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Original Article

Inducible Clindamycin Resistance in *Staphylococcus aureus* Isolated from Nursing and Pharmacy Students

Renushri, Avinandan Saha, Nagaraj, Veena Krishnamurthy

Department of Microbiology, Sri Siddharta Medical College, Tumkur, Karnataka, India

Address for correspondence: Dr. Renushri, E-mail: dr.renushree@gmail.com

ABSTRACT

Aims: Emergence of resistant isolates of *Staphylococcus aureus (S. aureus)* has resulted in failure of clindamycin therapy. The prevalence of inducible clindamycin resistance in *S. aureus* isolated from nursing students and pharmacy students (representing carriers exposed and not exposed to hospital environment respectively) was evaluated.

Materials and Methods: Nasal, throat, and palmar swabs were collected from 119 nursing students and 100 pharmacy students. *S. aureus* was identified and antibiogram obtained by Clinical and Laboratory Standards Institute guidelines. Inducible clindamycin resistance was detected by the D-test.

Results: 36 and 34 individuals in the exposed and non-exposed groups respectively were carriers of *S. aureus*. 16.7% and 5.9% isolates showed inducible clindamycin resistance in exposed and non-exposed groups, respectively. The percentage of inducible clindamycin resistance was higher among methicillin-resistant *S. aureus* (MRSA) (27.8%) compared to methicillin-sensitive *S. aureus* (5.8%).

Conclusion: *S. aureus* isolates resistant to β-lactams can also show inducible clindamycin resistance. Exposure to hospital environment was not found to be a risk factor for carriage of *S. aureus* with MLSBi phenotype.

Keywords: Inducible clindamycin resistance, MLSBi phenotype, MRSA, *S. aureus* carriers

INTRODUCTION

Clindamycin, an antimicrobial belonging to the macrolide-lincosamide-streptogramin B (MLS_B) family, is frequently used for treatment of skin and soft tissue infections caused by *Staphylococcus aureus* (*S. aureus*). However, the widespread use of the MLS_B family of antimicrobials has led to the emergence of resistance.[1] The common mechanism of resistance is mediated by *erm* genes that encode enzymes conferring inducible (MLS_Bi) or constitutive (MLS_Bc) resistance to MLS_B agents by reducing binding by these agents to the bacterial ribosome.[2-4]

Isolates with inducible clindamycin resistance are found to be resistant to erythromycin but susceptible to clindamycin when these discs are not placed adjacent to each other during antimicrobial sensitivity testing. Consequently, laboratory identification of such isolates is often missed, resulting in inappropriate therapeutic use of clindamycin and treatment failure.[2] These isolates can be detected by the D-test, a disc diffusion test in which induction of clindamycin resistance by erythromycin is tested.[2,5,6]

S. aureus can colonize healthy community-dwelling individuals, who are not only at an increased risk for developing subsequent infections, but also transmit the pathogen to other individuals.[7-9] Methicillin-resistant *S. aureus* (MRSA) is an important nosocomial pathogen and healthcare professionals, who are known to be carriers of MRSA, can transmit the pathogen to patients under their care, thereby leading to various complications associated with MRSA infections (like pneumonia and septicemia) in the patients.[7]

In this study, the prevalence of inducible clindamycin resistance in *S. aureus* isolated from nursing students and pharmacy students (representing carriers exposed and not exposed to hospital environment, respectively) was evaluated, with particular regard to MRSA.

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MATERIALS AND METHODS

The present study was conducted at the department of microbiology of our medical college from 30 June, 2010 to 31 August, 2010. Institutional ethical committee approval was obtained.

One hundred nineteen students of the age group 18-23 years of the college of nursing attached to our hospital were included in the study. All students attended rotating sessions for at least 4 h daily in various hospital departments for the last 6 months. They represented the group exposed to hospital environment.

One hundred age-matched students of the college of pharmacy in our city were also studied. None of the students in this group had a history of hospitalization or regular visits to a hospital in the last 6 months. They represented the group not exposed to hospital environment.

None of the subjects had a history of illness or treatment with an antibiotic in the last 6 months. An informed written consent was obtained from each of the subjects.

Nasal, throat, palmar, and web-space swabs were collected from each of the subjects. *S. aureus* was identified phenotypically by growth on mannitol salt agar, Gram's stain, catalase test, and slide and tube coagulase tests.[10-12] Antimicrobial susceptibility testing of the isolates to penicillin (10 U), cefoxitin (30 μg), erythromycin (15 μg), and clindamycin (2 μg) (HiMedia, Mumbai) was carried out by the standard disc diffusion test as per Clinical and Laboratory Standards Institute (CLSI) guidelines.[13] The erythromycin and clindamycin discs were placed 15 mm apart edge to edge.[2,5]

Isolates showing resistance to erythromycin (zone size ≤ 13 mm) and sensitivity to clindamycin (zone size ≥ 21 mm), as well as giving a D-shaped zone of inhibition around clindamycin with flattening adjacent to the erythromycin disc were considered to show inducible clindamycin resistance [Figure 1].[5,6] *S. aureus* BAA 977 and *S. aureus* BAA 976 were used as the positive and negative controls, respectively.

MRSA was detected by the cefoxitin disc diffusion test, using a 30 μg disc (HiMedia, Mumbai) (an inhibition zone diameter of ≤ 21 mm was reported as oxacillin or methicillin resistant and a zone diameter of ≥ 22 mm was considered sensitive) and by growth on oxacillin screen agar, incorporating 4% NaCl and 6 μg/ml of oxacillin (HiMedia, Mumbai), as per CLSI guidelines.[12-14]

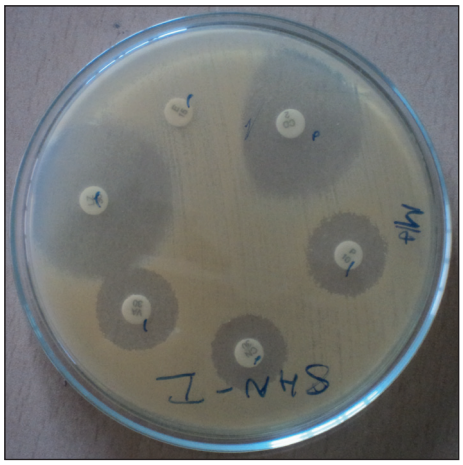

Figure 1: D-test showing a blunted zone of inhibition around the clindamycin disc adjacent to the erythromycin disc

Quality control strains—MRSA ATCC 43300 and methicillin-sensitive *S. aureus* (MSSA) ATCC 25923—were used as positive and negative controls, respectively.

Association of exposure to hospital environment with carriage of *S. aureus* showing MLS_Bi phenotype, and association between methicillin resistance and expressionof MLS_Bi phenotype were evaluated using the chi-square (χ^2) test.

RESULTS

In the exposed group, 36 individuals were found to be carriers of *S. aureus*. Isolates from six (16.7%) individuals showed inducible clindamycin resistance. From the non-exposed group, 34 individuals were found to be carriers of *S. aureus*. Isolates from two (5.9%) individuals showed inducible clindamycin resistance.

The number of isolates showing MLS_Bi and MS (resistance to erythromycin but sensitivity to clindamycin without forming a D-zone around the clindamycin disc) phenotypes in the groups exposed and not exposed to a hospital environment, as well as their categorization as MRSA and MSSA, is shown in [Table 1].

None of the isolates showed constitutive clindamycin resistance (MLS_Bc phenotype).

The percentage of inducible clindamycin resistance was higher among the group exposed to a hospital environment than among the group not exposed. However, this was not found to be statistically significant ($\chi^2 = 2.02$; $P > 0.05$).

The percentage of inducible clindamycin resistance was also higher among MRSA isolates compared to MSSA isolates [Table 2] and this was found to be statistically significant ($\chi^2 = 6.38$; $P < 0.05$).

Table 1: Number of isolates exhibiting MLS_Bi and MS phenotypes in the two study groups. The table also shows the number of isolates with MLS_Bi and MS phenotypes that were methicillin resistant and sensitive

Study group	Total no. of carriers of *S. aureus*	No. of isolates showing MLS_Bi phenotype		No. of isolates showing MS phenotype	
		MRSA (%)	MSSA (%)	MRSA (%)	MSSA (%)
Exposed	36	4 (11.1)	2 (5.6)	6 (16.7)	1 (2.8)
Non-exposed	34	1 (2.9)	1 (2.9)	0 (0)	5 (14.7)

Table 2: Number of MRSA and MSSA isolates exhibiting the MLS_Bi phenotype from both exposed and non-exposed groups

Nature of isolate	Total no.	With MLS_Bi phenotype (%)	Without MLS_Bi phenotype (%)
MRSA	18	5 (27.8)	13 (72.2)
MSSA	52	3 (5.8)	49 (94.2)

MRSA: Methicillin-resistant *S. aureus*, MSSA: Methicillin-sensitive *S. aureus*

Of the 36 *S. aureus* isolates obtained from the group exposed to hospital environment, 13 were resistant to erythromycin; of the 34 *S. aureus* isolates obtained from the non-exposed group, 7 were resistant to erythromycin.

The distribution of *S. aureus* isolated from different carriage sites is given in Table 3.

Table 3: Number of *S. aureus* isolated from different carriage sites in exposed and non-exposed groups

Site of isolation	Number of isolates	
	Exposed group	Non-exposed group
Nose	16	18
Throat	10	7
Web space	1	7
Nose and throat	3	1
Nose and web space	4	1
Throat and web space	2	0
Nose, throat and web space	0	0

DISCUSSION

Clindamycin provides an appropriate alternative for treatment of infections caused by isolates of *S. aureus* that are resistant to other antimicrobials like β-lactams, fluoroquinolones, and macrolides. However, isolates that are resistant to erythromycin may also show inducible resistance to clindamycin which can lead to treatment failure.

In our study, 11.4% (8 out of 70 individuals in both the study groups taken together) were colonized with *S. aureus* isolates showing the MLS_Bi phenotype. Other Indian studies on clinical isolates of *S. aureus* showed MLS_Bi prevalence of 14.5% and 13.1%.[5,15] Results of studies in other countries varied considerably with MLS_Bi prevalence of 25.4% and 52% being reported among *S. aureus*.[2,16]

The group exposed to a hospital environment had a larger percentage (16.7%) of individuals colonized with *S. aureus* isolates with the MLS_Bi phenotype compared to the group not exposed (5.9%) [Table 1]. This could be attributed to the fact that antibiotic resistance is more likely to emerge among *S. aureus* isolated from a hospital due to widespread antibiotic use and the resultant selection pressure created in a hospital environment. However, we found that the association between exposure to hospital environment and acquisition of isolates with the MLS_Bi phenotype was not statistically significant. This could be attributed to the limited number of isolates with the MLS_Bi phenotype that we obtained in our study.

More MRSA isolates showed MLS_Bi phenotype (27.8%) compared to MSSA isolates (5.8%) [Table 2]. Our results vary a little compared to other Indian studies that reported MLS_Bi prevalence of 27.6% and 38.4% among MRSA, and 1.6% and 12.9% among MSSA.[5,15] Association of methicillin resistance with the presence of the MLS_Bi phenotype was found to be statistically significant in our study.

It was found that in the exposed group, most isolates showing the MS phenotype were also resistant to methicillin, whereas in the non-exposed group, all isolates showing MS phenotype were sensitive to methicillin [Table 1].

In conclusion, it is very likely that isolates of *S. aureus* resistant to β-lactams will also show inducible clindamycin resistance. Exposure to hospital environment is not found to be a risk factor for carriage of *S. aureus* with the MLS_Bi phenotype. However, given that (to the best of our knowledge), this is the first study to explore the prevalence of the MLS_Bi phenotype in *S. aureus* isolated from carriers, further evaluation with a larger sample size is required for confirmation of the existence of an association between exposure to hospital environment and carriage of *S. aureus* with the MLS_Bi phenotype.

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