Implications of Reported Penicillin Allergies in Treatment of MSSA Bacteremia

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Abstract

Background: While 8% of patients report penicillin allergy, fewer than 5% are proven on testing. Reportedly allergic patients frequently receive alternative antibiotics which may increase cost, risk of treatment failure and prevalence of drug-resistant pathogens. Preparatory for a penicillin allergy testing protocol, we conducted a retrospective chart review examining the influence of reported penicillin allergy and antibiotic choice on treatment of methicillin-sensitive *Staphylococcus aureus* (MSSA) bacteremia.

Methods: Adults admitted between 2010 and 2015 with MSSA bacteremia were identified by DEDUCE search. Patients expiring before anti-microbial susceptibilities resulted were excluded. Outcomes included rates of 30- and 90-day mortality, 90-day recurrence and allergic reactions. Analyses were performed according to reported allergy and antibiotic choice. A binary logistic regression model was created in SAS adjusting for confounding factors (age, infection site and co-morbidities).

Results: 335 patients were included. Penicillin-allergic patients had similar 30- (17%) and 90-day (20%) mortality rates to non-allergic patients (16%, p=0.84 and 22%, p=0.67, respectively) but an 11-fold higher 90-day recurrence rate (p<0.01). Patients receiving vancomycin had substantially higher 30- (26%, p=0.002) and 90-day (28%, p=0.02) mortality rates compared to nafcillin (9%) or cefazolin (6%, see figure 1). Even after logistic regression modeling, beta-lactam use significantly reduced 30- (OR 0.26, p=0.001) and 90-day (OR 0.43, p=0.02) mortality rates (figure 2). No allergic reactions were detected.

Conclusions: Treatment of MSSA bacteremia with vancomycin was associated with significantly higher mortality rates than beta-lactams. Penicillin-allergic patients were more likely suffer recurrent bacteremia, but not higher mortality. Frequent use of cefazolin in supposedly penicillin allergic patients may explain the absence of any mortality difference by reported allergy: 45% of penicillin allergic patients received cefazolin without any allergic reactions reported. Beta-lactams should be strongly preferred over vancomycin for MSSA bacteremia, and can be safely given to select penicillin-allergic patients.

References

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Background

- 8% of patients report penicillin allergy, yet fewer than 5% are proven on testing
- As a result of reported allergies, patients frequently receive alternative antibiotics resulting in:
  - Greater risk of treatment failure
  - Higher cost
  - Increased prevalence of resistance
- **Objective:** To examine the effect of both reported penicillin allergy and eventual treatment choice on a variety of outcomes – including mortality, time to culture clearance and recurrence of bacteremia.

Methods

- Retrospective cohort study of adults admitted to our tertiary care hospital between 2010 and 2015 with methicillin sensitive *Staphylococcus aureus* bacteremia (n=335)
- Exclusion criteria:
  - Polymicrobial bacteremia
  - Comfort care
  - Expiration in <72 hours
- Primary outcomes:
  - 30- and 90-day mortality
  - 90 day recurrence rates for bacteremia
- Multivariate binary regression model to assess for outcomes while adjusting for potential confounding factors (e.g., age, infection site, co-morbidities)

Treatment	Non-allergic	Penicillin Allergic	p-values
Vancomycin	39 (15%)	30 (42%)	0.00
Cephalosporin	98 (37%)	29 (41%)	0.57
Nafcillin	113 (43%)	3 (4%)	0.00
Other	14 (5%)	9 (13%)	0.03

Observations Regarding Antibiotic Choice.

Outcomes	Vancomycin	Cefazolin	Nafcillin	p-value
Days to clear	5.1	4.5	4.2	
Acute renal inj	0	0.8%	0.9%	n/a
Drug reaction	0	0	0	n/a

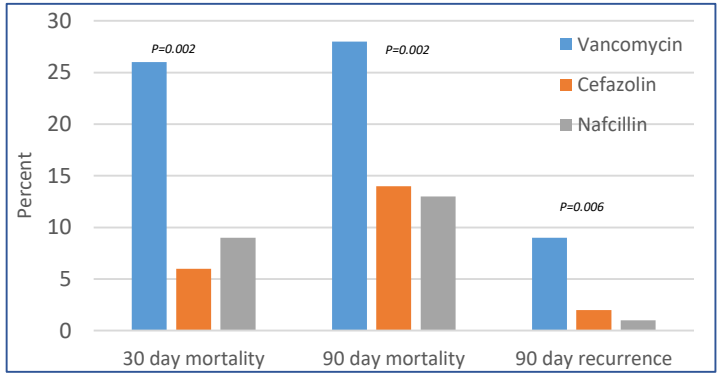
Observations Regarding Adverse Effects.

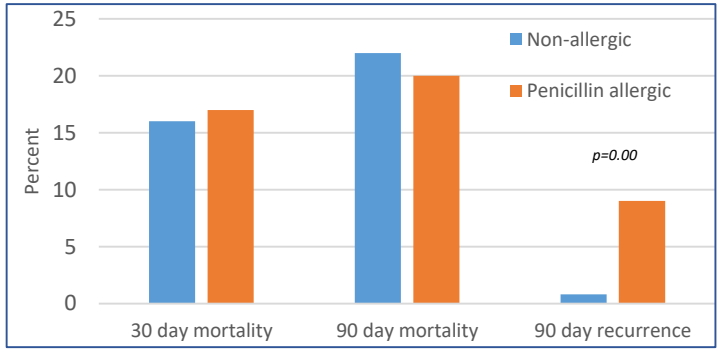
Results

Characteristics	Vancomycin	Cefazolin	Nafcillin
Number	53	127	116
Male	31 (59%)	82 (65%)	79 (68%)
Mean age	55.5	59.3	56.5
Co-morbidities			
CCmI, mean	6.5 p=0.00	6.4 p=0.00	4.3
MI	16 (30%)	33 (26%)	26 (22%)
CHF	26 (49%)	61 (48%)	44 (38%)
PVD	14 (26%)	35 (28%)	24 (21%)
CVA	24 (45%)	43 (34%)	41 (35%)
Dementia	2 (4%)	3 (2%)	5 (4%)
Pulmonary	20 (38%)	52 (41%)	35 (30%)
CTD	7 (13%)	13 (10%)	15 (13%)
PUD	6 (11%)	14 (11%)	13 (11%)
Liver	7 (13%)	16 (13%)	6 (5%)
Diabetes	35 (66%) p=0.04	65 (51%)	57 (49%)
Diabetes +	24 (45%) p=0.00	48 (38%)	20 (17%)
Paraplegia	3 (6%)	5 (4%)	7 (6%)
Renal	37 (70%) p=0.00	83 (65%)	49 (42%)
Cancer	14 (26%)	42 (33%)	23 (20%)
Metastatic cancer	5 (9%)	24 (19%)	7 (6%)
Severe liver	6 (11%) p=0.04	15 (12%)	4 (3%)
HIV	0	0	0
Infection Site			
Catheter	9 (17%)	24 (19%)	11 (9.5%)
Pneumonia	6 (11%)	9 (7%)	6 (5%)
Endovascular	12 (23%)	24 (27%)	19 (16%)
Osteoarticular	4 (8%) p=0.01	9 (7%)	28 (24%)
Soft tissue	11 (21%)	24 (19%)	31 (27%)
Unknown	14 (26%)	25 (20%)	28 (24%)

Table 1: Multivariate model. Created in SAS. Beta-lactam use predicted survival.

Variable	Maximum Likelihood Estimate	Odds Ratio Estimate	95% confidence limits	p-value
Beta-lactam	-1.34	0.26	0.12-0.60	0.001
Soft tissue site	-0.79	0.45	0.15-1.40	0.17
Age >65	0.63	1.87	0.84-4.16	0.12
Variable	**Maximum Likelihood Estimate**	**Odds Ratio Estimate**	**95% confidence limits**	**p-value**
Beta-lactam	-0.85	0.43	0.2-0.9	0.02
CHF	0.79	2.2	1.1-4.2	0.02
Cancer	1.06	2.9	1.5-5.6	0.002





Conclusions

- Vancomycin use was associated with four-fold higher mortality rates vs beta-lactams at 30 and 90 days
- Risk of recurrent MSSA bacteremia at 90 days was ten-fold higher with vancomycin vs beta-lactams
- Even after logistic regression modeling, beta-lactam use significantly reduced 30- (OR 0.26, p=0.001) and 90-day (OR 0.43, p=0.02) mortality
- Limitations: selection bias, C-statistics from multivariate modeling, poor sensitivity for adverse events