Molecular Characterization of Ofloxacin-Resistant *Mycobacterium tuberculosis*

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Minimum inhibitory concentrations (MICs) of ofloxacin (OFX) and moxifloxacin (MXF) were investigated against 69 clinical strains of *Mycobacterium tuberculosis* isolated in Hong Kong. Nineteen isolates were resistant to OFX. Molecular characterization of the 120-bp quinolone resistant determining region (QRDR) was determined by PCR-DNA sequencing of gyrase A (*gyrA*) gene. All strains harbored a Ser95Thr which is a natural polymorphism among clinical isolates in Hong Kong. For the 50 OFX-susceptible isolates, mutations associated with OFX-resistance in the QRDR were not detected. Overall, 84.2% (16 of 19) of the OFX-resistant strains harbored mutations in *gyrA* gene. Thirteen OFX-resistant isolates exhibited mutations at hotspot positions Ala90Val, Ser91Pro and Asp94 (Gly/Ala/Asn/Tyr/His). Three novel mutations were found at positions 70, 74 and 126. The mutant prevention concentrations (MPCs) of OFX and MXF were further investigated for the 50 OFX-susceptible isolates among which 10 were multidrug-resistant tuberculosis (MDR-TB) strains. The activity of MXF was higher than that of OFX against all isolates tested, with lower MIC_{90} (0.25 mg/L) and MPC_{90} (0.6 mg/L). Simultaneously, MXF displayed higher ratios of $Cmax/MIC_{90}$, $AUC_{0\text{-}24}/MIC_{90}$, $Cmax/MPC_{90}$ and $AUC_{0\text{-}24}/MPC_{90}$. Our findings revealed that MXF served as a promising drug for treatment of both non-MDR and MDR-TB in Hong Kong.

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