

TITLE: QUINOLONES AND ANTISEPTIC RESISTANCE AND PRESENCE OF EFFLUX PUMPS GENES IN METHICILLIN-RESISTANT *Staphylococcus aureus* ISOLATES FROM HOSPITALS IN RIO DE JANEIRO

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ABSTRACT:

MRSA isolates are often isolated from healthcare-associated infections. Resistance based on the presence and expression of efflux pumps has been associated with a high minimum inhibitory concentration (MIC) of antibiotics and antiseptic agents, such as chlorhexidine. The aim of this study was to characterize the resistance to antibiotics and antiseptics and identify the presence of efflux pumps and related genes in clonal lineages of MRSA isolates from Rio de Janeiro hospitals. Eighty MRSA isolates were evaluated to determine MIC for ciprofloxacin, moxifloxacin, and chlorhexidine (CHX) by the broth microdilution method. Detection of efflux pump genes *qacA/B* and *smr* was performed. Phenotypic expression of efflux pumps was analyzed by cartwheel method. Study of cross-resistance mediated between antibiotics and CHX has been determined in ten isolates exposed to sublethal doses of these compounds for up to 14 days and changes in the susceptibility were determined by MICs analysis for 6 drugs (moxifloxacin, vancomycin, ciprofloxacin, tetracycline, gentamicin and CHX). Among all isolates, MIC₉₀ for ciprofloxacin, moxifloxacin and CHX were $\geq 256 \mu\text{g/mL}$, $32 \mu\text{g/mL}$, and $1 \mu\text{g/mL}$, respectively. Among 18 (22.5%) isolates positive for active efflux pump systems, eight presented the highest efflux potential and four of them belonged to the USA100/ST5 lineage. For 14 isolates positive to the *qacA/B* gene, 10 (71.4%) were also associated with the USA100/ST5 lineage. On the other hand, among 21 isolates positive to the *smr* gene, 15 (71.4%) of them carried the SCCmecIV. Moreover, two isolates belonging to USA100/ST5 lineage were positive for both *qacA/B* and *smr* genes. Exposure to sublethal doses of ciprofloxacin evidenced nine isolates with increased resistance to fluoroquinolones (>16-fold MIC increase). Cross resistance was also found to tetracycline, gentamicin and CHX. When isolates were exposed to sublethal doses of CHX, one isolate show cross resistance for ciprofloxacin. The data show that specific hospital lineages of MRSA isolates present active efflux pump systems and related genes, such as USA100/SCCmec II isolates (*qacA/B* genes) and isolates carrying SCCmec IV (*smr* gene). It is important to note that cross-resistance between antibiotics and biocides reinforces the importance of rational use of both in the hospital environment.

Keywords: MRSA; efflux pumps; multidrug resistance; chlorhexidine; cross-resistance

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