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THE INFLUENCE OF SINGLE NUCLEOTIDE POLYMORPHISM (SNP) MUTATIONS IN *GYRA, GYRB, PARC* AND *PARE* ON THE ACQUISITION OF FLUOROQUINOLONE AND CROSS-RESISTANCES IN *SALMONELLA ENTERICA* SUBSPECIES *ENTERICA* SEROVAR ENTERITIDIS

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Fluoroquinolones (FQs), broad-spectrum bactericides, are the antibiotics of choice for treatment of invasive, life-threatening infections caused by *Salmonella enterica*. In this study, we aimed to identify and characterize non-synonymous single nucleotide polymorphisms (nsSNPs) mutations in the *gyrA, gyrB, parC* and *parE* genes, responsible for FQ-resistance in four resistant (MIC 8-16 µg/mL) and four highly resistant (MIC>128 µg/mL) *S. enterica serovar* Enteritidis strains, respectively. Initially, we used four clinical FQ-susceptible (MIC 0.06–0.12 µg/mL) *S. Enteritidis* strains (A5-S, A7-S, A21-S, and A33-S) and selected four spontaneous FQ-resistant (A5-R, A7-R, A21-R, and A33-R) and four FQ-highly resistant (A5-HR, A7-HR, A21-HR, and A33-HR) *S. Enteritidis* strains *via* a stepwise assay using ciprofloxacin as a selective agent. Among both, the resistant and highly resistant strains, no nsSNP were found in the gyrB and parE. In contrast, all the resistant strains had a substitution of S (Ser) for Y (Tyr) and F (Phe) at position 83 of the GyrA. The highly resistant strains together with A5-R strain acquired a second substitution of D (Asp) to G (Gly) at position 87 of the GyrA. For the ParC enzyme, we found a substitution of G for D at position 78 in the A7-HR strain and S for R (Arg) and I (Ile) at position 80 in the A5-R and A5-HR, respectively. By performing a cross-resistance assay using the resistant and highly resistant strains, we found that exposure of *S. Enteritidis* to FQ selects for additional resistance to cefoxitin, amikacin, chloramphenicol, and ceftiofur, antibiotics that do not belong to FQ class of antibiotics. Our study showed that amino acid substitution at position 83 of the GyrA is crucial for the acquisition of FQ-resistance, while substitution at position 87 of the same enzyme provides a high-level FQ-resistance. In addition, we showed that FQ exposure selects for the cross-resistance to some beta-lactam (cefoxitin and ceftiofur), aminoglycoside (amikacin) and chloramphenicol classes of antibiotics.

Biography

Sinisa Vidovic completed his PhD program in 2008 at the University of Saskatchewan, Canada and Postdoctoral trainings at the Medical College, University of Ottawa and the Vaccine and Infectious Disease Organization, University of Saskatchewan. Presently, he works as an Assistant Professor at the Department of Veterinary and Biomedical Sciences, University of Minnesota, USA. He has published over 20 peer-reviewed articles.

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