

Evaluation of vancomycin exposure on outcomes in a cohort of patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infective endocarditis (IE)

A.M. Casapao*, S. Patel, R. Kullar, S.L. Davis, D.P. Levine, M.J. Rybak (Detroit, US)

Objective: To evaluate a cohort of patients (pts) treated with vancomycin (VAN) for MRSA IE and characterize the association of outcomes and VAN exposure. **Methods:** A retrospective cohort study of pts with MRSA IE treated with VAN \geq 72 hours from 2004-2012 at Detroit Medical Center were included into study. Initial VAN trough levels and VAN area under the curve in 24 h (AUC24) to minimum inhibitory concentration (MIC) was evaluated for vancomycin exposure for each patient. Initial MRSA isolate was collected and VAN MIC was determined by broth microdilution per Clinical Laboratory Standard Institute. Modified population analysis profile was used to measure VAN susceptibility. Primary outcome was composite VAN treatment failure defined as persistent bacteremia (\geq 7 days on VAN) or all cause 30-day mortality. Classification and regression tree analysis (CART) was used to select VAN failure breakpoint between initial VAN trough and VAN AUC24:MIC ratio. **Results:** A total of 128 pts were included for evaluation; 75% (96/128) had right-sided IE, 19% (24/128) had left-sided IE, and 6% (8/128) had both left and right-sided IE. The median (IQR) APACHE II score was 11 (7-16). Seventeen percent (22/128) of the MRSA isolates were identified as heterogeneous vancomycin-intermediate *Staphylococcus aureus*. Overall VAN failure rate was 65% (83/128). Characteristics significant for failure were initial VAN trough level $<$ 15 mg/L ($p = 0.02$) and VAN AUC24:MIC $<$ 400 ($p = 0.03$), see Table 1. Using logistic regression analysis, initial VAN trough level $<$ 15 mg/L (aOR 3.7; 95% CI 1.6-8.6) was independently associated with VAN failure while young age $<$ 40 years old (aOR 0.96; 95% CI 0.93-0.99) was associated as an independent predictor of VAN success. CART breakpoint between VAN failure and success for initial VAN trough level and VAN AUC 24:MIC were 17.3 mg/L and 583, respectively. **Conclusion:** VAN failure rate was high among pts with MRSA IE treated with VAN. Initial VAN trough levels at steady state $<$ 15 mg/L and VAN AUC24:MIC $<$ 400 were significant for VAN treatment failure for pts with MRSA IE. Initial VAN trough levels $<$ 15 mg/L in pts with MRSA IE is an independent predictor for VAN failure. Further research is warranted to evaluate the breakpoints for initial VAN trough levels and VAN AUC24:MIC for persistent bacteremia and 30-day mortality in patients with MRSA infective endocarditis.

Table 1. Vancomycin exposure and association to clinical outcomes.

Outcomes	Initial VAN trough		p value	VAN AUC24:MIC		p value
	$<$ 15 mg/L n = 67	\geq 15 mg/L n = 61		$<$ 400 n = 50	\geq 400 n = 78	
Composite VAN Failure	50 (75%)	33 (54%)	0.015	39 (78%)	45 (58%)	0.027
Persistent Bacteremia	48 (72%)	28 (46%)	0.003	35 (70%)	43 (55%)	0.097
30-Day all-cause mortality	14 (21%)	12 (20%)	0.864	15 (30%)	11 (14%)	0.027