

TITLE: *Salmonella* Enteritidis PERSISTER CELLS PRESENT SMALL COLONY VARIANT AFTER EXPOSURE TO CIPROFLOXACIN

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ABSTRACT:

Salmonella Enteritidis usually causes self-limited gastroenteritis, but may be able to trigger asymptomatic, acute and even persistent infections. In order to survive a hostile environment, microbial populations may produce persister cells, which comprise a small subpopulation of cells able to survive lethal concentrations of bactericidal antimicrobials, even being genetically susceptible to them. Another phenotype has been described as a variant colony grown on agar plates after antimicrobial exposure that differs from the regular phenotype by its smaller size, called small colony variant (SCV). These phenotypes may present great importance in public health due to recurrent therapy failures, especially in infections associated with biofilms. In this sense, we investigated the presence of persister cells from *S. Enteritidis* after exposure to ciprofloxacin in planktonic and biofilm cultures for 72 h. Persister cells levels of 0.0108% and 0.1% were found in planktonic and biofilm cultures, respectively, when exposed to supra-lethal doses of ciprofloxacin (100-fold MIC). In both experiments, a biphasic killing curve was observed with a heterogeneous pattern represented by rapid death of susceptible cells, followed by a plateau. A small portion of colonies formed by persister cells showed a smaller size after incubation for 24 h, presenting ~ 0.5 mm diameter in contrast to the 2 mm diameter presented by regular colonies (RC). Scanning electron microscopy (SEM) was performed in order to view possible changes in cell morphology after ciprofloxacin exposure. It was possible to observe a decrease in cell size comparing persister cells from RC and SCV in both planktonic and biofilm cultures with cells from cultures without antimicrobial treatment. Therefore, we confirmed that *S. Enteritidis* presented persister cells, especially under biofilm culture, when exposed to ciprofloxacin, a common drug used for treatment of invasive salmonellosis. In addition, the experiments carried out in this study show at the first time SCV in *S. Enteritidis* persister cells formed after exposure to ciprofloxacin.

Keywords: biofilm, fluoroquinolone, persistence, *Salmonella*.

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