Original article

TO TEST THE IN *VITRO* ACTIVITY OF VANCOMYCIN, TEICOPLANIN AND LINEZOLID AGAINST *METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS* ISOLATES FROM TERTIARY CARE HOSPITAL, KANPUR.

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ABSTRACT-

Background:- Among gram positive bacteria, *Methicillin-resistant staphylococcus aureus* is a major nosocomial pathogen worldwide. Glycopeptides such as Vancomycin are frequently the choice of antibiotics for the treatment of infections caused by *Methicillin resistant staphylococcus aureus.* For the last few years incidence of vancomycin intermediate *S. aureus* and vancomycin resistant S. aureus has been increasing in various parts of the world. **Aim:-** To test the in *vitro* activity of vancomycin, teicoplanin and linezolid against *Methicillin resistant staphylococcus aureus,* in order to help formulate a better treatment plan. **Material and method:-** The study was conducted at Rama Hospital from June 2018 to November 2018 in 400 hospitalized patients, from various clinical samples. Susceptibility was tested by E test method and disk diffusion method. **Results:-** In this study we found that out of 400 samples, 147 (35%) MRSA were isolated. Out of 147 MRSA patients, 80(54%) were males, 67(45%) were females including all age groups. The samples collected were from 83 (56.4%) pus, 47 (31.9%) blood, 17 (11.5%) CSF. All isolates were sensitive to teicoplanin and linezolid. Of the other antibiotics, amikacin showed the best in vitro activity with 81%, followed by vancomycin 76%, clindamycin & erythromycin 40%, 30% ofloxacin, 21% gentamycin, lowest sensitivity was penicillin with 11%. **Conclusion:-** In this study Linezolid and teicoplanin had similar in-vitro efficacies for all

the MRSA. So, teicoplanin and linezolid can be a good alternative for the treatment of MRSA as compared to vancomycin.

INTRODUCTION

Methicillin resistant *Staphylococcus aureus* (MRSA) has emerged as one of the commonest causes of hospital acquired infections worldwide. The infection caused by MRSA increases the length of hospital stay and it is also responsible for raising health care expenses and morbidity. Resistance to all antibiotics which are available for use against *Staphylococcus aureus* has been reported. 63.2% MRSA were found to be resistant to gentamycin, cotrimoxazole, cephalexin, erythromycin and cephotaxim [1]. Ciprofloxacin usage has already been known to be associated with development of resistance of MRSA [2]. In a past few decades, vancomycin has been established as treatment of choice for MRSA infection. But due to excessive use of this drug, emergence of MRSA strains with reduced vancomycin susceptibilities (2-4 μg/ml) has been reported in past few years.

Currently, measures which are being taken to control *Staphylococcus aureus* infections are being challenged by a large and continuing increase in the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA), the spread of highly virulent community-associated MRSA, and the emergence of *Staphylococcus aureus* with reduced susceptibilities to vancomycin and other glycopeptides [3]. The condition has been further worsened by the emergence of vancomycin intermediate sensitive *Staphylococcus aureus* (VISA)(MIC 4-8 μg/ml) and vancomycin resistant *Staphylococcus aureus* (VRSA)(MIC ≥16 μg/ml) [4]. Among MRSA strains for which vancomycin MICs are elevated (1-2 μg/ml or 2-4 μg/ml), failure of vancomycin therapy or reduction in its efficacy has been widely reported [5].

The recently developed antimicrobial drug, linezolid, is probably one of the few choices for treatment of vancomycin resistant MRSA. Linezolid is the first drug among a new class of antibiotics, the oxazolidiones. This drug, unlike other protein synthesis inhibitors, acts early in translocation by disrupting the interaction of formyl methionine t- RNA with the 50s ribosomal subunit during initiation of pre initiation complex [6].Its spectrum includes medically important gram-positive bacteria such as methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) [7,8].

Teicoplanin is an antibiotic used in the prophylaxis and treatment of serious infections caused by Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* and *Enterococcus faecalis*. It is a glycopeptide antiobiotic extracted from *Actinoplanes teichomyceticus*, with a similar spectrum of activity to vancomycin. Its mechanism of action is to inhibit bacterial cell wall synthesis. Oral teicoplanin has been demonstrated to be effective in the treatment of pseudomembranous colitis and Clostridium difficile-associated diarrhoea, with comparable efficacy to vancomycin

So, the present study aimed to determine the activities of vancomycin,Teicoplanin and Linezolid and against *Methicillin Resistant Staphylococcus aureus* so as to formulate a better empirical therapy.

MATERIAL AND METHODS

The study was conducted at Rama Hospital from June 2018 to November 2018 in 400 hospitalized patients, from various clinical samples. Susceptibility was tested by E test method and disk diffusion method.

RESULTS

In this study we found that out of 400 samples, 147 (35%) MRSA were isolated.Out of 147 MRSA patients, 80(54%) were males, 67(45%) were females including all age groups. The samples collected were from 83 (56.4%) pus, 47 (31.9%) blood, 17 (11.5%) CSF. All isolates were sensitive to teicoplanin and linezolid. Of the other antibiotics, amikacin showed the best in vitro activity with 81%, followed by vancomycin 76%, clindamycin & erythromycin 40%, 30% ofloxacin, 21% gentamycin, lowest sensitivity was penicillin with 11%.

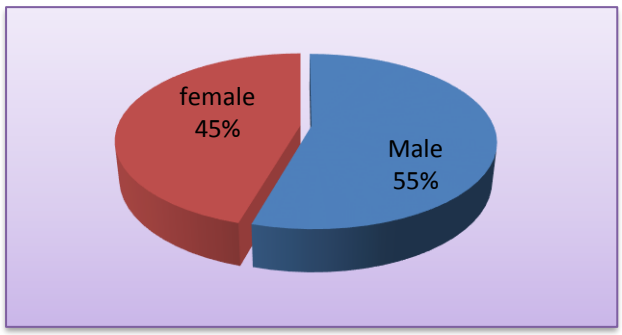

FIG-1. Age wise distribution

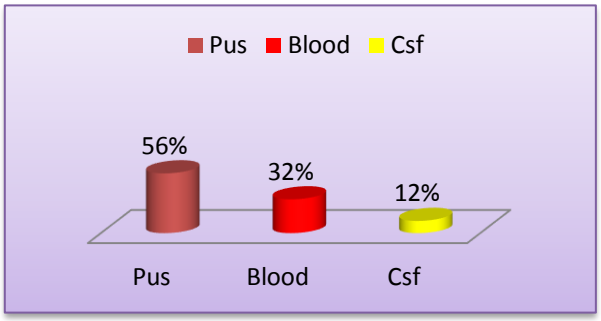

FIG-2. Sample wise distributions

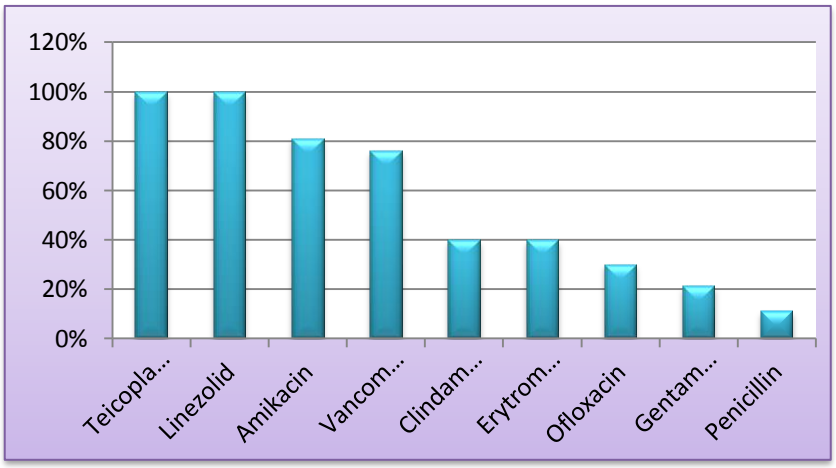

FIG- 3 Antibiotic susceptibility against MRSA.

DISCUSSION

In recent years, *Staphylococcus aureus* has become one of the most dangerous pathogens due to its increased resistance to β-lactam antibiotics and vancomycin [9,10,11] Studies showed that MRSA is a causative agent of hospital-acquired infection and an incipient community pathogen in many geographical regions [12,13,14,15].

In our study we found that out of 400 samples, 147 (35%) MRSA were isolates.Out of 147 MRSA patients, 80(54%) were males, 67(45%) were females including all age groups which was similar to the study conducted by (Dechen C) [16] where the rate of MRSA was more in Males as compared to Females.

The samples collected were from 83 (56.4%) pus, 47 (31.9%) blood, 17 (11.5%) CSF.. In other study, *Staphylococcus aureus* was found to be the commonest pathogen which was isolated from patients with localized pyogenic and surgical wound infections admitted to surgery ward, which was in accordance with the findings of other workers, who had also reported that *Staphylococcus aureus* was the commonest pathogen which was isolated from surgical site infections [12]

Vancomycin showed comparatively higher MICs than linezolid by agar dilution method demonstrates the MICs of vancomycin and linezolid for MRSA strains. Based on MIC levels of vancomycin and linezolid for MRSA strains , we can say that MRSA strains were also more susceptible to linezolid(Sachin Kishore) [17].

In our study we found that all isolates were sensitive to teicoplanin and linezolid. Of the other antibiotics, amikacin showed the best in vitro activity with 81%, followed by vancomycin 76%, clindamycin & erythromycin 40%, 30% ofloxacin, 21% gentamycin, lowest sensitivity was penicillin with 11%. Few other studies have also described linezolid as a good therapeutic option for MRSA, for reduction of burden on vancomycin for treatment of MRSA strains.

Similarly, low MIC values for linezolid were also reported by other investigators [18].

In current study, no linezolid resistant strain was isolated. This was similar to that which was seen in other studies which had reported that clinical isolates were linezolid sensitive. Rajaduraipandi reported 2.4% linezolid resistant *Staphylococcus aureus* (LRSA) in south India in year 2006 , which was found by Kirby-Bauer Disc diffusion method and recently, linezolid resistant strains were isolated in Nagpur from patients who were admitted to orthopaedics ward of a hospital [1, 19,20,21] But in UP, no linezolid resistant *Staphylococcus aureus* strain has been isolated [21].

In a multicentre study done in 2008-2009 also, no isolate was found to be resistant to linezolid by Indian Network for Surveillance of Antimicrobial Resistance (INSAR) [21] Previous studies have reported that strains with upper levels of minimum inhibitory concentrations (MICs) of vancomycin were in the sensitive range (1-4 μg/ml); which would result in more morbidity and mortality among patients, as compared to those which had lower ranges of vancomycin MICs (less than 1 μg/ml) [22] Further this agent, however, requires intravenous (i.v.) administration,

continuous monitoring of levels and occasionally, patients experience some unacceptable side effects. Linezolid, on the other hand, is also available in oral form [6]. This drug is rapidly and completely absorbed after oral administration, with a mean bioavailability of approximately 100% and it does not require continuous monitoring. Further, the oxazolidiones have a unique mechanism of action and they do not exhibit cross resistance with existing agents [23]. In a study done by Benjamin P Howden, he described improved outcomes obtained with linezolid for MRSA infection as compared to those which were obtained with use of vancomycin [24] .So, we suggest that linezolid is a good alternative for treatment of multidrug resistant *Staphylococcus aureus* strains. Our study was comparable with other studies which have also concluded that linezolid and teicoplanin was superior to vancomycin in treating patients.

CONCLUSION

In this study Linezolid and teicoplanin had similar in-vitro efficacies for all the MRSA. So, teicoplanin and linezolid can be a good alternative for the treatment of MRSA as compared to vancomycin.

We would also stress here again that the indiscriminate use of antibiotics without doing antibiotic susceptibility testing and prolonged and inappropriate use of antibiotics lead to emergence of resistance. A good antibiotic policy should be laid down between clinicians and microbiologists in all tertiary care hospitals and a strict antibiotic regimen should be applied by clinicians. As only limited drugs are available for the treatment of VISA, irrational use of antibiotics should be avoided and a rational antibiotic policy must be adopted.

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