AMINOCRHOME INDUCES DOPAMINERGIC NEURONS DEATH IN ORGANOTYPIC MIDBRAIN

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BACKGROUND: Parkinson's disease (PD) is the second most common neurodegenerative disease in developed countries. The motor symptoms manifested in PD are clearly linked to the degeneration and death of dopaminergic neurons of the substantia nigra. It is believed that the main reason is the formation of the semiquinone-o-leucoaminochrome from aminochrome (oxidized form dopamine and precursor of neuromelanin), which is extremely reactive and may cause mitochondrial damage and subsequent activation of apoptotic mechanisms, besides favoring formation of neurotoxic protofibrils. OBJECTIVE: Evaluate the neurotoxicity of aminochrome in organotypic cultures of midbrain. METHODOLOGY: We used organotypic midbrain cultures from 8 days postnatal Wistar rats. The slices were cultivated for 3 days with DMEM F12, incubated in 5% CO2 at 35°C. After, we treated the slices with the aminochrome at concentrations of 1nM, 2,5nM and 5 nM, for 48h. Then evaluated the neurotoxicity induced by aminochrome using lactate dehydrogenase (LDH) test, measuring this enzyme in the supernatant of cultures. Moreover we used Western Blot with detecting of enzyme tyrosine hydroxylase, a specific dopaminergic neurons marker.

DISCUSSION AND RESULTS: Analyzing cell viability by LDH test, we observed an increase in the amount of this enzyme in the culture supernatant, showing cell death by membrane damage and extravasation of this enzyme to the extracellular medium. By Western-blot assay we marked tyrosine hydroxylase and observed a decreased expression of this enzyme in cultures exposed to 2.5nM of aminochrome, suggesting a dopaminergic neuronal degeneration. CONCLUSIONS: This results show a neurotoxic action of aminochrome in organotypic midbrain cultures.

Key-words: Parkinson disease, aminochrome, organotipic midbrain culture

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