EFFECT IN VITRO OF HALOPERIDOL AND RISPERIDONE IN INFLAMMATORY RESPONSE OF RAW 264.7 MACROPHAGES CELLS

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Introduction: Antipsychotic drugs, such as Haloperidol and Risperidone, when used in long-term, can increase the risk of obesity and other endocrine dysfunctions in psychiatric patients. There are evidences suggesting that these drugs have pro-inflammatory effect, which contributes to the establishment of these disorders. However, results produced until now are contradictory. Therefore, investigations into isolated cells of the immune system that are directly involved in the inflammatory process are of interest. Objective: To investigate the in vitro effect of three concentrations of Haloperidol and Risperidone (20, 30 and 40 µM) on activation of RAW 264.7 macrophages lineage. Methods: The macrophages were cultured in RPMI 1340 with 10% fetal bovine serum and 1% antibiotic at 37°C in a 5% CO2 atmosphere. We analyzed the nitric oxide levels, cell viability 24, 48, 72 hours after exposure, production of inflammatory and proinflammatory cytokines and induction of apoptosis, by examining the expression of Bcl-2 and BAX genes and quantifying caspases 3 and 8. Results: Macrophages exposed to different concentrations of these drugs show increased in nitric oxide levels and decreased in viability after 24, 48 and 72 hours of exposure. Initial apoptosis was significantly higher in cells treated with 40 µM Haloperidol and in all treatments with Risperidone after 24 hours exposure. Bcl-2 / BAX ratio was lower than 1 in cells treated with the drugs, indicating apoptotic induction. The levels of caspases 3 and 8 levels also increased in a dose-dependent manner. The inflammatory cytokines levels increased in all treatments (IL-1β, IL-6, TNF, INFγ), while levels of IL-10 anti-inflammatory cytokine decreased. Conclusion: The results suggest that these drugs acts on macrophages activation and can exacerbate inflammatory processes. The activation of macrophages could contribute to the development of obesity caused by the use of these drugs for long time. Acknowledgments: Fapergs/CAPES/CNPQ. Keywords: antipsychotics, inflammation, macrophages.