

TITLE: High prevalence of ceftaroline non-susceptibility among MRSA clinical isolates from three Brazilian regions

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ABSTRACT:

Infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) are of major concern. Ceftaroline is a cephalosporin that inhibits bacterial cell wall synthesis by binding to penicillin binding proteins (PBPs) including PBP2A, which provides the activity against MRSA. Ceftaroline resistant *S. aureus* isolates are rare. The objective of this study was to evaluate the *in vitro* activity of ceftaroline against MRSA clinical isolates. A cross-sectional study was performed; samples were collected from in- and outpatients from three Brazilian regions. Methicillin resistance was initially screened by ceftazidime disk-diffusion. The presence of *mecA* gene was confirmed by polymerase chain reaction (PCR); *Staphylococcal cassette chromosome mec* (SCC*mec*) typing was performed by multiplex PCR assay. Ceftaroline minimum inhibitory concentration (MIC) was evaluated by Etest® (bioMérieux, France) and interpretation was based on the Brazilian Committee on Antimicrobial Susceptibility Testing (BrCAST) criteria. A total of 61/231 non-consecutive MRSA isolates were included – a 26.5% prevalence. Ceftaroline MIC range 0.19-4.0 µg/ml, and M50/M90 were 1.0 and 2.0 µg/ml. Twenty-seven isolates presented ceftaroline MIC results of ≥ 2 µg/ml, nonsusceptible according to BrCAST criteria: 19 (70.4%) were intermediate (MIC=2 µg/ml) non-pneumonia, 06 (22.2%) were resistant (MIC=2 µg/ml) pneumonia and 2 (7.4%) were resistant (MIC=3 µg/ml e MIC=4 µg/ml). SCC*mec* types II (77.8%), III (3.7%) and IV (18.5%) were detected in this study, and most ceftaroline-nonsusceptible isolates were SCC*mec* types II (19; 70.3%) and IV (5; 18.5%). This study highlights the high prevalence of MRSA among the *S. aureus* infections, and, more concerning, the high ceftaroline non-susceptibility that was evidenced. The potential advantage of ceftaroline over other β -lactams is its activity against *S. aureus* isolates, including drug-resistant strains – this fact could

jeopardize this agent as a treatment option in some settings. Comprehensive studies for the characterization of these isolates and the mechanism involved in this resistance are needed.

Keywords: MRSA, ceftaroline, antimicrobial resistance.