Abstract

The frequency of resistance to aminoglycoside resistance in *Staphylococcus aureus* isolates collected from clinical specimens in teaching hospitals affiliated to Ardabil University Medical Science 2017.

Background & Objectives: Treatment of *Staphylococcal* infections caused by MRSA strains represents a major clinical challenge. Aminoglycoside antibiotics are usually use in combination with a cell wall active agent in treatment of serious SA infections. The objective of this study was to determine the frequency of aminoglycosides resistance, distribution of aminoglycoside-modifying enzymes (AMEs) genes and *staphylococcal* cassette chromosome *mec* (*SCCmec*) elements among clinical isolates of MRSA in Ardabil, Iran.

Methods: In this cross-sectional study, a total of 118 SA isolates were collected from clinical specimens in four teaching hospitals in 2017 and 2018. The SA was identified using standard microbiological and molecular methods. Methicillin resistance was determined by cefoxitin disk test and oxacillin MIC testing. *mecA* methicillin resistance encoding gene, and SCC*mec* typing was determined using PCR method. Phenotypic aminoglycoside resistance was determined using disk diffusion assay and the MICs were determined using agar dilution method. AMEs genes were detected using PCR testing. Spa type of aminoglycoside resistant SA isolates were determined based on highly variable Xr region sequences of the spa-gene. The heterogeneity and clonal relatedness of aminoglycoside resistant SA isolates were determined using ERIC-PCR assay.

Results: Totally, 50 (42.4%) and 68 (57.6%) isolates were determined as MRSA and MSSA respectively. All MRSA were *mecA*-positive by PCR. Among MRSA isolates SCC*mec* type Iva 17 (34%) was predominant, followed by IVc, V, III, II, I. For aminoglycoside antibiotics the resistance rate to gentamicin, kanamycin, tobramycin and amikacin were 19 (16.1%), 21 (17.8%), 10 (8.5%) and 10 (8.5%) respectively. For non-aminoglycosides antibiotics, higher resistance rate observed for penicillin 50 (42.4%) and lower resistance rate observed for nitrofurantoin 1 (0.8%). Of the genes examined for aminoglycoside resistance, *aac (6')-Ie-aph (2'')* 30 (76.9%) was the most frequently identified gene followed by *aph(2'')Ib* 22 (56.4%), *ant (4')-Ia* 14 (35.9%) respectively. The genes *aph(2'')Ic, aph(2'')Id and aph(3'')IIIa* were not detected. The coexistence of multiple AME genes was detected in most aminoglycoside resistant isolates. spa-typing results divided the isolates into t030 types with t310 as the most common one. According to ERIC-PCR results, no significant genetic relatedness between the aminoglycoside resistant isolates were identified. The 19 distinct clusters were identified among aminoglycoside resistant isolates.

Conclusions: Resistance to at least one aminoglycoside antibiotic was found in 39 (33%) of isolates. Overall, the resistance to aminoglycoside and most of the non-aminoglycoside antibiotics were significantly higher in MRSA versus MSSA isolates. The *aac (6')*-Ie-aph (2'') was the predominate gene responsible for aminoglycoside resistance. The aminoglycoside resistant isolate were not closely related.

Keywords: *Staphylococcus aureus*, Aminoglycoside, Gentamicin, MRSA