Ciprofloxacin and the Brain: Unraveling Anxiety-Like Effects and Proteomic Alterations in Mice

Karliane Rodrigues da Silva[1], Paula Ruani Farias Barata[1], Karen Renata Herculano Matos Oliveira[1], Luana Ketlen Reis Leão [1], Juliana Silva Cassoli[1]

[1.] UFPA , Federal University of Pará, Rua Augusto Corrêa, 1 - Bairro: Guamá/ Belém (PA);

Introduction: Ciprofloxacin, a broad-spectrum antimicrobial agent from the fluoroquinolone family, is effective against both gram-negative and gram-positive bacteria and is commonly used to treat urinary tract, respiratory, and gastrointestinal infections. Despite its widespread application, ciprofloxacin is associated with adverse neurological effects, including headache, dizziness, agitation, sleep disturbances, and seizures. These neurological manifestations are purportedly linked to the binding of quinolones to GABAA receptors in the brain, which inhibits the neurotransmitter gamma-aminobutyric acid (GABA), resulting in central nervous system (CNS) stimulation and anxiety-like behaviors. **Aim:** This study aims to investigate the effects of varying doses of ciprofloxacin on anxiety-like behavior and to elucidate the protein profile of brain samples from Balb/c mice. **Materials and Methods:** Balb/c mice were administered intraperitoneal doses of ciprofloxacin at 20 mg/kg, 35 mg/kg, and 50 mg/kg and vehicle (control) over a period of 7 days (n=10 each group). Behavioral assessments were conducted using the open field test to evaluate locomotor and exploratory activities and the elevated plus maze test to assess anxiety-like behaviors. Post-behavioral testing, the mice were euthanized, and brain tissues were collected via craniotomy and stored at -80°C. For proteomic analysis, the samples were subjected to cell lysis (chemical and mechanical), alkylated with iodoacetamide, and digested with trypsin. The resulting peptides were desalted and analyzed using mass spectrometry. **Results:** In the open field test, ciprofloxacin-treated mice demonstrated reduced locomotor activity compared to controls, with increased time spent in the periphery ($p = 0.8775$; $F [3, 24] = 0.2258$) and decreased time in the center ($p = 0.1899$; $F [3, 16] = 1.789$), indicating anxiety-like behavior, albeit without statistical significance. Significant differences in \'grooming\' behaviors were observed between treated and control groups ($p < 0.0001$; $F [3, 27] = 15.76$), while \'rearing\' behaviors showed no significant differences ($p = 0.6346$; $F [3, 25] = 0.5785$). In the elevated plus maze test, the number of entries into the open arms was significantly reduced in treated groups at doses of 35 mg/kg and 50 mg/kg compared to controls ($p < 0.0001$; $F [3, 25] = 17.48$), with no significant difference at the 20 mg/kg dose. No significant differences were observed in entries into the closed arms, though treated groups exhibited increased closed arm entries compared to controls. Vertical exploration (rearing) did not show significant differences ($p = 0.1023$; $F [3, 28] = 2.270$), though a reduction in vertical activity was noted. **Conclusion**: Preliminary data suggest that ciprofloxacin administration may induce anxiety-like behaviors in mice, characterized by decreased locomotor activity and alterations in grooming, vertical, and horizontal exploratory behaviors. These findings warrant further investigation into the neurobiological mechanisms underlying these effects.

Agradecimentos: