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Determination of Vancomycin and Linezolid Resistance among Staphylococcal Isolates from a Tertiary Care Hospital

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A B S T R A C T

Methicillin resistant *Staphylococcus aureus* (MRSA) has emerged as one of the commonest causes of hospital acquired infections. Vancomycin is the drug of choice for the treatment of MRSA. Increase in Minimum inhibitory concentration (MIC) of Vancomycin has been observed in both Methicillin sensitive and resistant *Staphylococcal* isolates. In critically ill patients, Vancomycin has become a poor therapeutic antibiotic whereas; Linezolid has emerged as an alternative drug in treating such patients. This study was undertaken to determine the sensitivity pattern among clinical isolates of *Staphylococcus aureus (S. aureus)* to Vancomycin and Linezolid, in order to formulate a better treatment.100 *S. aureus*were isolated from various clinical specimens. Antibiotic sensitivity testing was performed by Kirby Bauer disc diffusion method and MICs of Vancomycin and Linezolid were determined by E-test following CLSI guidelines. Out of 100 *S. aureus* isolated, 68 were MRSA strains. Among 68 strains of MRSA for which MIC levels of Vancomycin 4 µg/ml, 2µg/ml and 1 µg/ml were 4, 27, and 37 respectively. Similarly, out of total MRSA strains MIC levels of Linezolid 4 µg/ml, 2µg/ml and 1 µg/ml were 1, 25, and 42 respectively. All 100 strains showed similar in-vitro efficacy for Vancomycin and Linezolid by Kirby Bauer disc diffusion method, but the number of strains with higher ranges of MICs of Vancomycin were more as compared to those which had higher ranges of MICs for Linezolid. Hence we suggest that Linezolid can be used as an alternative for the treatment of MRSA.

Introduction

Methicillin resistant *Staphylococcus aureus* (MRSA) has been emerged as one of the commonest causes of hospital acquired infections globally. The infections caused by MRSA prolong the duration of hospital stay and also increases the financial burden and morbidity. Many studies have reported resistance to all antibiotics available for use against *Staphylococcus aureus*. Vancomycin has been the most authentic therapeutic agent against MRSA (Rajaduraipandi *et al.*, 2006). The condition has been further worsened by

the emergence of Vancomycin intermediate sensitive *Staphylococcus aureus* (VISA) and Vancomycin *Resistance Staphylococcus aureus* (VRSA) (Loomba P S *et al.,* 2010). Failure of Vancomycin therapy or reduction in its efficacy has been reported among MRSA strains with increased Vancomycin MICs (1-2 µg/ml or 2-4 µg/ml) (Tandel *et al.,* 2012). The newly developed Linezolid drug belongs to class of Oxazolidones is probably one of the few choices for the treatment of Vancomycin resistant MRSA (Zurenko *et al.,* 1996).

Hence, this present study was conducted to determine the in-vitro activities of Vancomycin and Linezolid against *Staphylococcus aureus* and to know the various MICs of both drugs for formulation of better empirical therapy.

Materials and Methods

This study was conducted in the Department of Microbiology, AH&RC, B.G. Nagara, between January 2020 to December 2020, with ethical committee approval. 100 *Staphylococcus aureus* strains were isolated from various clinical specimens like pus, wound swabs, blood, urine, cerebrospinal fluid, catheters, sputum, high vaginal swabs and other body fluids from patients attending OPD and admitted in different wards of AH&RC. All specimen was processed in the Central laboratory of department of Microbiology. Only non-repetitive clinical isolates were included in this study.

The collected specimens were inoculated on Blood agar, MacConkey's agar plates and they were incubated at 37°C for 24-48 hours. A presumptive identification of organism was done by colony morphology, Gram's staining, Catalase test and Slide coagulase test. A confirmation was done by tube coagulase test, growth on Mannitol salt agar, DNAse test. Antibiotic susceptibility was done by Kirby Bauer disc diffusion method. Detection of MRSA was done by using Cefoxitin disc (30 µg). The *Staphylococcus aureus* strains with Zone of diameter of <21mm were considered as MRSA and those with > 22mm as sensitive. The MICs of Vancomycin and Linezolid were detected by E-test (HiMedia laboratories) as per CLSI guidelines 2019 (Bauer *et al.,* 1966). The zone of inhibition was observed. The zone edge intersecting the graded strip at the minimum concentration of the antibiotic was interpreted as MIC (Fig1 and Fig 2). *S. aureus* ATCC 29213 was used as control strain. The MICs were interpreted in (Table 1).

Results and Discussion

A total of 100 *Staphylococcus aureus* were isolated from 250 clinical specimens from various departments. Majority of the isolates were from pus followed by blood and urine (Table.2).

Out of 100 *Staphylococcus aureus* isolates, 68 isolates were Methicillin Resistant *Staphylococcus aureus* and the remaining isolates were Methicillin sensitive. All 100 isolates were sensitive to Vancomycin (30 µg) and Linezolid (30 µg) by Kirby Bauer disc diffusion method. No Vancomycin or Linezolid Resistant *Staphylococcus aureus* strains were detected by determination of MICs using E- test. MICs between 0.5-2 µg/ml for Vancomycin and 1-4 µg/ml for Linezolid were obtained for all 100 strains isolated from clinical specimens by E-test. Table 3 and Table 4 shows number of strains with various concentrations of MICs for Vancomycin and Linezolid. Fig 3 shows comparison of MIC of Vancomycin and Linezolid.

Out of 68 MRSA strains for which MIC levels of Vancomycin 4 µg/ml, 2µg/ml and 1 µg/ml were 4, 27 and 37 respectively. Similarly, out of total MRSA strains MIC levels of Linezolid

4 µg/ml, 2µg/ml and 1 µg/ml were 1, 25, and 42 respectively (Figure 4).

In this study, *Staphylococcus aureus* was the commonest pathogen isolated from various clinical specimens especially from pus, wound swabs collected from patients with localized pyogenic and surgical wound infections admitted in surgery and orthopedic wards, which is in correlation with other studies (Gupta *et al.,* 2003).

All 100 *Staphylococcus aureus* isolates were sensitive to both Vancomycin and Linezolid by Kirby Bauer disc diffusion method, but Vancomycin showed comparatively higher MICs than Linezolid by E-test. All 68 MRSA strains were also more susceptible to Linezolid. These findings are similar with the studies of Sachin *et al.,* (2015), Srinivasan *et al.,* (2006) and Kaleem *et al.,* (2011). These studies also emphasize that Linezolid is a good therapeutic option for treatment of MRSA.

In this study, 4 *Staphylococcus aureus* strains showed MIC of 4µg/ml for Vancomycin, these strains were isolated from the patients admitted in Orthopedic (3) and Surgery wards (1). Long duration of stay in hospital and prolonged antibiotic therapy for these patients may be the cause of higher MICs and multidrug resistance. The chronic exposure for antibiotics may lead to selective antibiotic resistant strains, these findings are in correlation with other studies (Rajaduraipandi, *et al.,* 2006, Sachin, *et al.,* 2015). In the present study, all 100 *Staphylococcus aureus* were sensitive to Linezolid by Kirby Bauer disc diffusion method, which is similar to other studies (Sachin K *et al.,* 2015)

Table.1

MIC interpretation	MICs of Antibiotics in µg/ml	
	Vancomycin	Linezolid
Sensitive	≤ 2	4
Intermediate	4-8	-
Resistance	16	-

Table.2 Distribution of *Staphylococcal aureus* isolated from the various clinical specimens

Type of specimen	Number of specimen	*S.aureus* (%)
Pus	126	52
Blood	50	22
Urine	55	18
Sputum	6	3
High Vaginal swabs	6	3
CSF	2	-
Catheters and Other body fluids	5	2
Total	250	100

Table.3 MICs of *Staphylococcus aureus* for Vancomycin using E-test

Minimum Inhibitory Concentration	Vancomycin
No of Strains with MIC ≤ 4 µg/ml	4
No of Strains with MIC ≤2 µg/ml	30
No of Strains with MIC ≤1 µg/ml	66

Table.4 MICs of *Staphylococcus aureus* for Linezolid using E-test

Minimum Inhibitory Concentration	Linezolid
No of Strains with MIC ≤ 4 µg/ml	1
No of Strains with MIC ≤2 µg/ml	54
No of Strains with MIC ≤1 µg/ml	45

Fig.1 Vancomycin E-strip test showing sensitive MIC

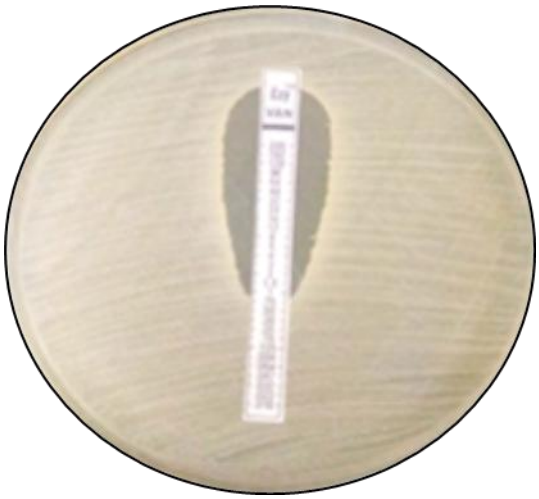


Fig.2 Linezolid E-strip test showing sensitive MIC

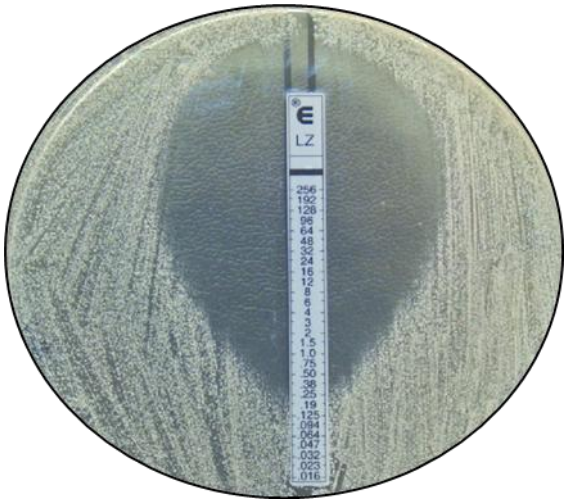


Fig.3 Comparison of MIC of Vancomycin and Linezolid

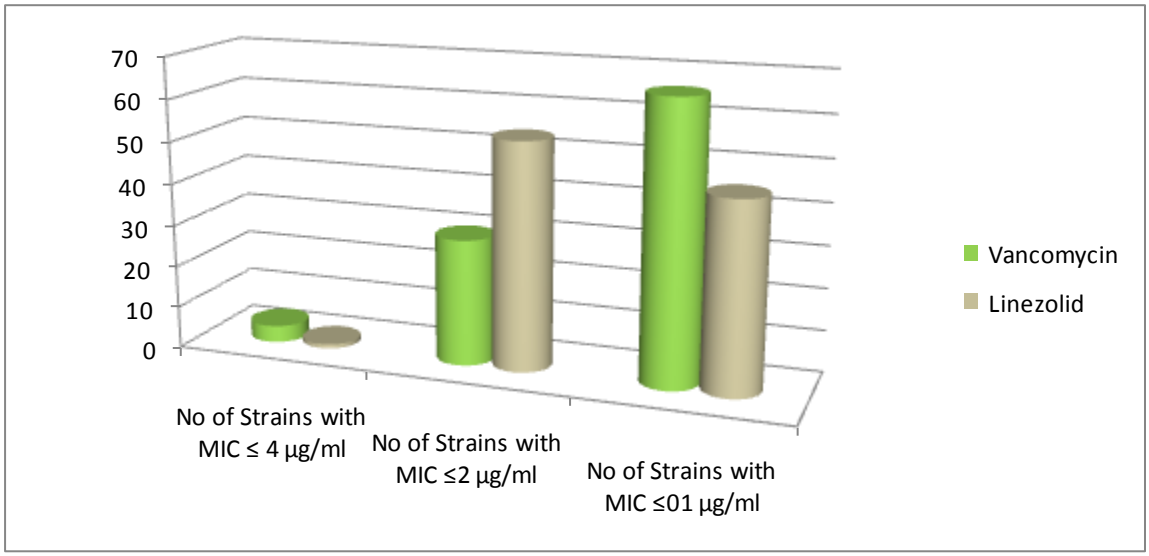
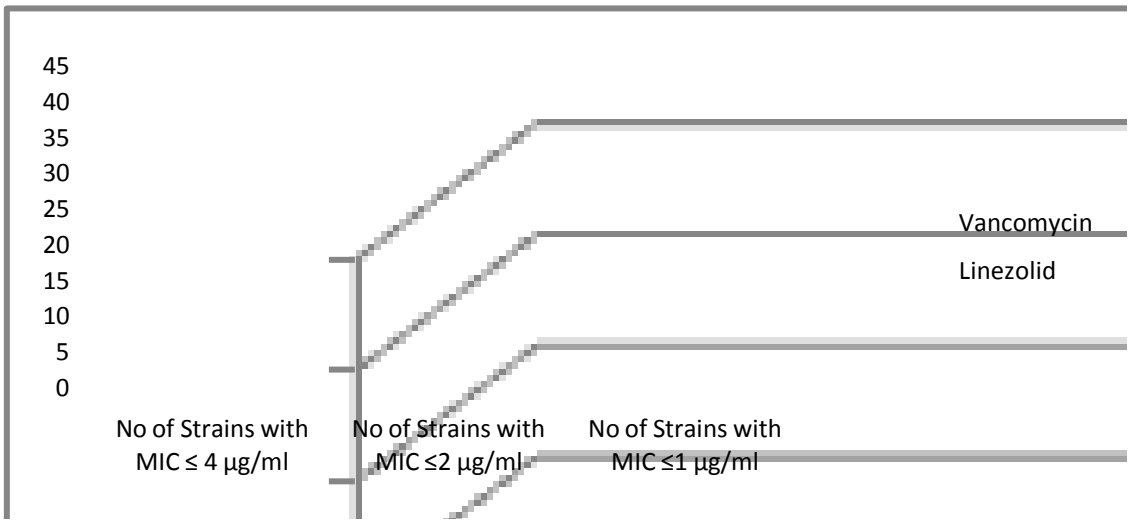


Fig.4 Comparison of MIC of Vancomycin and Linezolid for MRSA strains



Other studies have reported that *Staphylococcal* strains with upper level MICs of Vancomycin will lead to more morbidity and mortality among patients compared to those with lower MICs (Price *et al.*, 2009).

Vancomycin requires intravenous administration, monitoring of levels and rarely patients may experience some side effects. However, Linezolid is available in both intravenous and oral form. Linezolid can be rapidly and completely absorbed following oral administration; it doesn't require continuous monitoring (Shinabarger *et al.*, 1997). In one of the study for MRSA infections Linezolid showed desired, improved outcome compared Vancomycin (Howden Benjamin *et al.*, 2004).

According to this study, both Vancomycin and Linezolid have similar in-vitro efficacies for MRSA infections. Oral dosing of Linezolid leads to earlier discharge of patients and cost effective. Along with in-vitro efficacies Linezolid also have good in-vivo efficacy, which makes it an important therapeutic

alternative to Vancomycin in treatment of MRSA infections.

The indiscriminate use of antibiotics leads to emergence of resistance. As only limited drugs are available for the treatment of MRSA, a good antibiotic policy should be implemented in all tertiary care hospitals and a strict antibiotic regimen should be applied by clinicians. So we suggest that Linezolid is a good alternative therapeutic drug for the treatment of multidrug resistant *Staphylococcus aureus*.

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