The discrepancy of MRSA MIC results in Etest and 4 commercially available broth micro dilution (BMD) methods: analysis of MIC measurement results of Vancomycin(VCM), Teicoplanin(TEIC), Linezolid(LZD), Daptomycin(DPT), Arbekacin(ABK) and Quinupristine/Dalfopristine (QPR/DPR) on 55 MRSA colonized isolates

Sari Umekawa, M.D., Yuka Kitano, M.D., Haruaki Wakatake, M.D., Ph.D., Shigeki Fujitani, M.D., Ph.D., Yoshihiro Masui, M.D., Ph.D., Yasuhiko Taira, M.D., Ph.D.
St. Marianna University School of Medicine, Department of Emergency and Critical Care Medicine, Kanagawa Japan

Corresponding contact: Sari Umekawa, M.D.
E mail: 99013su@jichi.ac.jp
TEL: +81-44-977-8111 FAX: +81-44-979-1522

Presentation # 356

Abstract

■ Background: It has been speculated that there exists discrepancy of Methicillin Resistant *Staphylococcus aureus* (MRSA) Minimal Inhibitory Concentration (MIC) results between variable methods. The association between higher MRSA MIC and worse clinical outcomes has been previously reported and has become a major clinical concern in managing MRSA infections. Therefore, it is clinically essential to investigate whether discrepancy exists between different MIC measurements, especially between Etest and BMD methods.

■ Methods: From November 2009 to March 2011, a prospective observational study was performed at two metropolitan tertiary Emergency Departments in Japan. Patients with high risk of MRSA colonization were determined a priori and MRSA surveillance culture was obtained. We used these previously accumulated 55 clinical MRSA isolates to compare MIC results in Etest (SYSMEX ® bioMerieux Co.Ltd.) and BMD methods (BD Phoenix®, Microscan ®(SIEMENS, CA, USA), Eiken ® (Eiken Chemical Co., Ltd. Japan), VITEK 2 system ® (bioMérieux, Inc)). MIC results of VCM, TEIC, LZD, DPT, ABK and QPR/DPR were evaluated. The statistical analysis was performed using Wilcoxon signed rank test with continuity correction.

■ Results: There was constant and significant discrepancy of MIC results in between Etest and BMD methods for MRSA isolates. The averages of VCM MIC were 1.86 μg/ml and 0.74 μg/ml in Etest (SYSMEX ®) and in BD Phoenix ®, respectively. In TEIC, they were 1.86μg/ml and 0.60μg/ml, and in LZD they were 2.55μg/ml and 1.18μg/ml. The Wilcoxon signed rank test showed p-values between Etest and BD Phoenix ® were all less than 0.001 in VCM, TEIC and LZD, respectively.

■ Conclusion: Our study demonstrated the significant and constant discrepancy between Etest and BMD methods. The MIC results with Etest were significantly higher compared to those with BMD methods.

Background

■ Background: It has been speculated that there exists discrepancy of MRSA MIC results between variable methods. The association between higher MRSA MIC and worse clinical outcomes has been previously reported and has become a major clinical concern in managing MRSA infections.
■ It is clinically essential to investigate whether discrepancy exists between different MIC measurements, especially between Etest and BMD methods.

Methods

■ Periods: From November, 2009 to March, 2011.
■ Places: Two metropolitan tertiary Emergency Departments in Japan.
■ Study design: A prospective observational study.
■ Patients with high risk of MRSA colonization were determined a priori and MRSA surveillance culture was obtained.
■ We used previously accumulated 55 clinical MRSA isolates to compare MIC results in Etest (SYSMEX ® bioMerieux Co.Ltd.) and micro dilution test (BD Phoenix®, Microscan ®(SIEMENS, CA, USA), Eiken ® (Eiken Chemical Co., Ltd. Japan), VITEK 2 system ® (bioMérieux, Inc)). MIC results of VCM, TEIC, LZD, DPT, ABK and QPR/DPR were evaluated.
■ Statistical analysis: Wilcoxon signed rank test with continuity correction.

Results

■ A total of 55 MRSA colonization isolates were studied.

Table 1. Comparison of VCM MICs in MRSA

VCM MIC (μg/ml)	No. of isolates (%) with MIC (μg/ml) determined by:					
	Etest	BMD methods				
		Phoenix®	Eiken®	MicroScan® (turbidity)	MicroScan® (prompt)	Vitek2®
0.5	0(0)	29(52.7)	8(14.5)	0(0)	1(1.8)	7(12.7)
1	2(3.6)	26(47.3)	45(81.8)	24(43.6)	23(41.8)	45(81.8)
1.5	12(21.8)	-	-	-	-	-
2	41(74.5)	0(0)	2(3.6)	27(49.1)	30(54.5)	3(5.5)
4	0(0)	0(0)	0(0)	4(7.3)	1(1.8)	0(0)
Modal MIC (μg/ml)	2	0.5	1	2	2	1
MIC average (μg/ml)	1.86	0.74	0.96	1.70	1.58	0.99

Table 2. Comparison of TEIC MICs in MRSA

TEIC MIC (μg/ml)	No. of isolates (%) with MIC (μg/ml) determined by:					
	Etest	BMD methods				
		Phoenix®	Eiken®	MicroScan® (turbidity)	MicroScan® (prompt)	Vitek2®
<=0.5	0(0)	48(87.3)	36(65.5)	-	-	54(98.2)
0.75	2(3.6)	-	-	-	-	-
1	9(16.4)	5(9.1)	10(18.2)	-	-	1(1.8)
1.5	11(20.0)	-	-	-	-	-
2	26(47.3)	2(3.6)	6(10.9)	(<=2) 55(100)	(<=2) 53(96.4)	0(0)
3	5(9.1)	-	-	-	-	-
4	2(3.6)	0(0)	3(5.5)	0(0)	2(3.6)	0(0)
Modal MIC (μg/ml)	2	0.5	0.5	<=2	<=2	0.5
MIC average (μg/ml)	1.86	0.60	0.94	2.00	2.07	0.51

Table 3. Comparison of LZD MICs in MRSA

LZD MIC (μg/ml)	No. of isolates (%) with MIC (μg/ml) determined by:					
	Etest	BMD methods				
		Phoenix®	Eiken®	MicroScan® (turbidity)	MicroScan® (prompt)	Vitek2®
<=0.5	-	2(3.6)	-	-	-	-
1	0(0)	42(76.4)	19(34.5)	2(3.6)	3(5.5)	18(32.7)
1.5	4(7.3)	-	-	-	-	-
2	23(41.8)	11(20.0)	34(61.8)	50(90.9)	43(78.2)	35(63.6)
3	24(43.6)	-	-	-	-	-
4	4(7.3)	0(0)	2(3.6)	3(5.5)	9(16.4)	2(3.6)
Modal MIC (μg/ml)	3	1	2	2	2	2
MIC average(μg/ml)	2.55	1.18	1.70	2.07	2.27	1.50

Figure 2: Comparison of VCM MIC by each method

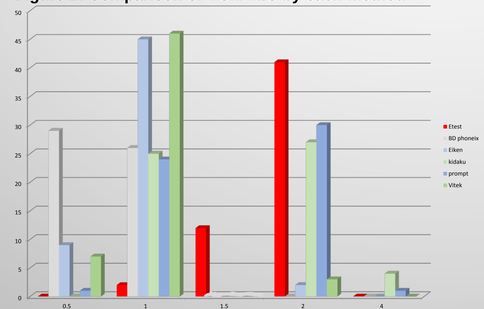


Figure 1-A. VCM: Number of isolates, Etest vs. Phoenix®

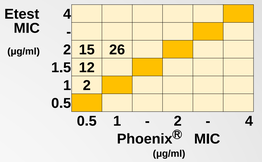


Figure 1-B. VCM: Number of isolates, Etest vs. Eiken®

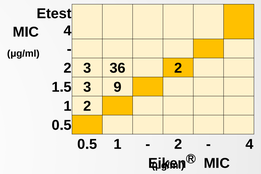


Figure 1-C. VCM: Number of isolates, Etest vs. Vitek®

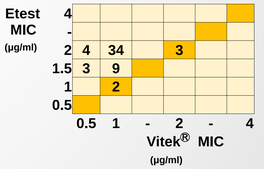


Figure 1-D. VCM: Number of isolates Etest vs. MicroScan®(turbidity)

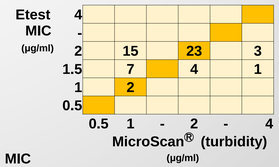
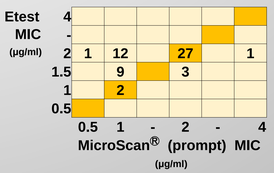


Figure 1-E. VCM: Number of isolates, Etest vs. MicroScan®(prompt)



Discussions

■ Higher MIC is known to be associated with worse clinical outcome[1,2] . In these studies, MIC was measured with Etest.
■ It has been speculated that there may be a discrepancy of MIC results among different measurement methods.
■ Previous studies suggested that MIC measured with Etest tends to be higher than BMD methods[3].
■ Our study showed there is a tendency of higher MIC with Etest, which means Etest may overestimates MIC, besides BMD may underestimates MIC.
■ Therapeutic recommendations/guidelines may need to specify which MIC measurement method should be used[4].
■ It is recommended that clinicians take the MIC testing methods into consideration in choosing antimicrobial chemotherapy for MRSA because there may be discrepancy between Etest and BMD methods.
■ Limitations: ①This study was conducted at only two tertiary Emergency Departments, ②Only MRSA colonies which were obtained by nasal screening were used.

Conclusions

■ Our study demonstrated significant and constant discrepancy of anti-MRSA antibiotics MIC between by the Etest and BMD methods.

■ The MIC results measured by Etest were significantly higher compared to those by BMD methods. Careful interpretation should be made especially when MRSA MIC were measured with BMD methods so that clinicians do not falsely underestimate MRSA MIC.

References

1. *Influence of vancomycin minimum inhibitory concentration on the treatment of methicillin-resistant Staphylococcus aureus bacteremia. Clin Infect Dis. 2008 Jan 15;46(2):193-200.*
2. *Clinical outcomes and nephrotoxicity associated with vancomycin trough concentrations during treatment of deep-seated infections. Expert Opin Drug Saf. 2010 Jan;9(1):9-14.*
3. *Determination of vancomycin and daptomycin MICs by different testing methods for methicillin-resistant Staphylococcus aureus. J Clin Microbiol. 2011 Jun;49(6):2272-3.*
4. *Vancomycin MICs for methicillin-resistant Staphylococcus aureus isolates differ based upon the susceptibility test method used. Antimicrob Agents Chemother. 2008 Dec;52(12):4528.*