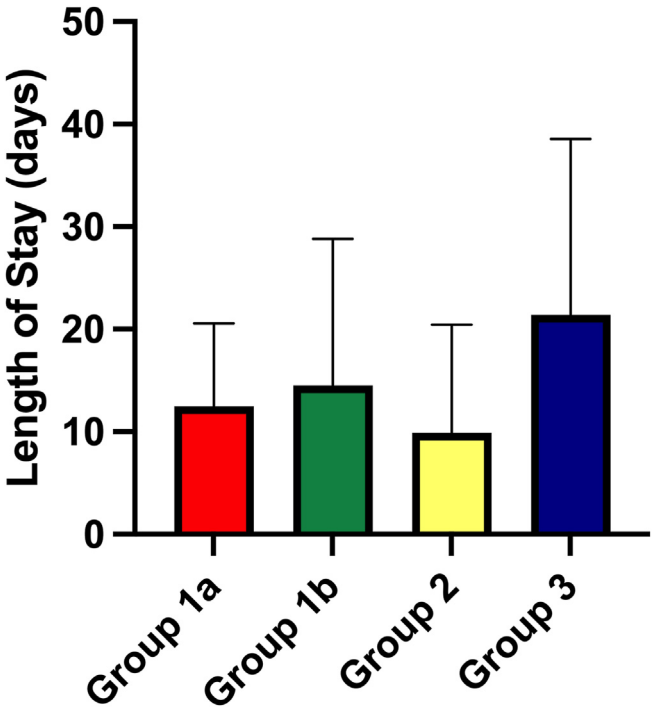

FIG 1. LOS for the groups. Statistical analyses: group 1a versus group 2, $P = .043$; group 1a versus group 3, $P = .010$; and group 2 versus group 3, $P = .002$.

patients were admitted under surgical specialties or general medicine, and the inability to facilitate delabeling may be attributed to number of variables, such as busy ward environment, staffing numbers, and possible lack of familiarity. In this latter context, further awareness of β-lactam cross-reactivity in addition to a refined AMS may be beneficial.[16]

Additionally, limited medical and nursing support by our allergy service remains a significant continued barrier. Although other centers, including those in Australia,[17] have implemented a strong collaborative liaison with infectious disease physicians, nursing, and pharmacy staff to provide this service via risk stratification and delabeling in a safe and cost-effective manner, this has yet to come to fruition in our center. This is supported by a recent review of our outpatient drug allergy clinic waiting list, which demonstrated that 65% of referrals were from clinicians in the inpatient setting, ultimately reflecting the fact that education and continued work are needed to address this issue.[18]

Our study has demonstrated that the overall rates of readmission were high, especially in group 1a. A high readmission rate has previously been reported for inpatients with a history of a penicillin allergy versus for those without such a history.[19] An Australian study reported that an antibiotic allergy label was associated with more readmissions within 4 weeks: 29% versus 18% for patients without a drug allergy label.[20] Our small patient numbers prohibit definitive conclusions, but the presence of higher rates of readmission within 30 days in group 1b (66.6%) than in group 1a (46.2%) indicates that allergy service review, recommendation, and follow-through with the plan are valuable. Additionally, patients receiving alternate antibiotics, despite having no label, have a high rate of readmission within 30 days.

A limitation of the study is its retrospective nature and the low numbers in the cohort, including limited 1:1 matching of the patients. Since the completion of this study, institution funding for a prospective, matched cohort study to address this limitation has been received.

In conclusion, our study of inpatients within a brief period of time demonstrates that those taking a PCA have a lower LOS than others. A PCAAL increases LOS, with a high readmission rate, especially within 30 days, if not delabeled. In our institution, ongoing inpatient delabeling with assessment, LOS, and readmission rates will remain performance indicators that are key to both the patient and health care alike.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

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Clinical implications: A penicillin and or cephalosporin allergy label influences both hospital LOS and hospital readmission. Labeled patients are older and may benefit the most from proactive review and delabeling.

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