LEAD INDUCES APOPTOSIS (PROGRAMMED CELL DEATH) IN HUMAN LEUKEMIA (HL-60) CELLS VIA OXIDATIVE STRESS

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Abstract: Lead is a multi-targeted toxicant that affects many organ systems including; the gastrointestinal tract, hematopoietic system, cardiovascular system, central and peripheral nervous systems, immune system, and reproductive system. There are many published studies that have documented the adverse effects of lead in children and the adult population. Previous in vitro studies in our laboratory have shown that lead nitrate induces cytotoxicity to HL-60 cells in a dose-dependent manner. However, the molecular mechanisms of toxicity and carcinogenesis are still largely unknown. In this research, we hypothesized that oxidative stress plays a key role in lead nitrate-induced toxicity and cell death in human Leukemia (HL-60) cells. To test this hypothesis, we performed lipid hydroperoxide assay for assessing the levels of the degradation products of polyunsaturated fatty acid (PUFA) hydroperoxide in lead nitrate-treated HL-60 cells and the flow cytometric analysis of phosphatidylserine externalization to detect the percentage of death cell. Data generated from lipid hydroperoxide assay resulted in a significant increase (p < 0.05) in the production of hydroperoxides (degradation products of lipid peroxidation) with increasing doses of lead nitrate in treated cells. Upon 24 h of exposure, the hydroperoxide concentrations in the sample [μM] (mean ±SE, n = 3) compared to untreated control were 6.7 ± 2, 7.1 ± 1, 14.7 ± 2, 15.7 ± 6, 16.2 ± 4, and 15.2 ± 1 in 0, 10, 20, 30, 40, and 50 μg/mL of lead nitrate, respectively. The results of flow cytometric assessment (Annexin V) also showed a strong dose-response relationship between lead nitrate exposure and early stage apoptosis in HL-60 cells. In summary, these studies show that lead nitrate represents an apoptosis-inducing agent in human Leukemia (HL-60) cells and its apoptotic mechanism is mediated through oxidative stress and phosphatidylserine externalization.

Keywords: Lead nitrate, annexin V, HL-60 cells, phosphatidylserine externalization, lipid peroxidation

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