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Original Research Article

Antimicrobial Profile of Inducible Clindamycin Resistant Strains of Staphylococcus Aureus Isolated From Clinical Samples

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ABSTRACT

Aims: Present study was undertaken to determine antimicrobial profile of inducible clindamycin resistant (ICR) strains of *Staphylococcus aureus*. In-vitro routine tests for clindamycin susceptibility may fail to detect inducible Clindamycin resistance due to *erm* genes resulting in treatment failure, thus necessitating the need to detect such resistance by simple D-test and their antibiotic sensitivity pattern on a routine basis.

Materials and methods: Erythromycin resistant strains of *Staphylococcus aureus* were detected by using erythromycin (15µg) disc as per standard disc diffusion method. Erythromycin resistant strains were further subjected to antimicrobial sensitivity testing as per CLSI guidelines. MLS_B phenotypes were detected by using D-test and interpreted as per CLSI guidelines.

Result: Total 176 erythromycin resistant strains of *Staphylococcus aureus* were included in the study. Of these, 46 isolates were inducible clindamycin resistant. Out of 46(26.13%) isolates of inducible clindamycin resistant (ICR) strains of *Staphylococcus aureus*, 42 (91.3%) isolates were MRSA and 4 (8.69%) isolates were MSSA.

Antimicrobial sensitivity testing of ICR strains of *Staphylococcus aureus* revealed that, 42(91.3%) isolates were sensitive to Linezolid. Among ICR strains exhibiting MRSA, 38 (90.4%) isolates were sensitive to Linezolid.

Key words: *Staphylococcus aureus, $iMLS_B$ resistance, AST.*

INTRODUCTION

Emergence of variety of drugs resistance in *Staphylococcus aureus* is major concern. First challenge to this organism was offered by sulfonamide in 1930, for which it developed resistance. The problem was later tackled by introducing benzyl penicillin in 1941. The continued usage of this agent caused selection of resistant strains producing Beta-lactamases. Again temporary relief was obtained by introducing newer synthetic penicillins like methicillin, cloxacillin etc. [1]

In the year 1962, methicillin resistant Staphylococcus species started to emerge, that have evolved resistance to all penicillin group of drugs and also newer synthetic penicillins. [2] Methicillin resistance in *Staphylococcus aureus* is mediated by production of low affinity Penicillin binding

proteins (PBP-2a) that is encoded by a gene called *mec*A. [3]

In such cases, the Macrolide-Lincosamide-Streptogramin-B (MLS_B) family of antibiotics serves as one such alternative, with clindamycin being the preferred agent due to its excellent pharmacokinetic properties. Widespread use of MLS_B antibiotics hassled to an increase in number of staphylococcal strains acquiring resistance to MLS_B. [4-6]

Three unrelated groups of antimicrobial agents share the same ribosomal binding site in the bacterial cell-macrolide, lincosamide and streptograminB. Therefore, it is possible that to one group of antibiotics (macrolides) might predict resistance to the other groups. Resistance to erythromycin is used as an indicator of possible resistance to clindamycin. [1]

Most common mechanism for such resistance is target site modification mediated by *erm* genes which can be expressed either constitutively (constitutive MLS_B phenotype) or inducibely (inducible MLS_B phenotype). [7, 8-11]

Strains with inducible resistance to clindamycin are difficult to detect in the routine laboratory as they appear erythromycin resistant and clindamycin sensitive in vitro when not placed adjacent to each other. In such case, in vivo therapy with clindamycin may select constitutive *erm* mutants leading to clinical therapeutic failure. [11]

In case of another mechanism of resistance, *Staphylococcus aureus* can also develop isolated macrolide resistance based on the presence of an efflux pump, encoded by msrA gene which leads to resistance to macrolide and type B streptogramins but not to lincosamide. These isolates known as MS phenotype also shown in vitro resistance to erythromycin and sensitive to clindamycin same as in inducible resistance phenotype, but clindamycin therapy can be safely given in infections with this phenotype and there is no risk of clinical failure. [7,10-12]

Molecular markers for the *erm* genes are available, but they are costly and inconvenient for everyday use. The simple, reliable and inexpensive D-test perform on routine basis in laboratory can be of help to deal with this problem. [13]

Clinical and Laboratory standard Institute (CLSI) recommends the double disk diffusion test (D-test) to detect the presence of phenotypic inducible clindamycin resistance. [14]

So it is mandatory to detect inducible clindamycin resistant strains and their antibiotic sensitivity pattern for appropriate therapy.

MATERIALS AND METHODS

The study was conducted at Department of Microbiology, MGM Medical College, Aurangabad. Erythromycin resistant strains of *Staphylococcus aureus* were detected by using erythromycin (15µg) disc as per standard disc diffusion method. [14]

Erythromycin resistant strains were further subjected to antimicrobial sensitivity testing as per CLSI guidelines. MLS_B phenotypes were detected by using D-test and interpreted as MS_B phenotype, Inducible MLS_B phenotype, and Constitutive MLS_B phenotype as per CLSI guidelines. [14]

Quality control: *Staphylococcus aureus (*ATCC 25923) stains were used according to the standard disc diffusion quality control procedure. [15]

RESULTS

Total 176 erythromycin resistant strains of *S. aureus* were included in the study. Of these, 46 isolates were inducible Clindamycin resistant. Out of 46 isolates of inducible clindamycin resistant (ICR) Strains of *Staphylococcus aureus,* 42

isolates were MRSA and 4 isolates were MSSA.

Antimicrobial sensitivity testing of erythromycin resistant strains of *Staphylococcus aureus* revealed that, 130 (73.86%) strains were sensitive to linezolid followed by doxycyclin 121(68.75%) (table-1)

Amongst ICR strains of *Staphylococcus aureus*, 42(91.3%) isolates were sensitive to Linezolid followed by Amikacin and Doxycyclin (67.3%). (Table-2). And ICR strains exhibiting MRSA, 38 (90.4%) isolates were sensitive to Linezolid and ICR strains exhibiting MSSA, 4(100%) isolates were sensitive to Linezolid and Amikacin. (Table-3).

Table-1: Antibiotic sensitivity pattern of erythromycin resistant *Staphylococcus aureus*. n=176

Antibiotics	Susceptible
Levofloxacin	102 (57.95%)
Doxycyclin	121 (68.75%)
Amikacin	110 (62.5%)
Co-trimoxazole	45 (25.56%)
Penicillin	6 (3.40%)
Linezolid	130 (73.86%)
Ciprofloxacin	39 (22.15%)

Table-2: Antimicrobial sensitivity pattern of ICR strains of *Staphylococcus aureus*. (n=46)

Antibiotics	Susceptible
Levofloxacin	27(58.6%)
Doxycyclin	31(67.3%)
Amikacin	31(67.3%)
Co-trimoxazole	10(21.7%)
Penicillin	00 (00%)
Linezolid	42(91.3%)
Ciprofloxacin	05(10.8%)

Table-3: Antibiotic sensitivity pattern of ICR strains of S. aureus exhibiting MRSA & MSSA. (n=46)

Antibiotics	Susceptible	
	MRSA (n=42)	MSSA (n=4)
Levofloxacin	24 (57.1%)	03 (75%)
Doxycyclin	28 (66.6%)	03 (75%)
Amikacin	27 (64.2%)	04 (100%)
Co-trimoxazole	07 (16.6%)	03 (75%)
Penicillin	00 (00%)	00 (00%)
Linezolid	38 (90.4%)	04 (100%)
Ciprofloxacin	03 (7.1%)	02 (50%)

DISCUSSION

Staphylococcus aureus is an important pathogen causing pyogenic infections, toxin mediated infections, and urinary tract infection. [16]

Resistance to antimicrobial agents is a major concern worldwide and is exemplified by the global spread of methicillin resistant *Staphylococcus aureus* and development of resistance to Microlide-Lincosamide-StreptograminB (MLS_B) group of antibiotics. [17]

The determination of antimicrobial susceptibility of a clinical isolates is often crucial for optimal antimicrobial therapy of infected patients. This is particularly important considering the increase of resistance and emergence of multidrug resistant organisms.

Reporting *Staphylococcus aureus* as susceptible to clindamycin without checking for inducible resistance may result in institution of inappropriate clindamycin therapy. On other hand negative result for inducible clindamycin resistance confirms clindamycin susceptibility and provides a very good therapeutic option. [11, 18]

A total of 392 *Staphylococcus aureus* were isolated during the study period of 12 months (January 2012 to December 2012) in the department of microbiology. Out of 392 *Staphylococcus aureus* isolates, 176 (44.89%) were erythromycin resistant; of these 46 (26.13%) strains were ICR. Out of 46 isolates of ICR strains of Staphylococcus aureus, 42(91.3%) isolates were MRSA while 4 (8.69%) isolates were MSSA.

Present study was undertaken specially focused on Antimicrobial sensitivity pattern of ICR strains of *Staphylococcus aureus*, and it revealed that; 42(91.3%) isolates were sensitive to Linezolid (Table-1). Among ICR exhibiting MRSA strains, 38 (90.4%) isolates were sensitive to Linezolid (table-2)

Fahriye Eksi et.al [19] reported all the isolates of *Staphylococcus aureus* were sensitive to linezolid. Although a few

isolates of linezolid resistant of *Staphylococcus aureus* reported elsewhere, [20, 21] this is in concordance with present study.

The incidence of resistance is highly variable with regards to geographic locality; hence local data regarding inducible clindamycin resistance is helpful in guiding anti-staphylococcal therapy. [18]

CONCLUSION

As the resistance conversion may result in clindamycin treatment failure, [19, 22] accurate detection of ICR is necessary to improve the empirical approaches to the therapy. And further study of antimicrobial susceptibility of such ICR strains may helps in judicial use of drugs in serious infection caused by staphylococci.

In conclusion, we recommend detection of ICR strains of staphylococcus aureus and their antibiotic sensitivity pattern on routine basis for the judicial use of drugs and optimal therapy.

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