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**The investigation of in vitro activity of ceftaroline, vancomycin and teicoplanin for methicillin-resistant *Staphylococcus aureus* isolates**

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**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) strains were considered as resistant to all beta-lactam agents, however the introduction of cephalosporins with anti-MRSA activity, i.e. ceftaroline and ceftobiprole, necessitated an update in this consideration. Until recently, vancomycin was used as the first choice treatment option for the serious infections due to MRSA, however the demonstration of treatment failure and increased mortality in infections due to MRSA strains with vancomycin minimal inhibitory concentration (MIC) of  $\geq 1$  mg/L resulted in search for alternative agents. Ceftaroline fosamil is indicated for the treatment of community acquired bacterial pneumonia and acute bacterial skin and skin structure infections. In our study we aimed to determine the MIC values for vancomycin (VA), teicoplanin (TEC) and ceftaroline fosamil (CFT) in a collection of clinical MRSA isolates.

**Material/methods:** MRSA strains (n=105) isolated from clinical specimens between 2012 and 2015 were included in the study. The isolates were identified with MALDI-TOF MS instrument (Bruker Daltonics, Germany). The antimicrobial susceptibility testing was performed using VITEK 2 instrument (bioMérieux, France). Isolates stored at  $-80^{\circ}\text{C}$  in cryo vials were retrieved and broth microdilution (BMD) was performed for CFT (Astra Zeneca), VA and TEC (Sigma) following the EUCAST methodology. For an MRSA isolate with VA MIC value of 4 mg/L, VA and VA/TEC MIC test strips (Liofilchem, Italy) were used. *Staphylococcus aureus* ATCC 29213 was used as the control strain.

**Results:** MIC<sub>50</sub> and MIC<sub>90</sub> values of the strains were determined as 0.5 mg/L and 1 mg/L for VA, 0.5 mg/L and 2 mg/L for TEC and CFT, respectively (Table 1). When evaluated with the current EUCAST

clinical breakpoints, nonsusceptibility was observed in 0.9% (n=1), 1.9% (n=2) and 23.8% (n=25) of the study isolates for VA, TEC and CFT, respectively. The MRSA isolate with VA MIC of 4 mg/L in BMD method also demonstrated an MIC of 4 mg/L with VA gradient strip test, and with VA/TEC gradient strip the values 4/16 mg/L were obtained.

**Conclusions:** Among the study MRSA isolates we detected an isolate with VA MIC of 4 mg/L which should be categorised as “vancomycin resistant” according to EUCAST breakpoints. We also observed two teicoplanin resistant isolates with TEC MIC of 4 mg/L. Even though ceftaroline fosamil has not entered into clinical practice in our country yet, ceftaroline susceptibility among clinical MRSA isolates was determined as 76.2%.

**Table 1.** The *in vitro* activity of vancomycin, teicoplanin and ceftaroline for clinical MRSA isolates (n=105)

	MIC (mg/L)			Susceptibility (%)
	MIC range	MIC <sub>50</sub>	MIC <sub>90</sub>	
<b>Vancomycin</b>	0.125 - 4	0.5	1	99.1
<b>Teicoplanin</b>	0.125 - 4	0.5	2	98.1
<b>Ceftaroline</b>	0.125 - 2	0.5	2	76.2