Abstract # 996

Impact of Penicillin Allergy Labels on Carbapenem Use in a Multi-Center Study

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Abstract

Background: Antibiotic allergy labels lead to excess exposure to broad-spectrum antibiotics and can result in patient harm. We aimed to describe the prevalence of penicillin allergy labels (PAL) across a variety of hospital settings and its association with carbapenem exposure.

Methods: We performed a retrospective cohort analysis of inpatient admissions from 14 hospitals in the Duke Antimicrobial Stewardship Outreach Network (DASON) and Duke Health System from 2016 to 2018. Data was collected from the DASON central database which is derived from electronic health record extracts. Penicillin allergy label (PAL) was defined from drug allergy documentation indicating any reaction to penicillin or its related agents, but did not include labels for other beta-lactam agents (e.g. cephalosporin). Carbapenem exposure was defined as a binary variable indicating receipt of at least one dose of meropenem, ertapenem, doripenem or imipenem on an inpatient unit. The association between PAL and carbapenem exposure was assessed using multivariable logistical regression. Variables that did not have significant confounding or selection bias were eliminated using backward elimination. Interaction terms were compared using a likelihood ratio test (LRT). Hospital-level PAL prevalence was defined as percentage of inpatient admissions. Hospital-level carbapenem use rates were assessed as days of therapy (DOT) per 1000 patient days and stratified by PAL to understand the portion of use associated with PAL.

Results: Of the 727,168 admissions included in this study, 84,033 (11.6%) patients had a PAL. The majority of admissions with documented PAL were in patients >65 years old (47.9%, n= 40,240) and female (57.8%, n= 418,472). PAL prevalence varied among hospitals (median 14%, IQR 12.8-16.2%). Hospitals with antibiotic allergy-focused stewardship programs (A-ASP) had a lower PAL prevalence to those without (median 13.8 vs 15.9%, p=0.08), but the percent of carbapenem DOT used in patients with PAL was similar (median 23% vs 24%, p=0.6). In the final multivariate logistic regression model, PAL was associated with a 1.6-fold odds of receipt of carbapenem (adjusted odds ratio 1.63, 95% CI 1.41- 1.88, p<0.0001). Increasing age, inpatient mortality, admission to teaching hospital and carbapenem restricting hospital were also found to be significant risk factors for carbapenem receipt. We detected interactions between PAL and teaching hospitals as well as carbapenem restricting hospitals.

Conclusion: PAL was associated with increased carbapenem exposure. A-ASP activities may affect PAL but it is unclear if it reduces carbapenem use based on these observational data.

Background

- Approximately 10-15% of the population has a penicillin allergy label, most of which are incorrect.[1]
- Antibiotic allergy labels lead to excess exposure to broad-spectrum antibiotics, inferior patient outcomes and antimicrobial resistance.[1]
- The use of carbapenems in the US has risen by 50% in recent years.[2]
- De-labelling incorrect allergies and educating on appropriate allergy assessment is one strategy proposed to reduce carbapenem use.

1. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Lancet. 2019;393:183-98.
2. Baggs J, Fridkin SK, Pollack LA, Srinivasan A, Jernigan JA. JAMA Intern Med. 2016;176(11):1639-48.

Methods

- Setting: 14 hospitals in DASON and Duke Health System
- Study period: 1/1/2016 to 12/31/2018.
- Inclusion criteria: Electronic health record extracts of all inpatient admissions during the study period.
- Statistical approach:
  - The association between PAL and carbapenem exposure was assessed using multivariable logistical regression, adjusted for clustering by hospital.
  - Variables that did not have significant confounding or selection bias were eliminated using backward elimination. Interaction terms were compared using a likelihood ratio test.

Definition of key terms	
Exposure	Penicillin allergy label (PAL) was defined from drug allergy documentation indicating any reaction to penicillin or its related agents, but did not include labels for other beta-lactam agents (e.g. cephalosporin).
Outcome	Carbapenem exposure was defined as a binary variable indicating receipt of at least one dose of meropenem, ertapenem, doripenem, or imipenem on an inpatient unit.
Antibiotic allergy-focused antimicrobial stewardship program (A-ASP)	Presence of an established (minimum 1 year) antimicrobial stewardship program with a focus on addressing antibiotic allergy-related issues.

Results

Table 1: Baseline patient characteristics, n= 727,168.

	PAL (n=643,135)	No PAL (n= 84,033)	OR (95% CI)	P-value
Age				
19-64yo, n (%)	41,758 (11.5)	322,418 (88.5)	0.98 (0.97-1.00)	0.02
≥ 65yo, n (%)	40,240 (14.8)	231,724 (85.2)	1.63 (1.61-1.66)	<.0001
Female, n (%)	57,006 (68.1)	361,466 (56.5)	1.65 (1.62-1.67)	<.0001
Race				
White, n (%)	56,543 (67.3)	373,974 (58.2)	1.48 (1.45-1.50)	<.0001
Comorbidities, n (%)				
COPD	12,053 (14.3)	64,125 (10.0)	1.51 (1.48-1.54)	<.0001
CHF	78,412 (12.2)	14,293 (17.0)	1.48 (1.48-1.50)	<.0001
Malignancy	1,922 (2.3)	21,219 (3.3)	0.69 (0.65-0.72)	<.0001
ICU admission	11,392 (13.6)	84,645 (13.2)	1.03 (1.01-1.07)	0.0015
Carbapenem receipt, n (%)	2,839 (3.4)	10,701 (1.7)	2.07 (1.98-2.16)	<.0001

Results

- 84,033 (11.6%) patients had a PAL. PAL prevalence varied among hospitals (median 14.3%, IQR 12.8-16.2%).
- 7 (50%) hospitals had A-ASP and 5 (35%) offered skin testing. 9 (64%) had carbapenem restriction policies, including all 7 with A-ASP.
- Hospitals with A-ASP had lower PAL prevalence compared to those without (median 13.4 vs 15.7%, p=0.08, Fig 1). The proportion of carbapenem DOT used in patients with PAL was similar among A-ASP and non-A-ASP hospitals (median 23% vs 25%, p=0.6).
- Carbapenem restricting hospitals had lower rates of total carbapenem use (Fig 2).
- Modeling:
  - We detected significant interactions of the main effect for teaching (LRT p=0.01) and carbapenem restriction (LRT p<0.001, Table 2).
  - A-ASP was not a significant predictor of carbapenem exposure and was dropped during modeling.
  - PAL was associated with a 1.6-fold odds of carbapenem receipt (adjusted odds ratio 1.63, 95% CI 1.41-1.88, p<.0001).

Figure 1: PAL prevalence by hospital

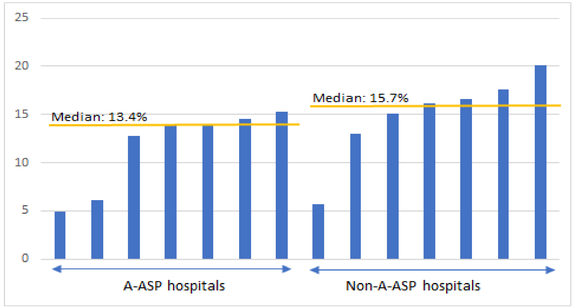

Figure 2: Effect of A-ASP and carbapenem restriction (Carb-R) on carbapenem use

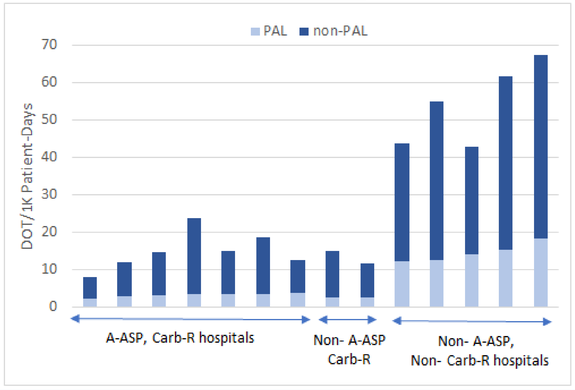

Table 2: Risk factors for carbapenem receipt (Final model)

Variable	OR (95% CI)	P value
PAL	1.63 (1.41- 1.88)	<.0001
Age, per 1 year increase	1.01 (1.00- 1.02)	0.0144
Inpatient mortality	5.53 (3.98- 7.67)	<.0001
Admission to teaching hospital	1.65 (1.19- 2.30)	0.0030
Admission to carbapenem restricting hospital	0.29 (0.21- 0.41)	<.0001
PAL x teaching hospital (interaction)	1.05 (0.86- 1.28)	0.6527
PAL x carbapenem restricting hospital (interaction)	1.13 (0.95- 1.33)	0.1734

Conclusions

- PAL was associated with a 1.6-fold increased odds of carbapenem exposure.
- A-ASP activities may affect PAL prevalence but it is unclear if it reduces carbapenem use, especially in hospitals with existing carbapenem restriction policies.