

***In vitro* and *in vivo* studies of antibacterial effect of ceftriaxone moxifloxacin combination against methicillin resistant *Staphylococcus aureus* biofilms formed on biomedical implants**

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Methicillin resistant *Staphylococcus aureus* (MRSA) is the etiologic agent of a wide range of diseases worldwide including the Middle East. Biofilm production is an important virulence attribute in the pathogenesis of device-related MRSA infection. Our aim was to study the bactericidal effect of cephalosporin/fluoroquinolone combinations against MRSA biofilm *in vitro* and *in vivo*. The minimal inhibitory concentrations (MICs) were evaluated by microdilution method. All studied MRSA strains were highly resistant to cephalosporins (MIC₉₀, 500 - 1,000 µg/ml). Moxifloxacin showed higher activity than levofloxacin (MIC₉₀, 6.25 and 12.5 µg/ml, respectively). The combinations were studied using checkerboard technique. Ceftriaxone/moxifloxacin revealed 50% synergistic effect contrary to ceftriaxone/levofloxacin combination (16.7%). Rate of biofilm inhibition was determined by the time kill assay. When biofilm coated catheter was exposed to ceftriaxone and/or moxifloxacin, the combination showed 3–7.5 log reduction compared to the starting point after 24 h while it was only 1–3 and 2–4 log reduction with ceftriaxone and moxifloxacin, respectively. Levels of inflammatory markers as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) were evaluated by enzyme-linked immunosorbent assay (ELISA). Co-administration of both antibiotics to bacterial strain challenged rats showed significant reduction in TNF-α and IL-6 levels ($P < 0.001$).

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