Risk Factors for Therapeutic Failure to Vancomycin in Adults with Methicillin-Resistant Staphylococcus Aureus Infection Treated in a Hospital in Cali, Colombia

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Introduction

For a long time, glycopeptides such as vancomycin have been the first-line antibiotics for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections. However, in recent years they have shown a decrease in effectiveness. For this reason, it is important to determine the risk factors are for the therapeutic failure of vancomycin.

Materials and methods

OBJECTIVES: To determine the risk factors associated with vancomycin treatment failure in adult patients with MRSA infection using electronic medical records.

METHODS: In a case-control design study, all adult patients hospitalized between January 2015 and December 2021 with MRSA infection with a confirmed MRSA microbiological isolation were included. Cases were those patients with therapeutic failure to vancomycin (as defined by mortality, no clinical improvement, change of antibiotic required, early relapse, or persistence of positive blood cultures) while controls were those who had a good clinical response. The significant variables of the bivariate analysis were included in a multiple analysis with an asymmetric logistic regression model.

Results

A total of 105 patients (28 cases and 77 controls) were included. Median age was 49 years, and 59 (56%) were males. Age (OR 1.034; 95% CI 1.007-1.061, p = 0.011), osteomyelitis/septic arthritis (OR 6.035; 95% CI 2.282-15.956, p = 0.000) and minimum inhibitory concentration (MIC) (OR 5.971; 95% CI) 1.321-26.979, p = 0.020), were independent risk factors associated with vancomycin treatment failure. Vancomycin trough levels (measured in only 47 patients) were not different between cases and controls (OR 0.976; 95% CI 0.911-1.044, p = 0.478)

Table 1. Demographic characteristics and risk factors of patients with MRSA

	Therapeutic failure		
Variables	Controls (n=77)	Cases (n=28)	General (n=105)
	n (%)	n (%)	n (%)
Age, median (IQR)	43 (28-58)	61 (50-73)	49 (30-65)
Mean (SD)	44.5 (18.7)	59.3 (18.4)	48.4 (19.7)
Gender			
Females	31 (40.3)	15 (53.6)	46 (43.8)
Males	46 (59.7)	13 (46.4)	59 (56.2)
Diabetes	10 (13.0)	9 (32.1)	19 (18.1)
Cirrhosis	0 (0)	0 (0)	0 (0)
CKD	4 (5.2)	1 (3.6)	5 (4.8)
Endocarditis	1 (1.3)	1 (3.6)	2 (1.9)
HIV	1 (1.3)	1 (3.6)	2 (1.9)
Immunosuppressive treatment or chemotherapy	25 (32.5)	8 (28.6)	33 (31.4)
Osteomyelitis or septic arthritis	6 (7.8)	7 (25.0)	13 (12.4)
Skin or soft tissue infection	41 (53.3)	13 (46.4)	54 (51.4)
Catheter-related infection	8 (10.4)	2 (7.1)	10 (9.5)
Pneumonia	10 (13.0)	7 (25.0)	17 (16.2)
Central nervous system infection	7 (9.1)	1 (3.6)	8 (7.6)
Bacteremia	25 (32.5)	15 (53.6)	40 (38.1)
Vancomycin trough levels (µg/mL), median (IQR), n = 47	17.6 (12.5-23.6)	15.7 (10.7-23.8)	17.2 (11.6-23.8)
Mean (SD)	19.8 (10.6)	17.5 (9.4)	19.2 (10.3)
Minimum inhibitory concentration (µg/mL), median (IQR), n = 104	1 (1-1)	1 (1-1)	1 (1-1)
Mean (SD)	0.98 (0.17)	1.05 (0,28)	1 (0.20)
Charlson index, median (IQR)	2 (0-3)	3.5 (2-5)	2 (0-4)
Mean (SD)	2.15 (2.5)	3.64 (2.6)	2.55 (2.6)
Previous use of vancomycin, n = 73	19 (24.7)	6 (21.4)	25 (23.8)
***IQR interquartile range**			
†SD standard deviation			

Table 2. Multiple analysis of factors associated with therapeutic failure to vancomycin

	OR not adjusted 95% CI				OR adjusted 95% CI			
Variables (Factors)	OR	Inf	Sup	p-value	OR	Inf	Sup	p-value
Age	1.04	1.017	1.069	0.001	1.03	1.007	1.061	0.011
Osteomyelitis or septic arthritis	3.94	0.997	15.68	0.018	6.03	2.282	15.95	0.000
Pneumonia	2.23	0.632	7.430	0.139	1.97	0.827	4.712	0.125
MIC	4.91	0.60	40.30	<0.138	5.97	1.321	26.97	0.020
Charlson index	1.23	1.046	1.463	0.013	1.14	0.967	1.360	0.114

Discusion

There was an association between osteomyelitis/septic arthritis and therapeutic failure, suggesting that a good analysis should be performed before initiating vancomycin treatment in these patients. Age was also an independent risk factor, which could be explained by an inefficient immune system in older patients. We found no association with trough levels of vancomycin, but the power to measure that variable was low. Having a higher MIC was also associated with therapeutic failure.

Conclusion

In our cohort, only three variables were found to be significant risk factors for therapeutic failure to vancomycin in MRSA infected patients: age, osteomyelitis and/or septic arthritis, and MIC. Due to sample size limitation, other risk factors described in the literature might have gone undetected.

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