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Original Article

In Vitro Activity of Tigecycline against Methicillin Resistant *Staphylococcus Aureus*

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Abstract

Introduction: Methicillin resistant *Staphylococcus aureus* (MRSA) emerged with increasing resistance to most of the antimicrobial agents used for treatment of infections. The incidence of hospital acquired MRSA varies from 25% in western part of India, to 50% in South India. There is need of new antimicrobial agents, as increase in resistance and spread of multi drug resistance among many pathogenic species. Tigecycline is a newer glycylcycline antimicrobial agent very active against bacteria resistant to other classes of antibiotics, including the quinolones & betalactams. *Aims & Objective:* To evaluate in vitro activity of Tigecycline against Methicillin resistant *Staphylococcus aureus*. *Material and methods:* A total of 50 MRSA were isolated from various clinical samples of patients attending to tertiary care hospital. The organisms were identified by conventional method and antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method as per CLSI guidelines. Tigecycline MIC was determined by using E strips according to manufacturer's instruction. *Result:* In our study all MRSA isolates were sensitive linezolid and teicoplanin. All MRSA isolates were inhibited by concentration of ≤0.5µg / ml of tigecycline. Most of strains in our study had MIC value less than 0.125µg / ml which was much below the US FDA cut offs for the susceptibility. *Conclusion:* Tigecycline is a potent anti microbial agent against MRSA. In the view of its excellent activity against MDR pathogens, it is prudent to reserve tigecycline for life threatening infections when other options fail.

Keywords: MRSA; Tigecycline; *Staphylococcus Aureus*; MDR Pathogens; E-Test.

Introduction

Significant changes in causative organism of nosocomial bacterial infections have been observed globally over past 100 yrs. In the first of half of 20th century, Gram positive organism particularly *Staphylococcus aureus & Streptococcus spp.* were of primary concern. By the end of 1970s, Methicillin resistant *Staphylococcus aureus* (MRSA) had also emerged with increasing resistance to most of the antimicrobial agent used for treatment of infections [1]. MRSA is now endemic in India. The incidence of hospital acquired MRSA varies from 25% in western part of India, to 50% in south India. Isolation of community acquired MRSA has also been identified & increasingly reported from India [2].

Resistance to currently available antibiotics is increasing at an alarming rate. At the same time, development of new antimicrobial agent to treat such serious bacterial infections is decreasing. As a result of the emergence and spread of multidrug resistance in many pathogenic species, the need for new antimicrobial agent is more urgent & greater than ever [3].

Tigecycline is a newer glycylcycline antimicrobial agent that induces its bacteriostatic effect by binding to high affinity intracellular site of the bacterial 30s

ribosome. Tigecycline is very active against bacteria resistant to other classes of antibiotics, including quinolones & betalactams. Tigecycline additionally, resist deactivation by most known tetracycline resistance mechanism [6]. Because of this promising profile against clinically important bacteria, as well as promising pharmacodynamic & pharmacokinetic data tigecycline is good alternative to treat MDR pathogens [3-5]. So considering multidrug resistance among MRSA, we tried to evaluate in vitro activity of tigecycline by E test.

Aims & Objectives

To evaluate in vitro activity of tigecycline against Methicillin resistant *Staphylococcus aureus* from various clinical samples by E test.

Material & Methods

A total of 50 MRSA were isolated from various clinical samples of patients attending to tertiary care hospital for period of three months. The strains were isolated from pus (n=36), blood (n=9) and urine (n=8). The organisms were identified by conventional method using Gram positive panel. Antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method using different antimicrobial agents; penicillin G [10 U], cefoxitin [30µg] gentamycin [10 µg], ciprofloxacin [5µg] erythromycin [15µg] clindamycin[2µg] Amoxycillin-clavulanic acid [20 / 10 µg] Levofloxacin [5 µg] linezolid [30µg] Teicoplanin [30µg] as per CLSI guidelines. Tigecycline [15µg] disc diffusion testing was done by using US FDA breakpoints, tigecycline MIC was determined by using E strips according to manufacturer's instruction.

Results and Observations

In our study, all MRSA isolates were sensitive to linezolid and teicoplanin. In the present study, 80 % of MRSA isolates were sensitive to levofloxacin while only 20 % were sensitive to Gentamycin and ciprofloxacin. (Table 1).

In our study, all MRSA isolates were inhibited by concentration of d"0.5µg / ml of tigecycline. Most of strains in our study had MIC value less than 0.125µg / ml which was much below the US FDA cut offs for the susceptibility (Table 2).

Table 1: Antimicrobial susceptibility pattern of MRSA isolates (n= 50)

Antimicrobial agent	S	I	R
Penicillin (10U)	0	0	100%
Cefoxitin (30µg)	0	0	100%
Gentamycin (10µg)	20%	0	80%
Ciprofloxacin (5µg)	20%	0	80%
Amoxycillin-clavulanic acid (20 / 10 µg)	0	0	100%
Erythromycin (15µg)	30%	0	70%
Clindamycin (2µg)	40 %	0	60 %
Levofloxacin (5 µg)	80%	0	20%
Lenozolid (30µg)	100%	0	0
Teicoplanin (30µg)	100 %	0	0
Tigecycline (15µg)	100%	0	0

S-sensitive, I-intermediate sensitive, R-resistant.

Table 2: Minimum inhibitory of concentration of MRSA strains for tigecycline obtained by E test

	MIC of tigecycline (ug/ml)		
	< 0.5 to 0.25	0.25-0.125	< 0.125
MRSA (n=50)	6	10	34

Discussion

Emergence of multidrug resistance among methicillin resistant *Staphylococcus aureus* strains have led to limited therapeutic options, resulting in increased morbidity and mortality. The development of new anti-microbial agents with novel modes of action is critically needed to keep in pace with development and spread of drug resistance mechanisms among bacteria [7].

Tigecycline is a glycylcycline compound with broad spectrum of bacteriostatic activity against Gram positive pathogens including MRSA [3]. It acts by inhibiting the 30s subunit of the ribosome.

Tigecycline does not exhibit co-resistance with known mechanisms of resistance. Its capacity to penetrate into various tissues makes it useful in the treatment of infections of skin and soft tissue as well intra abdominal infections [8-0].

In our study, 100 % strains were sensitive to linezolid and teicoplanin. Similar observations were shown by manisha mane et a [10].

In present study, 80 % strains were sensitive of levofloxacin similar result were obtained by Manoharan et al [7] while Shanthi M et al in his study reported only 25 % sensitivity to levofloxacin [11]. In comparison to our study Manisha mane et al reported somewhat higher sensitivity to ciprofloxacin and gentamycin [10].

In our study all strains were sensitive to tigecycline. Most of strains had MIC value less than 0.125µg / ml which was much below the US FDA cut offs for the susceptibility. Many other Indian and foreign studies reported MIC90 of tigecycline ranging from 0.125µg / ml to 0.5µg / ml against MRSA isolates[7, 12-14]. The activity of tigecycline against *Staphylococcus Aureus* is completely unaltered by the presence of methicillin or glycopeptides resistance genes. It is the most potent antimicrobial agent when tested against glycopeptides-intermediate resistant *Staphylococcus Aureus [15].*

To conclude, the present study shows tigecycline is a potent anti microbial agent against MRSA. In the view of its excellent activity against MDR pathogens, it is prudent to reserve tigecycline for life threatening infections when other option fails.

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