OXIDATIVE STRESS AS A FACTOR INVOLVED IN MALAOXON-INDUCED NEUROTOXICITY

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Introduction and Objectives: Organophosphates (OPs) represent a class of compounds that include many of the most common agricultural and commercial pesticides used worldwide. The acute toxicity induced by OPs is primarily caused by the irreversible inhibition of acetylcholinesterase (AChE) enzyme. However, there is substantial evidence that OP low levels exposures can be associated with neurobehavioral and cognitive deficits even in the absence of the classical (cholinergic) signs of acute toxicity. Although, molecular mechanisms related to this non-cholinergic neurotoxicity, especially with regard to oxidative stress, are not yet fully understood. So, this study aimed to investigate the role of oxidative stress in the neurotoxicity induced by exposure to malaoxon (Mx), the active metabolite of the OP Malathion, in an in vitro model of mouse primary cell cultures of cortical neurons.

Materials and Methods: Primary cultures of cortical neurons were incubated with different concentrations of Mx (0.01 - 100 µM) and cell viability was determined at 24 and 48 hours or 6 days in vitro by the MTT method. AChE enzyme activity was determined by the production of thiocholine from the hydrolysis of acetylthiocholine. Superoxide anion production was determined by using fluorescent dye dihydroethidium (DHE).

Results and Conclusions: A significant decrease in cell viability was observed at 48 hours (1-100 µM) and 6 days (0.1-100 µM) after Mx treatment. In addition, a significant increase in pro-oxidative stress-related parameters was observed in 24 hours after Mx treatment (0.01-100 µM). Pretreatment of the cells with the antioxidant ascorbic acid (200 µM) prevented the oxidative damage, either exhibited partial neuroprotective effects by preventing Mx-induced cell death. Finally, Mx treatment (100 µM) significantly decreased AChE activity in a time-independent manner. These results indicate the occurrence of oxidative stress in neuronal cortical cells soon after Mx exposure, which seems to have a partial role in Mx-induced neurotoxicity.

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Key Words: Malaoxon, cell culture, oxidative stress