ARSENIC TRIOXIDE-INDUCED GENOTOXICITY AND MORPHOLOGICAL CHANGES OF APOPTOSIS IN LUNG CELL

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Abstract: Lung cancer is one of the most lethal and common of cancers in the world, causing up to 3 million deaths annually. The drugs used for treatment are toxic in patients and patients have developed a resistance to them. Therefore, the prognosis of lung cancer is still very poor. There is a need to discover new strategies for the treatment of lung cancer. One strategy is to investigate the mechanisms of action of arsenic trioxide to determine whether arsenic trioxide can be a possible treatment for lung cancer. Arsenic trioxide, the trade name Trisenox, has been used for the treatment of relapsed/refractory acute promyelocytic leukemias. Arsenic trioxide has been shown to induce genotoxicity in liver and colon as well as induce apoptosis in liver, breast, lung and colon cancer cells. The cellular and molecular studies of arsenic trioxide on lung (A549) cancer cells are poorly understood. Therefore, the purpose of this study is to investigate arsenic trioxide-induced genotoxicity and apoptosis in lung (A549) cancer cells. To achieve these aims, A549 cells were cultured following standard protocols, and exposed to various doses (0, 2, 4, and 6 µg/ml) of arsenic trioxide for 48 h. The 4’, 6-diamidine-2 phenylindole (DAPI) staining of A549 was conducted to observe the nuclear morphological changes in ATO-induced apoptotic cells. To evaluate the genotoxic potential of arsenic trioxide in A549 cells, the comet assay was conducted to measure DNA damage associated with arsenic trioxide toxicity. The DAPI staining revealed characteristic morphology of apoptosis (condensed chromatin and apoptotic bodies) at 4 and 6 µg/ml of arsenic trioxide. In addition, our studies have shown that arsenic trioxide induced apoptosis as evidence of cell shrinkage, membrane blebbing and condensed chromatin. This study confirmed that arsenic trioxide exposure caused genotoxicity as revealed by the dose-dependent increase in percentage of DNA damage, tail moment and tail length. This study enhances our understanding of arsenic trioxide as a potential chemotherapy agent in treating certain forms of lung cancer in particular non-small cell lung cancer. However, further studies are warranted to understand the cellular and molecular implications of arsenic trioxide.

Keywords: Trisenox, genotoxicity, 4’, 6-diamidine-2 phenylindole (DAPI).

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