Title: A molecular analysis of quinolone-resistant haemophilus influenzae: Validation of the mutations in quinolone resistance-determining regions

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Body: OBJECTIVE We validated the genetic mechanisms of quinolone resistance in H. influenzae. MATERIALS AND METHODS We used 29 H. influenzae strains included 11 quinolone-resistant strains. We analyzed each sequences of Quinolone Resistance-Detamining Regions (QRDRs) and made a comparison of their mutations between resistant and susceptible strains. Furthermore, we induced mutations in susceptible strains by selection with quinolone, and investigated the associations between these mutations of QRDRs and decreased susceptibilities to quinolones. RESULTS Figure 1 showed, several amino acid changes in GyrA (at Ser84 and Asp88) and ParC (at Gly82, Ser84 and Glu88) are closely related to the MICs against quinolones. The strains with MFLX MICs of 0.125-1 and 2-4 µg/ml had one and two amino acid changes of GyrA and ParC, respectively. Especially, the five strains with MFLX MIC of ≥8 µg/ml had three or more amino acid changes in their QRDRs. The isolates induced mutations with MFLX MICs of <2 and ≥2 µg/ml had one and two amino acid mutations in their QRDRs, respectively. CONCLUSION The isolates induced mutations had the same mutations as resistant strains. From this result, we confirmed the several mutations of GyrA (at Ser84, Asp88) and ParC (at Gly82, Ser84, Glu88) closely contribute to quinolone resistance. In addition, more these mutations of QRDRs, became highly quinolone-resistant.