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Original Article

INCREASED VANCOMYCIN MINIMUM INHIBITORY CONCENTRATION (MIC) AMONG MRSA ISOLATES IN A TERTIARY CARE HOSPITAL

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Abstract :

Introduction : Methicillin Resistant Staphylococcus aureus (MRSA) is not only an important nosocomial pathogen but also an incipient community pathogen in many geographical areas. Recommended therapeutic agent for treatment of MRSA infections are glycopeptides, in particular vancomycin. The distribution of vancomycin Minimum Inhibitory Concentration (MIC) values among MRSA isolates in our hospital is unknown. We conducted this study to Determine the distribution of vancomycin MIC values among MRSA isolates from clinical samples in our hospital.

Materials & Methods : Fifty six MRSA isolates were included in the study. These isolates were obtained from different clinical samples received in the department of Microbiology over a period of six months from august 2012 to January 2013. Screening for MRSA was done by disc diffusion method using Cefoxitin disc. Determination of vancomycin MIC of all the isolates was done by macro broth dilution method.

Results : All 56 isolates were sensitive to vancomycin. Out of the 56 isolates tested, 25 (44.64%) and 12 (21.4%) had Vancomycin MIC of 1µg/ml and 2 µg/ml respectively.

Conclusion : The high vancomycin MIC values observed among our strains are a cause of concern, as this may have an impact on the success of treatment with vancomycin.

Keywords : Methicillin Resistant Staphylococcus aureus, vancomycin MIC.

Introduction :

Methicillin Resistant Staphylococcus aureus (MRSA) is not only an important nosocomial pathogen but also an incipient community pathogen in many geographical areas.[1] MRSA isolates are usually resistant to multiple classes of antimicrobial agents including macrolides, lincosamides, tetracyclines, fluroquinolones and aminoglycosides.[2] Recommended therapeutic agent for treatment of MRSA infections are glycopeptides, in particular vancomycin.[3]

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The glycopeptide antibiotic, vancomycin, was first released in 1958. For many years there was no indication that vancomycin resistance in Staphylococcus aureus was likely to be a problem. Initial reports of reduced vancomycin susceptibility in clinical isolates of Staphylococcus aureus, from Japan in 1997, generated significant concern in the medical community. The first clinical isolate of Vancomycin Resistant Staphylococcus aureus (VRSA) was reported from The United States in 2002.[4] Strains of Vancomycin Intermediate Staphylococcus aureus (VISA) have been reported from Japan, France, The UK, Germany and India.[1]

The distribution of vancomycin Minimum Inhibitory Concentration (MIC) values among MRSA isolates in our hospital is unknown. We conducted this study to determine the distribution of vancomycin MIC values among MRSA isolates from clinical samples in our hospital.

Materials and methods :

Fifty six MRSA isolates were included in the study. These isolates were obtained from different clinical samples received in the department of Microbiology over a period of six months from august 2012 to January 2013. All the isolates were identified by conventional methods[5]. Screening for MRSA was done by disc diffusion method using Cefoxitin disc (30µg). [6]

In view of the fact that VISA is detected by dilution based susceptibility test methods, Determination of MIC of all the isolates was done by macro broth dilution method. Vancomycin stock solution, to a final concentration of 10,000µg/ml, was prepared in sterile distilled water. Five hundred micro liters of two fold dilution of vancomycin, ranging from 0.5µg/ml- 256µg/ml was prepared in cation adjusted Mueller Hinton broth. Five hundred micro liters of inoculum containing 10^5CFU/ml of actively multiplying MRSA was added to each tube and incubated at 37^0 C for 24 hours. The final concentration of vancomycin is half the original concentration in each tube (0.25-128µg/ml). The lowest concentration of vancomycin that inhibited growth of MRSA, as detected by lack of visual turbidity, matching with negative control included with the test was taken as the MIC and recorded in microgram/milliliter.[7] The results were interpreted according to CLSI guidelines as shown in table 1.[6]

Results :

A total of 56 isolates of MRSA were obtained from various clinical samples. Pus and wound swabs accounted for majority of the isolates (48.21 %), followed by blood (44.64%) and urine (7.14%) samples.

The vancomycin MIC of the MRSA isolates is shown in table 2

All 56 isolates were sensitive to vancomycin. Out of the 56 isolates tested, 25 (44.64%) and 12 (21.4%) had vancomycin MIC of 1µg/ml and 2 µg/ml respectively.

Discussion :

Vancomycin is one of the very few antibiotics available for the treatment of infections caused by MRSA. After the emergence of Vancomycin Resistant Enterococci (VRE) in the 1980's, significant concerns existed with regard to the potential for large outbreaks of VRSA, due to acquisition of *VanA* gene from Enterococci. However, to date, only eleven cases of VRSA have been reported, nine from the USA and one each from India and Iran. After the first reports of VISA and hetero resistant VISA (hVISA) from Japan, it did not take long for this strain phenotype to be recognized around the world. They have now been reported from various countries including the USA, Australia, South Korea, India and others.[4]

In our study, no VRSA or VISA strains were found. However, we did not look for hVISA, as there is currently no standard guideline for the accurate detection of hVISA.[4]

Although VRSA and VISA strains are not very common among clinical isolates of Staphylococcus aureus, there is a great concern about the emergence of Staphylococcus aureus with reduced susceptibility to vancomycin. Furthermore, analysis of clinical and microbiological data from patients for whom vancomycin therapy failed, suggest that the increasing vancomycin MIC's, even those which are well within the susceptible range, might be a significant risk for treatment failure.[8]

Increasing vancomycin MIC within the susceptible range was associated with a significant risk of vancomycin treatment failure in MRSA bacteraemia.[9] Higher clinical failure in MRSA bacteraemia was noted with vancomycin MIC $\geq$1.5 µg/ml. [10,11]

In our study, 21.42% of MRSA had MIC values of 2µg/ml and a MIC of 1 µg/ml in 44.64% of isolates. Even though we did not correlate the clinical outcome of treatment of MRSA infection, the possibility of treatment failure, if treated with Vancomycin, cannot be ruled out and is an area of concern.

Conclusion

The high vancomycin MIC values observed among our strains are a cause of concern, as this might have an impact on the success of treatment with vancomycin.

Table 1: Vancomycin MIC interpretation criteria

Vancomycin MIC in µg/ml	Interpretation
≤ 2	Vancomycin Sensitive Staphylococcus aureus (VSSA)
4-8	Vancomycin intermediate Staphylococcus aureus (VISA)
≥16	Vancomycin resistant Staphylococcus aureus (VRSA)

Table 2: Distribution of Vancomycin MIC

Concentration of Vancomycin (µg/ml)	No. of isolates (n=56)	Percentage
<0.25	1	1.79
0.5	18	32.14
1	25	44.64
2	12	21.42

References :

1. Tiwari HK, Sen MR. Emergence of Vancomycin resistant Staphylococcus aureus (VRSA) from a tertiary care hospital from northern part of India . BMC Infect dis .2006; 6: 156-162.
2. Coyle MB. In: Manual of antimicrobial susceptibility testing. American Society of Microbiology, Washington 2005:101-115.
3. Dhanalakshmi TA, Umapathy BL, Mohan DR. Prevalence of methicillin, Vancomycin and multidrug resistance among Staphylococcus aureus. Journal of Clinical and Diagnostic Resarch.2012; 6(6): 974-977.
4. Howden BP, Davies JK, Johnson PDR, Stinear TP, Grayson ML. Reduced Vancomycin susceptibility in Staphylococcus aureus, including Vancomycin –intermediate and heterogenous Vancomycin-intermediate strains: resistance mechanisms, laboratory detection and clinical implication. Clin Microbiol Rev. 2010; 23(1):99-139.
5. Collee JG, Fraser AG, Marimon BP, Simmons A. In: Mackie and McCartney Practical medical microbiology.14 ed. Elsevier publication, New Delhi 2006:245-261.
6. Clinical and Laboratory Standards Institute: Performance standards for antimicrobial susceptibility testing; seventeenth informational supplement M 100-S17. Approved standard. Wayne, PA, USA, 2007.
7. Schwalbe R, Steele-Moore L, Godwin AC.In: Antimicrobial susceptibility testing protocols.CRC press, New York 2007:75-80.
8. Ahmad N, Nawi S, Rajasekaran G, Maning N, Aziz MN, Husin A et al. Increased vancomycin inhibitory concentration among Staphylococus aureus isolates in Malaysia. J Med Microbiol. 2010; 59:1530-1532.
9. Sakoulas G, Moise-Broder PA, Schentag J, Forest A, Mollering RC, Eliopoulos GM. Relationship of MIC and bactericidal activity to efficacy of vancomycin for treatment of methicillin-resistant Staphylococcus aureus bacteremia. J Clin Microbiol. 2004; 42(6):2398-402.
10. Lodise TP, Graves J, Evans A, Graffunder E, Helmecke M, Lomaestro BM et al. Relationship between Vancomycin MIC and Failure among Patients with Methicillin-Resistant Staphylococcus aureus Bacteremia Treated with Vancomycin. Antimicrob Agents Chemother. 2008; 52(9): 3315–3320.
11. Sariano A, Marco F, Martinez JA, Pisos E, Almela M, Dimova VP et al. Influence of Vancomycin minimum inhibitory concentration on the treatment of methicillin resistant Staphylococcus aureus bacteraemia. Clin Infect Dis.2008; 46: 193-200.