Abstract

The Mechanism of ROS Activity, P53 and Caspase 3 Expression, and Neuron Cell Death in Mice (Mus musculus) Embryonic Cerebral Cortex of Carbofuran Insecticide Exposure

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The aim of this study was to describe the process of neuronal cell death in cerebral cortex caused by exposure to insecticide carbofuran in embryonic period. This laboratory experimental study used 81 mice fetuses from 27 breeding mice and carbofuran was exposed with gavage in 6-15 days gestation in a dose of 0.0417 mg/kg BW and 0.0208 mg/kg BW. At 17 days of gestation the mice were sacrificed and the fetuses were taken to measure cerebral activity of ROS (malondialdehyde/MDA and superoxide dismutase/SOD) and calculating the average number of embryonic cerebral cortex neuron cells that undergo apoptosis using Apoptag Apoptosis Detection Kit and necrosis using HE staining. Assessment of p53 and caspase 3 expression used immunohistochemistry. The results of calculation of ROS activity, necrosis, apoptosis, calculation of p53 and caspase 3 expression were averaged and analyzed by analysis of variance (Anova) and least significant difference test (LSD). It was concluded that the insecticide carbofuran exposure during embrionic period may increase the activity of embryonal cerebral ROS characterized by elevated levels of MDA ($p<0.05$), and decreased SOD ($p<0.01$), increased p53 and of caspase 3 expression, and cerebral cortical neurons cell death either by necrosis or apoptosis ($p<0.05$). At the low dose (0.0208 mg/kg), carbofuran insecticide can lead to increased expression of p53, caspase 3 and apoptosis. At the high dose (0.0417 mg/kg), it can lead to increased levels of MDA and necrosis. There is a correlation between the dose of carbofuran exposure and MDA levels and p53 expression. There was a high correlation between the dose of exposed carbofuran and SOD activity. There is a correlation between the SOD activity and MDA levels and p53 expression. There is a correlation between the expression of p53 and caspase 3, and cells undergoing apoptosis and necrosis. There is a high correlation between the expression of caspase 3 with cells undergoing apoptosis. Increased expression p53 and caspase 3 and apoptosis showed that the insecticide carbofuran caused apoptosis through the intrinsic pathway. The fact that the increased apoptoric embryonal neurons open an opportunity of prevention and treatment of the effect of ROS activities due to carbofuran insecticide exposure during pregnancy.

Keywords: *carbofuran, ROS, p53, caspase 3, neuron cell death, embryonal cerebral cortex*