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Staphylococcus aureus: An Unusual Resistance Mechanism?

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Abstract

S. aureus resistance mechanism to lincosamides by enzymatic inactivation was detected. Lnu (A) was investigated by PCR and sequenced. From one hundred *Staphylococcus aureus* isolated from clinical samples, two (1 susceptible and 1 methicillin-resistant S. aureus) were erythromycin and clindamycin susceptibles, lincomycin resistant and Lnu (A) positive. We suggest to test lincomycin instead of clindamycin to detect this mechanism.

Keywords: *Staphylococcus aureus*; LnuA- lincomycin; Resistance mechanism

Introduction

Staphylococcus aureus (Sau) is one of the major causes of community-acquired and hospital-acquired infections. It´s a gram-positive coccus responsible for a wide range of human disease, including septicaemia, endocarditis and pneumonia; and wound, bone, and joint infections [1]. Macrolide, Lincosamide and Streptogramin (MLS) antibiotics are widely used in the treatment of staphylococcal infections. Resistance to macrolides and lincosamides is increasingly reported in clinical isolates of Sau and few reports have communicated the presence of resistance to lincosamide by enzymatic inactivation (lincosamide nucleotidyltransferase) [2-5]. Lincomycin is produced naturally by several species of actinomycetes, Streptomyces lincolnensis, Streptomyces espinosus, and Actinomycesroseolus, and clindamycin is a semisynthetic derivative obtained by chlorination of lincomycin [6]. These antibiotics act as inhibitors of protein synthesis by blocking the peptidyltransferase site of the 50 S subunit of the bacterial ribosome [7]. Lincosamides are principally used against gram-positive cocci (Staphylococcus, Streptococcus and Enterococcus) and anaerobes (Bacteroides, Clostridium).

The resistance mechanism to lincosamide by enzymatic inactivation is due to the presence to the Lnu (A) gene [8]. When evaluating susceptibility to this antibiotic by the disk diffusion method, resistance to lincomycin (LIN) is evident in strains carrying the Lnu (A) gene (L phenotype) [9]. However results for clindamycin (CLI) could be misinterpreted since it shows susceptible inhibition zones in vitro.

The aim of this study was to detect Sau resistance mechanism to lincosamides by enzymatic inactivation on isolates from patients attended at teaching hospital, Santa Fe city, Argentina. One hundred, consecutive, clinically important Sau isolates from adult patients were studied between January 1st and June 30th, 2011. Susceptibility test was performed by the automated Phoenix system (Phoenix™ BD). Lincomycin (2 µg) susceptibility was tested by diffusion method (CLSI). Lnu (A) and pvl genes were investigated by PCR [9,10] in all strains. Lnu (A) amplification products were sequenced. Fifty-seven (57) of 100 Sau were methicillin-sensible (MSSA) and 43 were methicillin-resistant (MRSA). The susceptibility tests results, phenotype and presence of Lnu (A) gene in Sau strains are shown in Table 1. Lnu (A) gene was confirmed by DNA sequencing of PCR products (321 pb). From all lincomycin resistant studied strains, only two of them carried Lnu (A) gene. They were recovered from skin and soft tissues, they showed ERY and CLI susceptibilities and carried pvl gene.

Susceptibility tests/ phenotype/Lnu (A) gene	100 Sau	
	57 MSSA	43 MRSA
S: ERY, CLI and LIN /susceptible/ negative	52	29
R: ERY, CLI and LIN /constituve MLSB / negative	1	5
R: ERY and inducible R to CLI and LIN/ inducible MLSB / negative	3	8
S: ERY and CLI; R: LIN /L phenotype/ positive (Figure 1)	1	1

Table 1: Characteristics of the *Staphylococcus aureus* strains included in this study. Sau: *Staphylococcus aureus*; MSSA: Methicillin-Susceptible Sau; MRSA: Methicillin-Resistant Sau; S: Susceptible; R: Resistance; ERY: Erythromycin; CLI: Clindamycin; LIN: Lincomycin; MLSB: Macrolides-Lincosamides-Streptogramin B.

Conclusion

We conclude that both isolates that carried LnuA gene (2%) were LIN resistant, ERY susceptible and they showed an apparent CLI susceptibility which could be misinterpreted. This resistance mechanism could be found either in MSSA or MRSA. We suggest, in all cases, to assay LIN to detect this phenotypic resistance mechanism by any susceptibility method.

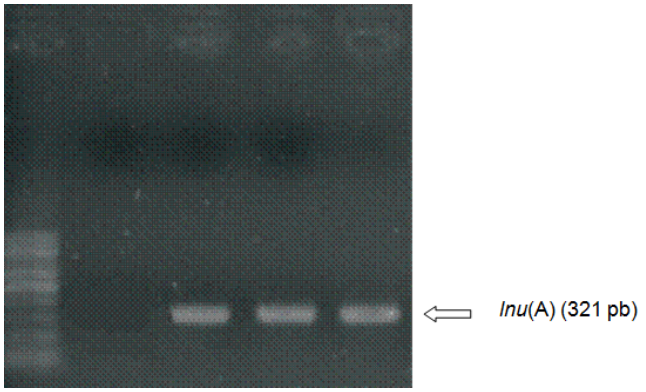

Figure 1: PCR detection. Lane 1: Molecular weight marker (MWM); Lane 2: Negative control (Sau ATCC 25923); Lane 3: Positive control (Sau LnuA positivo) ; Lane 4: LnuA positive methicillin-susceptible Sau; Lane 5: LnuA positive methicillin-resistant Sau.

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