عنوان مقاله:

PI۳K Inhibition Sensitize the Cisplatin-resistant Human Ovarian Cancer Cell OVCAR۳ by Induction of Oxidative Stress

محل انتشار:

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خلاصه مقاله:

Background: This study evaluates the effect of simultaneous AKT inhibition and cisplatin therapy in changes of Reactive Oxygen Species (ROS) production, apoptosis induction, and cell survival in cisplatinresistant OVCAR۳ cell. Methods: OVCAR۳ cancer cells were treated with cisplatin, Ly ۲۹۴۰۰۲ (LY), and cisplatin+Ly to investigate the cytotoxicity effect of the mentioned groups via MTT assay. Then, DCFH-DA (۲′, ۷′- dichlorodihydro fluorescein diacetate) assay kit is used to assess the potential of treated groups in intracellular ROS generation. Protein expression levels of caspase-۳, cleaved caspase ۳, PI۳K, Akt, p-Akt, XIAP, and Survivin are estimated through immunoblotting assay in all three experimental groups. Results: The results showed that all three treated groups, including cisplatin and Ly alone and coadministration of cisplatin+Ly, could reduce the cell vitality of OVCAR۳ cancer cells, induced intracellular production of ROS and increased the expression level of activated caspase ۳ and Akt protein, whereas downregulated the phosphorylation of Akt protein. However, the effect of combination therapy was more tangible compared to single therapy and control groups. In contrast, the expression amount of XIAP, Survivin, and PI۳K did not show detectable changes in comparison with the control group. Conclusions: The results showed that the AKT inhibition by Ly could sensitize the OVCAR۳ cancer cells to the cisplatin and lower the effective dose of cisplatin through hyperactivation of oxidative stress.

کلمات کلیدی:

Caspase-۳, Cisplatin, Ovarian cancer, PI۳K/Akt signaling.