Arсенный триоксид индуцирует апоптоз через гидроксид-перекисной-зависимый путь и активацию caspase-3 в клетках HeLa человека

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**Background** Inorganic arsenic trioxide (As₂O₃) at a low dose (1–2µmol/L) was shown to have a therapeutic effect against acute promyelocytic leukemia (APL) cells, even in patients resistant against all-trans-retinoic acid or conventional chemotherapy, by induction of apoptosis of APL cells. Furthermore, it has been shown that As₂O₃ induced apoptosis through activation of caspases in B-cell leukemia cell lines. This raised interest in its apoptotic effect in other solid tumors, therefore, we investigated apoptotic effects and its possible mechanisms of As₂O₃ in HeLa human cervical carcinoma cell lines.

**Methods** To investigate the potential effects of As₂O₃ in HeLa cells and its possible mechanisms, the cells were exposed to clinically achievable concentrations of As₂O₃ (1–2µmol/L). Apoptosis was characterized by FITC-annexin V/PI staining and nucleosomal DNA fragmentation. Caspase-3 activation was measured using flow-cytometric analysis and Western blotting. Loss of mitochondrial membrane potential was also measured by flow cytometry and intracellular H₂O₂ concentration was analysed with specific fluorescence dye.

**Results** Clinically achievable concentration of As₂O₃ induced apoptosis in HeLa cells characterized by FITC-annexin V/PI staining and nucleosomal DNA fragmentation. The induction of apoptosis by As₂O₃ involves an increase in H₂O₂ content and decrease in cellular mitochondrial membrane potential, followed by caspase-3 activation, and DNA fragmentation. As₂O₃ induced H₂O₂ production and apoptotic cell death was almost completely inhibited in the presence of N-acetyl-L-cysteine, a precursor of antioxidant glutathione. In addition, incubation of cells with catalase resulted in decrease of apoptotic cell death.

**Conclusion** As₂O₃ induces apoptosis mediated by hydrogen peroxide production, loss of mitochondrial membrane potential, and caspase-3 activation in HeLa cervical cancer cell line.