Dual Effects of Antipsychotic Drugs on the Viability of Neuro-2A Cells

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Introduction: The pathogenesis of some neuronal disorders has been associated to the cell death with involvement of the oxidative stress. Abnormal mitochondrial ROS generation associated to persistent changes in the mitochondrial permeability and integrity seems to play central role in this process. Psychotropic drugs has been associated to the modulation of mitochondrial functions conferring neuroprotective effects. However, there is a lot of controversy about the cytoprotective versus cytotoxic action of these drugs. In this work we evaluated the effects of the antipsychotic drugs, chlorpromazine (CPZ) and thioridazine (TR) on basal conditions and the hydrogen peroxide-induced oxidative stress in Neuro-2A cells.

Material and Methods: Cell viability was estimated by using the MTT reduction assay and LDH release was measured by kinetic method of pyruvate reduction. The mitochondrial transmembrane potential was determined spectrofluorimetrically with rhodamine 123.

Results and Discussion: The pre-incubation with 2.5 μM TR for 2 h before the exposition of cells to 0.5 mM H₂O₂ for 24 h decreased the observed cell death about 15%. In the same conditions, CPZ did not exhibit this cytoprotective effect. Both drugs did not protect Neuro-2A cells exposed to 0.5 mM H₂O₂ for 6 after pre-incubation with drugs for 24 h. LDH release, indicative of plasma membrane permeabilization, was not observed in the H₂O₂-induced cell death. At higher concentrations, both drugs induce cell death with EC₅₀ about 68 and 27 μM, CPZ and TR, respectively, for 24h incubation, associated to the mitochondrial depolarization.

Conclusions: TR, but not CPZ, protected Neuro-2A cells against H₂O₂-induced cell death at low concentrations and this effected was switched to cytotoxicity with mitochondrial involvement at higher concentrations.

Keywords: antipsychotic drugs, thioridazine, chlorpromazine, oxidative stress.
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