Iran. J. Radiat. Res., 2003; 1(1): 17- 22

Oxidative membrane damage and its involvement in gamma radiation-induced apoptotic cell death

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ABSTRACT

Background: Recent results have provided increasing evidence to support involvement of membrane damage in the mechanism of ionizing radiation induced killing of mammalian cells. These findings have stimulated renewed interest in evaluating the damage to membrane as a primary initiator in radiation-induced cell killing especially in apoptotic death. The present study was aimed to gain deeper insight on the molecular mechanisms of radiation-induced damage at membrane level with consequences to apoptotic cell death.

Materials and Methods: Radiation mediated changes in membrane fluidity in egg yolk lecithin (EYL) liposomal membrane were studied by employing 1,6-diphenyl hexatriene (DPH) fluorescence polarization and subsequent oxidative damage by measurement of malondialdehyde (MDA) by thiobarituric acid reactive species (TBARS) spectrophotometrically. Alterations in membrane permeability and nuclear dimensions in γ-irradiated immature mouse thymocytes were investigated by fluorescein diacetate (FDA) and propidium iodide (PI) method, respectively.

Results: Results on irradiated liposomes have shown dose dependent lipid peroxidation with concomitant alterations in bilayer fluidity. These parameters were found significantly modified, when liposomes were prepared with α-tocopherol or cholesterol suggesting the contributions of both the radical scavenging and matrix modifying factors in membrane peroxidative damage. In addition, studies on mouse thymocytes labeled with FDA and PI have shown increased permeability of the plasma membrane and decreased nuclear diameter following γ-irradiation of thymocytes. Alteration in membrane permeability with the time of post-irradiation incubation was found correlated with the induction of apoptotic death of thymocytes.

Conclusion: These results suggest that membrane associated radiation damage were correlated with changes in the nucleus of cells. Moreover, the membrane damage seems a primary trigger in radiation-induced apoptosis which may have implications in cancer radiotherapy. *Iran. J. Radiat. Res.; 2003; 1(1): 17 - 22.*

Keywords: *Liposomes, thymocytes, oxidative damage, membrane permeability, nuclear condensation, apoptosis.*

INTRODUCTION

Ionizing radiations interact with cells producing molecular lesions such as lipid peroxidation of membrane, oxidation of proteins and damage to cellular DNA. Involvement of radical mediated oxidative damage of cellular membrane by ionizing radiation and the consequent loss of cell function have been reported (Ramakrishnan *et al.* 1993, Pandey and Mishra 1999). It is generally accepted that oxidative damage to cellular membrane by ionizing radiation is mediated by reaction of reactive oxygen species (ROS) and / or the cytosolic free radicals. These radicals also react with cellular macromolecules like DNA, proteins and lipid

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