Increased Vancomycin Resistance associated with decreased methicillin resistance in *staphylococci*

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ABSTRACT

The treatment of staphylococcal infections has become problematic due to the emergence of resistance to methicillin, vancomycin and other antibiotics. Growing prevalence of MRSA has led to increased use of vancomycin which led to decreased susceptibility to vancomycin. Hence the present study was undertaken to determine methicillin and vancomycin resistance in *staphylococci* and to know whether vancomycin resistance is associated with methicillin resistance in *staphylococci* isolates in Medchal, A.P, India. Prospective study of 100 *Staphylococcus aureus* isolates from various clinical samples were studied for a period of one year. Screening for methicillin resistance and vancomycin resistance in these isolates was done as per CLSI guidelines. Vancomycin MIC’s of the isolates was determined. Vancomycin resistance in MRSA and non MRSA isolates was determined. 15% of the isolates were found to be methicillin resistant by cefoxitin disc diffusion method, 14% by oxacillin agar method and 12% by oxacillin disc diffusion method. Both Vancomycin agar screen and agar dilution method revealed 11% isolation of VISA. 50% of the isolates showed vancomycin MIC’s of 1-2 mg/ml. The non MRSA isolated showed higher percentage of VISA when compared to MRSA. Increased vancomycin MIC’s in staphylococcal isolates calls for limiting use of vancomycin only in situations where it is deemed appropriate by current CDC guidelines. Raised vancomycin MIC’s in all staphylococcal isolates and increased vancomycin resistance in non MRSA isolates when compared to MRSA isolates suggests misuse of this antibiotic not only in the treatment of MRSA isolates but in all staphylococcal infections.

Keywords: *Staphylococcus*, Methicillin resistance, Vancomycin resistance.

INTRODUCTION

*Staphylococcus* is one of the most common pathogens causing a variety of infections ranging from relatively benign skin infections to lifethreatening systemic illness. The treatment of *Staphylococcus aureus* infections has become problematic because of the emergence of resistance to Methicillin, Vancomycin and other antibiotics.[1] MRSA is a well recognised cause of nosocomial infection worldwide and these infections are responsible for several difficult to treat infections and impose a high burden on healthcare resources.[2, 3] Vancomycin has been considered the mainstay treatment of infections caused by methicillin resistant *staphylococcus aureus*. [4] The reports of the emergence of vancomycin intermediate and vancomycin resistant *Staphylococcus aureus* from various parts of the world have been of a great clinical concern.[5] Studies reveal that the growing prevalence of Methicillin resistant *Staphylococcus aureus* has led to increased use of vancomycin. This in turn has led to decreased susceptibility to vancomycin.[6] Hence the present study was undertaken to determine the current status of vancomycin susceptibility i.e for the possible presence of vancomycin resistant and vancomycin intermediate strains of *Staphylococcus aureus* in our hospital set up and also to know whether vancomycin resistance is associated with methicillin resistance in *staphylococcus aureus* isolates in our area.
MATERIALS AND METHODS

A total of 100 Staphylococcus aureus were isolated from various clinical samples during a period of one year from September 2011 – August 2012. Permission was obtained from Institute’s research council. The isolates were identified as staphylococcus by standard biochemical reactions. The screening for methicillin resistance in these isolates was done by oxacillin disc diffusion method, cefoxitin disc diffusion method and by inoculating the Staphylococcus aureus isolates on oxacillin screen agar i.e. Mueller hinton agar with 4 % NaCl +6 mic. g/ml oxacillin. Staphylococcus aureus ATCC 25923 strain was used as the control strain. Screening for Vancomycin intermediate staphylococcus aureus (VISA) and Vancomycin resistant staphylococcus aureus (VRSA) was done by vancomycin screen agar method using MHA with 5 mic.g/ml vancomycin obtained from Hi Media Mumbai, India. Staphylococcus aureus ATCC 29213 and 43300 strains were used as control strains. The vancomycin MIC’s of these isolates were determined by agar dilution method as per CLSI guidelines.

RESULTS

Out of the 100 staphylococcal isolates analysed, 15 % were found to be methicillin resistant by cefoxitin disc diffusion method, 14 % by oxacillin agar screen method and 12 % by oxacillin disc diffusion method. On vancomycin agar screen, 11 % staphylococcus aureus isolates were vancomycin intermediate resistant. By agar dilution also, the percentage of vancomycin intermediate resistant staphylococcus aureus (VISA) was 11 % and no vancomycin resistant staphylococcus aureus (VRSA) was detected (0 %). 50 % of the staphylococcal isolates showed vancomycin MIC of 1 -2 mic.g/ml. Among the MRSA isolates, 50 % of the isolates were VISA. Among the Non MRSA isolates, 82 % were VISA.

DISCUSSION

100 Staphylococcal isolates were analysed for Methicillin resistance and Vancomycin resistance.

There was 15 % isolation of MRSA by the cefoxitin disc diffusion test, 14 % isolation by Oxacillin agar screen test and 12 % isolation by Oxacillin disc diffusion method which was in agreement with another study [7] which showed methicillin resistance of 64 % by cefoxitin disc diffusion test, 60 % by oxacillin agar screen method and 56 % by oxacillin disc diffusion method. The increased percentage of MRSA isolation by cefoxitin method could be because oxacillin agar screen method does not detect borderline resistant strains and oxacillin disc diffusion method may be affected by various components of Mueller Hinton agar. Temperature and duration of incubation. Thus cefoxitin disc method is a reliable method and can be used as a sole method for detection of MRSA.

When the vancomycin resistance was analysed, in our study the isolation of VISA was 11 % and of VRSA was 0 %. by both vancomycin agar screen method and agar dilution method i.e there was 100 % concordance between the vancomycin agar screen method and agar dilution method. This shows that vancomycin screen agar showed 100 % specificity and 100 % negative predictive value for the detection of vancomycin resistance. Another study [8] also revealed no difference in the detection of vancomycin resistance by vancomycin agar screen and agar dilution methods which showed an isolation of 0 % VISA and 0 % VRSA by both these methods. This suggests that vancomycin agar screen test can be used as a reliable screening test for the detection of vancomycin resistance in staphylococcal isolates in rural hospitals were facilities are not available to perform both these tests.

In our study, 50 % of the staphylococcal isolates had a vancomycin MIC of 1-2 mic. g/ml which suggests heteroresistance in these isolates. Similarly increased vancomycin MIC’s were also observed in other studies [9,10,11]. MIC’s of vancomycin of 1-2 mic. g/ml could be associated with inferior vancomycin treatment outcomes in Pneumonias and bacteremias. Therefore vancomycin should be limited to only situations specified by the current CDC guidelines.

The comparative study of Methicillin and Vancomycin resistance revealed that Vancomycin resistance was low in MRSA isolates (54.5%) than in the nonMRSA isolates (82 %). Another study also showed that vancomycin resistance was less (0 %) in isolates of MRSA [12]. This supports the invitro finding that expression of the mutated PBP 2A is downregulated in vancomycin resistant isolates.

CONCLUSION

Prevalence of MRSA was 15 %. Prevalence of VISA was 11 %. Prevalence of VRSA was 0 %. Cefoxitin method is a reliable method and can be used as a sole method for detection of MRSA. Vancomycin screen agar method for detection of vancomycin resistance showed 100 % specificity & 100 % negative predictive value. Vancomycin
agar screen method can be used without agar dilution for detecting vancomycin resistance in staphylococcal isolates in rural hospitals where facilities are not available. Increased vancomycin MIC’s in Staphylococcal isolates calls for limiting use of vancomycin only to situations where it is deemed appropriate by current CDC guidelines. Vancomycin resistance being lower in MRSA isolates than in the non-MRSA isolates and raised MIC’s for vancomycin in our area suggests misuse of this antibiotic not only in the treatment of MRSA infections but also in the treatment of all staphylococcal infections.

REFERENCES