MICROGLIAL ACTIVATION AND NIGROSTRIATAL NEURONAL DEATH FOLLOWING CHRONIC DICHLORVOS EXPOSURE IN RAT

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In recent years, several lines of evidence have shown an increase in Parkinson’s disease (PD) prevalence in rural environments where pesticides are heavily used. The present investigation was carried out to elucidate a possible molecular mechanism of nigrostriatal neuronal death after chronic dichlorvos exposure with special emphasis on neuroinflammation. In this study, we report that chronic dichlorvos exposure (2.50 mg/kg b.wt. s.c/daily for 12 weeks) caused marked microglial activation leading to nigrostriatal dopaminergic neurodegeneration as evident from the immunohistochemistry and FACS analysis. Microglial marker (Mac-1) expression was increased at transcription as well as translational levels in the substantia nigra (SN) and corpus striatum (CS) of rats exposed to dichlorvos. Activated microglia were seen in SN and CS of dichlorvos treated animals but were rarely observed in controls. Double immunostain, revealed lesser number of TH positive neurons and higher number of activated microglia in SN and CS region after dichlorvos treatment. The mRNA and protein levels of the NADPH-oxidase, main subunit gp91\textsuperscript{phox} were significantly increased after dichlorvos administration. Increased gp91\textsuperscript{phox} immunoreactive cells were observed in activated microglia in the SN and CS of rats treated with dichlorvos. It also lead to increased levels of IL-1\textbeta, TNF-\alpha and IL-6 in ventral midbrain and CS at transcription as well as translational levels. Chromatin condensation was seen in the dichlorvos treated animals. Many mitochondria in neuropil of SN were greatly enlarged and swollen into spherical shape. All these findings taken together indicate that chronic dichlorvos exposure cause neuroinflammation leading to nigrostriatal neuronal death.