Antimicrobial activity of tigecycline against methicillin resistant Staphylococcus aureus in a tertiary care setting

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Abstract

Objective: To determine the in vitro efficacy of tigecycline against methicillin resistant Staphylococcus aureus (MRSA).
Place and Duration of study: Department of Microbiology Army Medical College and Armed Forces Institute of Pathology Rawalpindi, from Feb 2008 to Jan 2009.
Materials and Methods: One hundred clinical isolates of MRSA were taken. Detection of MRSA was done using 30µg disc of cefoxitin as recommended by Clinical laboratory Standard Institute (CLSI). Susceptibility of the isolates to tigecycline was done by employing modified Kirby Bauer disk diffusion technique, according to the guidelines provided by the Food and Drug Administration (FDA). Minimum inhibitory concentrations (MICs) of the isolates were determined by using E-strips (bioMerieux) of tigecycline. Results were interpreted according to FDA recommendations.
Results: All MRSA isolates were susceptible to tigecycline by disc diffusion method. The MICs of tigecycline revealed that all MRSA isolates were in sensitive range.
Conclusion: In an era of rapidly growing antibiotic resistance, tigecycline has been found to have very good in vitro efficacy against MRSA isolates.

Keywords : Antimicrobial activity, MRSA, Tigecycline.

Article

INTRODUCTION

Bacteria possess the ability to protect themselves from naturally occurring antibiotics by acquiring resistance through the exchange of genetic material with other bacteria. In the last two decades, however, the problem has escalated and multi-drug-resistant strains have emerged.1 Methicillin resistant Staphylococcus aureus is one of the frequent causative agents of many infections.2 Multidrug resistant properties of these bacterial isolates are limiting the armamentarium of potentially active antimicrobial agents in clinical use, especially in nosocomial infections.3,4 There has been a dramatic increase in the proportion of infections caused by MRSA worldwide.5 Among National Nosocomial Infections Surveillance system (NNIS) hospitals, the percentage of infections due to MRSA increased from 29% in 1991 to 59 % in 2003.6

According to a multi-centre study in Pakistan, the frequency of MRSA is estimated to vary between 2-61%, with highest frequency seen in major cities of the country.7 A study done at Armed Forces Institute of Pathology (AFIP) Rawalpindi revealed that the frequency of MRSA among all nosocomial isolates of S. aureus increased from 39% in 1996 to 51% in 2003.8 In order to counter these resistant organisms, the focus is to find newer antibiotics for future therapeutic use.

Tigecycline is a glycylcycline which is structurally related to minocycline, but alterations to the molecule have resulted in its expanded spectrum of activity and decreased susceptibility to the development of resistance when compared with other tetracyclines. It has a broad spectrum of activity covering multi drug-resistant gram-positive and negative organisms. It binds to the 30S subunit where it prevents transfer of amino acid into the elongating peptide chain with a subsequent inhibition of protein synthesis.9,10By 1980s with the notable exception of vancomycin, resistance to all the available antibiotics had been reported. With the emergence of vancomycin resistant enterococci, it was feared that this resistance might also spread to staphylococci. These fears became true when low-level vancomycin resistance in Staphylococcus aureus was reported in 1996.11 More alarming are the recent reports of high level vancomycin resistance in Staphylococcus aureus.12

Recently vancomycin resistant MRSA isolates have been reported in various parts of the world. Two

MRSA isolates with vancomycin MICs of 32 and >256µg/mL have been isolated from a tertiary care hospital in Tehran.13 Similarly two MRSA isolates which were vancomycin resistant were reported from a tertiary care hospital in northern India in 2006.14 Thirteen vancomycin intermediately resistant Saphylococcus aureus were reported in a study done by Hakim et al in Karachi, Pakistan in 2007.15 The rapid emergence of multidrug resistant organisms (MDRs) necessitates the study of new drugs. The objective of this study was to determine in vitro efficacy of tigecycline against MRSA isolates in our setup.

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MATERIAL AND METHODS

This study was performed in Microbiology Department of Army Medical College and Armed Forces Institute of Pathology Rawalpindi. One hundred clinical isolates of MRSA were taken.
Staphylococcus aureus isolates were tested for methicillin resistance by modified Kirby-Bauer disk diffusion technique using 30µg cefoxitin disk (Oxoid, Basingstoke, UK) on Mueller-Hinton agar (Oxoid, Basingstoke, UK). Plates were incubated at 33-35oC for 24 hours. Susceptibility to cefoxitin was interpreted as per CLSI criteria. A zone diameter of > 22 mm was taken as susceptible and < 21 mm as resistant.16
Bacterial suspensions of 0.5 McFarland turbidity standards were made. Control strain of MRSA (ATCC 33591) was used along with test organism. Suspension of MRSA isolates was plated on Mueller-Hinton agar, and then 15µg disks and E-strips of tigecycline were applied on the inoculated media. The plates were incubated aerobically at 33-35oC for 16-20 hours. The results of MIC and disk diffusion for tigecycline were interpreted according to FDA approved criteria9. (Table-1)

Table-1: FDA approved criteria for disc diffusion and MIC of tigecycline against MRSA[9]

MIC (µg/mL)			Zone diameters (mm)		
S	I	R	S	I	R
≤0.5	…	…	≥ 19	15 - 18	≤14

RESULTS

The microorganisms were isolated from specimens of patients admitted in different wards of Military Hospital and Combined Military Hospital Rawalpindi including medical ICU, gynaecology/obstetrics, medical wards, nephrology, surgical wards, surgical ICU, rehabilitation medicine and paediatric medicine. Majority of MRSA isolates (74%) were from pus/pus swabs and the rest of isolates were from blood (8%), catheter tips (6%), pleural fluids (4%), nasobronchial lavage (NBL) (4%), urine (2%) and throat swab (2%) Table-2.

Table-2: Source of MRSA isolates (n=100)

Sample source	Percentage
Pus/pus swab	74%
Blood	8%
Catheter tips	6%
Pleaural fluid	4%
NBL	4%
Urine	2%
Throat swab	2%

All MRSA isolates were sensitive to tigecycline with zone diameters ranging from 21-31mm by modified Kirby-Bauer disc diffusion method. Mean zone diameter was 25.48mm. The MICs of tigecycline against MRSA isolates revealed that all 100% isolates were in susceptible range with MICs from 0.047 to 0.32µg/mL, mean 0.097µg/mL.

DISCUSSION

The growing bacterial resistance is an increasing threat to the successful treatment of both community as well as hospital-acquired infections caused by multi-drug resistant (MDR) organisms.17 This global problem is due to the irrational use of antibiotics that has resulted in the emergence of these MDR bacteria through out the world. In developing countries, there is lack of infection control practices and formal antibiotic policies are nonexistent which has further aggravated the problem. Nosocomial pathogens like MRSA have been increasingly reported from all over the country.18

Our results showed that most of the MRSA isolates (74%) were from pus/pus swab specimens. Similar results (71%) were shown by Tiwari et al from a tertiary care hospital in western Nepal.19 These MRSA isolates were mostly isolated from surgical wards. Similar results were shown by Hussain et al from a tertiary care hospital in 2005.20

All MRSA isolates were sensitive to tigecycline by disk diffusion method and MICs were also in the sensitive range in our study. Similar results were seen in a study conducted by Reinert et al on the isolates collected from Asia/Pacific Rim, Europe, Latin and North America. Their results revealed 100% sensitivity of MRSA isolates to tigecycline by microdilution method.21 Kasbekar et al conducted a study on 265 MRSA isolates in university of Pennsylvania, Philadelphia and found MIC90 of 0.25 µg/mL.22 Gales et al conducted a study in Latin America and showed that MIC50 of tigecycline (0.25 µg/mL) was eight-fold more potent than MIC50 of minocycline (2 µg/mL) against oxacillin-resistant Staphylococcus aureus.23 Sauli et al showed that 99% of MRSA isolates were inhibited by tigecycline at a concentration of ≤0.5µg/mL.17

Our results are in concordance with similar studies done around the world recently. The excellent in vitro efficacy of tigecycline against MRSA makes it as an ideal choice in situations where other therapeutic options are limited. With the increasing reports of vancomycin intermediate and resistant Staphylococcus aureus, tigecycline may prove to be a flake of gold to combat infections caused by these isolates. Clinical studies are however required to substantiate the findings of in vitro efficacy of tigecycline.

Conclusion

Tigecycline showed excellent in vitro activity against MRSA. It is a promising antimicrobial agent that is likely to have a key role in the future treatment of nosocomial infections.

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