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EXTENDED ABSTRACT

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Evaluation of vancomycin susceptibility among isolates of *Staphylococcus aureus* infections between 2010 and 2018 in Aveiro, Portugal

Raquel Diaz[1,2], Elmano Ramalheira[1,2], Bruno Gago[1], Vera Afreixo[3]

[1] Department of Medical Sciences, University of Aveiro, Portugal
[2] Department of Medical Microbiology, Centro Hospitalar Baixo Vouga, Aveiro, Portugal
[3] CIDMA - Center for Research and Development in Mathematics and Applications, Department of Mathematics, University of Aveiro, Portugal

Background

Vancomycin is the primary treatment for methicillin- resistant *Staphylococcus aureus* (MRSA) [1]. Increasing proportions of MRSA isolates with high MICs (Minimum Inhibitory Concentration) have been observed within the susceptible range (MIC creep) [2,3]. These isolates with MIC creep have been associated with therapeutic failure [4].

The aim of this study was to assess the possibility of vancomycin MIC creep among *Staphylococcus aureus* isolates from various clinical sources and to identify trends and differences in vancomycin MICs by using different susceptibility testing methods.

Materials and Methods

A total of 488 clinical MRSA isolates obtained between January 2010 and December 2018 from Centro Hospitalar Baixo Vouga, Aveiro, were analysed. All isolates were identified using routine bacteriological procedures. Only one isolate per patient was included in this analysis. Isolates were recovered from various clinical sources, including respiratory tract (n= 124), blood (n=139), wounds (n=185), urine (n=15) and other source (n= 25).

In each case the MIC of vancomycin for *S. aureus* was evaluated, both for MSSA (methicillin- susceptible *Staphylococcus aureus*) and MRSA, using two methods, the automated system VITEK2 (bioMerieux) and the Broth Microdilution Method (BMD) testing method (*).

All statistical tests with p values <0.05 were considered significant and all statistical analyses were performed using IBM SPSS statistics 22.0.

Results

All 488 *S. aureus* infections studied were susceptible to vancomycin (EUCAST breakpoint ≤ 2mg/L). Figure 1 shows the mean of vancomycin MICs for each year. Compared the vancomycin MICs obtained by different methods we found significant differences between methodologies studied (p<0,001, by sign test).

Correlations between the methodologies and year were studied. The Spearman's correlation coefficient to MRSA between year and BMD was -0,041 (p=0.510) and between year and automated testing analysis was 0.281 (p<0.001), and the Speaman's correlation coefficient to MSSA between year and BMD 0,089 (p=0.183) and between year and automated testing analysis was 0.086 (p=0,198), as showed in Table 1.

Vancomycin MICs from automated testing were also significantly higher than those found by BMD analysis (p<0.001, by sign test).

Conclusion

With only automated testing analysis we can suppose that the MIC creep phenomenon exists, but with the BMD analysis the gradual increased of MIC does not appear to be evident. The MIC creeps are not accurately detected by automated systems. It is important in the next years to monitor the vancomycin MIC

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Corresponding author:
Raquel Diaz
raqueldiaz@ua.pt

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because in 2017 there was an increase in vancomycin MIC values that we don't expect. It appeared, for the first time, MRSA with vancomycin MIC = 2mg/L, that means a soft increase in vancomycin MIC values.

We suggest that all hospitals should monitor their local status of vancomycin MICs to screen this phenomenon and ensure the effectiveness of therapy with vancomycin, given so the vancomycin MIC creep phenomenon seems to be a regional problem.

(*) Vancomycin MIC data were generously provided by the SENTRY program (JMI Laboratories, Inc., North Liberty, IA).

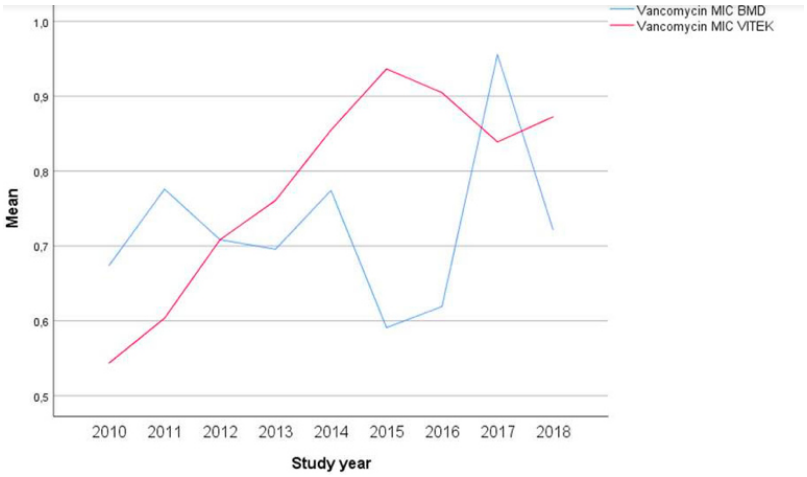

Figure 1 - The mean of vancomycin MICs over the years studied.

Table 1 - Results of the different methodologies studied.

		Mean	95% CI		Median	Spearman Correlation[a]	p value
			Lower bound	Upper Bound			
Vancomycin MIC BMD	MRSA	0,6937	0,6624	0,7250	0,5000	-0,041	0,510
	MSSA	0,7898	0,7506	0,8290	1,0000	0,089	0,183
Vancomycin MIC VITEK	MRSA	0,7844	0,7528	0,8159	1,0000	0,281	<0.001
	MSSA	0,8872	0,8507	0,9236	1,0000	0,086	0,198

[a]Speaman's correlation: correlation between year and vancomycin MIC for each method.

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