Mechanisms accounting for fluoroquinolone multidrug resistance Escherichia coli isolated from companion animals

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Abstract:

Multidrug resistance (MDR) is associated with fluoroquinolone (FQ) resistance in companion animal Escherichia coli (E. coli). In this study, gyrA, gyrB, parC, and parE quinolone resistance determining regions (QRDR) were sequenced among uropathogenic E. coli isolates with different resistant phenotypes. Also determined were porin, efflux pump and regulatory gene expression based on quantitative real-time reverse transcriptase PCR (qRT-PCR), the impact of efflux pump inhibition (Phe-Arg-β-naphthylamide) and the presence of plasmid-mediated quinolone resistance (PMQR). Using enrofloxacin as the prototypic FQ, we found that (i) the number of mutations in target genes correlate well with minimum inhibitory concentrations (MICs). A single mutation (Ser83Leu) in gyrA increases FQ MIC in susceptible isolates; subsequent mutations result in resistance that increases from low (enrofloxacin MICs 4-16 µg/ml) to high level (enrofloxacin MICs≥128 µg/ml) with each progressive mutation. (ii) as MIC increase, acrB activity and the number of drug classes contributing to the MDR phenotype increases; (iii) a consistent relationship between regulatory gene expression and MIC could not be identified; and (iv) qnrS and aac(6')-Ib-cr gene were detected in 14 and 5 ENR(R)-MDR isolates containing the target mutation, respectively. Of 13 isolates expressing PDR isolates, 10 (77%) were positive for qnrS gene, and 4 (40%) carried both qnrS and aac(6')-Ib-cr gene. These findings demonstrated that MDR-associated FQ resistance in canine and feline uropathogenic E. coli reflects a combination of point mutations, enhanced efflux pump activities, and PMQR mechanisms. Point mutations in DNA gyrase, however, are necessary to achieve a clinical level of FQ resistance.

Keywords:

E. coli; s-lactams; fluoroquinolone; antimicrobial resistance

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