

Investigation of lead-induced neurotoxicity in PC12 cell: Role of Nitric Oxide & Apoptosis

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Objective: The nervous system is one of most important targets of lead poisoning. Despite decades of study, the exact mechanism of lead neurotoxicity, has not been fully elucidated. Therefore the present study sought to examine role of apoptosis and nitric oxide (NO) production in lead induced neurotoxicity using PC12 cells as a suitable model of neuronal cell. **Methods:** PC12 Cells were grown in DMEM medium and incubated with various concentrations of lead acetate (0.01-180 μ M) for 24, 48 and 72 hours. The cell viability was determined using MTT assay. NO were determined by measuring nitrite (NO₂) and nitrate (NO₃) present in the culture medium using NO colorimetric method. Apoptosis was shown by two different methods: DNA fragmentation and expression of proteins involved in apoptosis (Bax & Bcl-2). **Results:** The present result showed lead could induce toxicity in PC12 cells after 24 hours as little as 1 μ M in a concentration- and time- dependent manner. The cytotoxicity was positively correlated with increased NO_x (nitrite and nitrate) production in these cells. L-NAME, a NOS inhibitor, treatment (2.5 mM) could reverse this cytotoxicity. On the other hand in Western blot analysis, the ratio of Bax/Bcl-2 protein expression in cells incubated with 3, 30 and 90 μ M lead acetate significantly increased compared to controls. Additionally DNA laddering pattern in lead treated cells were shown which could indicate nuclear fragmentation. **Conclusion:** It can be concluded nitric oxide could be an important mediator of lead-induced cell death. in which apoptosis or programmed cell death play an important role.