EVALUATION OF VANCOMYCIN MIC CREEP PHENOMENON IN MRSA ISOLATES FROM CLINICAL SAMPLES

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DOI: http://dx.doi.org/10.24327/ijrsr.2020.1103.5181

ABSTRACT

Background- Methicillin resistant Staphylococcus aureus (MRSA) is an important cause of nosocomial and community acquired infections. Increased use of vancomycin which has a cornerstone for MRSA treatment has resulted in the emergence of MRSA with reduced susceptibility to vancomycin with high MIC values in susceptible range, phenomenon referred to as MIC creep.[2-4]. Patients infected with such MRSA isolates experience poor clinical outcome, delayed response to therapy, increased relapse rates, increased mortality rates.[8-10].

Objectives- Study was undertaken to evaluate local status of Vancomycin MIC in our setup & presence of Vancomycin MIC creep phenomenon among MRSA isolates from clinical specimens

Methods- The prospective study was conducted over a period of 6 months from January 2019 to June 2019. Isolates identified as Staphylococcus aureus using routine bacteriological procedures were labelled as MRSA if they are cefoxitin resistant & further tested for different antimicrobials as per CLSI guidelines.[11]. Vancomycin MIC value was determined using Epsilometer test. Interpretation of results was done as per CLSI guidelines.

Results- Of total 90 isolates studied, Vancomycin MICs were 0.5, 0.6, 0.75, 1, 1.5, 1.75, 2 mcg/ml for 1, 1, 20, 24, 32, 5, 7 isolates respectively. No isolate showed MIC >2 mcg/ml.

Conclusion- The phenomenon consistent with Vancomycin MIC creep was found in our study, which alarms us about possibility of getting increasing number of MRSA isolates with intermediate value for Vancomycin susceptibility &/or isolates resistant to Vancomycin in near future. Strict adherence to local antibiogram pattern along with rational dosing & close monitoring of patients on Vancomycin therapy is recommended.

INTRODUCTION

Staphylococcus aureus is one of the most common pathogens that leads to severe infections, including skin and soft tissue infections, pneumonia, bacteremia, and endocarditis, either in community settings or hospitals. [1] Methicillin resistant Staphylococcus aureus (MRSA) is an important cause of nosocomial and community acquired infections. Vancomycin has been the cornerstone in the treatment of patients with serious methicillin-resistant Staphylococcus aureus (MRSA) infections. Increased use of vancomycin has resulted in the emergence of MRSA with reduced susceptibility to vancomycin with high MIC values in susceptible range, phenomenon referred to as MIC creep.[2-4]. Currently, there is a growing concern about MRSA with reduced susceptibility to vancomycin.[5,6]. Many reports have stated discrepancies between in vitro susceptibility test results for vancomycin and clinical outcomes of MRSA infections treated with it [7]. The use of vancomycin has been increasing since the mid-1980s, which results in the emergence of MRSA with reduced susceptibility to vancomycin.[3]. The emergence of MRSA with reduced vancomycin susceptibility has become a worldwide concern. Patients infected with MRSA isolates which exhibit Vancomycin MICs creep, may experience poor clinical outcome, delayed response to therapy, increased relapse rates, increased mortality rates.[8-10]. However, Vancomycin treatment failure is also common even in presence of Vancomycin susceptible MRSA isolates in vitro.

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Present study was undertaken with the aim of evaluating local status of Vancomycin MIC in our setup & presence of Vancomycin MIC creep phenomenon among MRSA isolates from clinical specimens.

**MATERIAL AND METHODS**

The prospective study was conducted over a period of 6 months from January 2019 to June 2019, in a rural teaching hospital in Pune.

**Selection of cases**

Only one isolate per patient was included in this study. For patients with more than one isolate, only the first isolate was tested.

All nonrepetitive MRSA isolates from different clinical specimens, received in the Microbiology laboratory during the study period were included in the study.

**Methodology**

All isolates were identified as Staphylococcus aureus using routine bacteriological procedures (Gram's stain microscopic examination, Catalase test and coagulase test, Mannitol fermentation test).

Isolates resistant to cefoxitin (30 mcg) were labelled as MRSA as per CLSI guidelines. MRSA isolates were subjected to antimicrobial susceptibility testing by the disk diffusion method for susceptibility to a panel of antibiotics using Mueller-Hinton agar (Himedia) medium. The antibiotic discs (Himedia) containing the following antibiotic concentrations (in µg) as per CLSI [11] guidelines were used: ampicillin (10), cefoxitin (30), gentamicin (10), erythromycin (15), ciprofloxacin (5), moxifloxacin (5) levofloxacin (5) clindamycin (2), trimethoprim-sulphamethoxazole (1.25/23.75), and linezolid (30), tetracycline (30). All plates were incubated at 350C for 24 hours.

**Epsilometer test (E test) for Vancomycin MIC determination**

Commercially available Vancomycin E-Test (Epsilometer) strips (Himedia) were used. These consisted of a strip of filter paper impregnated with a defined gradient of, two-fold dilutions of the antimicrobial agent being tested. The strips were applied to an agar plate on which a test bacterium has been lawn-inoculated according to the manufacturer’s instructions. After incubation, the MIC value for Vancomycin was interpreted as the zone of inhibition that corresponds to a concentration gradient on the E test strips, as per the manufacturer’s instructionssusceptibility breakpoint for Vancomycin was 2 mcg/ml [11].

**RESULTS**

Total 90 isolates were included in this study. Among the various samples, MRSA was isolated most commonly from pus (51) followed by Urine (23), Blood (9), followed by Miscellaneous samples (7) which included swabs & catheter tip. Most common age from which MRSA was isolated was 11-30 years (33 isolates) followed by age group of 51-70 years (25 isolates) followed by age group of 31-50 years (21 isolates) and with least no of cases in the age group of 71-90 years (11 isolates).

Vancomycin MICs were 0.5, 0.6, 0.75, 1, 1.5, 1.75, 2 mcg/ml for 1, 1, 20, 24, 32, 5 & 7 isolates respectively. (Fig.1)

Maximum number of isolates showed Vancomycin MIC value of 1.5 mcg/ml. 7 isolates showed MIC value of 2 mcg/ml. No isolate showed MIC value of >2 mcg/ml.

**DISCUSSION**

In this study, we included 90 isolates of MRSA. More number of the MRSA were isolated from male patients (51 out 90 i.e.56.66%) as compared to female patients (39 out of 90 i.e. 43.33%). MRSA was isolated from samples from IPD (90%) & ICU (10%).

We isolated MRSA from pus (56.66%) followed by urine (25.55%), blood (10%) & miscellaneous specimens (7.77%) including swabs, catheter tips etc.

In our study, no MRSA isolate was with MIC >2 mcg/ml. Lowest observed MIC value was 0.5 mcg/ml in only one isolate from a urine samples from a female patient. Overall MIC values appear to increase during the study period.

Over past few years, MRSA has been one of the most common causes of serious hospital- and community-acquired infections. Vancomycin has always been the primary antibiotic of choice for the treatment of serious MRSA infections. Although new anti-staphylococcal antibiotics such as linezolid and daptomycin have been developed recently, vancomycin remains as the only widespread therapeutic preference due to new drugs' high cost and the absence of large clinical trials.[12]

In this study, we observed an increase in the percentage of isolates with MIC value of > 1 mcg/mL with only one isolate with MIC of 0.5 mcg/ml; many other studies showed similar results. In a study by Golan et al.,[13] authors reported a statistically significant increase in vancomycin MIC from 2001-2005 in a regional medical centre in the United States. Study by Wang et al. reported an MIC increase in both MRSA and MSSA. [14] In Europe, very gradual increases in vancomycin MICs have been documented from France.[15] Many studies reported in past have produced conflicting results which did not report phenomenon of MIC creep.[16-18]
In a study done by Afzal Hussein, in 2014 to 2016, vancomycin MIC creep phenomenon was observed.[19]. The study done by Chang W et al, in 2010, in China, also showed phenomenon of Vancomycin MIC creep correlating with the results of our study.[4]

While the results from few studies did not show any such creeping of Vancomycin MIC.[19-21]

CONCLUSION

We observed gradual increase in number of isolates with increased Vancomycin MIC in our study, the phenomenon consistent with Vancomycin MIC creep. The apparent increase in Vancomycin MIC among MRSA, observed in recent years, can represent the first step towards the emergence of fully Vancomycin resistant isolates in near future. Though unclear, the cause for Vancomycin MIC creep phenomenon might be the overuse of drug along with improper dosing schedule. Hence, before starting empiric Vancomycin, it is necessary to take into account the institutional antibiogram pattern. Also, rational dosing with close monitoring & strict follow up of a patient receiving Vancomycin therapy will help to prevent treatment failure with this key drug & emergence of complete drug resistance.

Limitations

Number of isolates included in our study & also the study duration was small which may be problem for statistical calculations. We have tested MIC by Epsilometer (E strip) method. According to few studies, microbroth dilution testing & E test strip method to calculate Vancomycin MICs may give two fold different results.[22] We did not have data on antibiotic use in our hospital which would clarify the relationship between antibiotic use and changes in MIC pattern. The impact of vancomycin MIC creep on clinical outcome remain unexplored.

References


How to cite this article:
DOI: http://dx.doi.org/10.24327/ijrsr.2020.1103.5181

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