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Therapeutic efficacy of hydrogen-rich saline alone and in combination with PI3K inhibitor in non-small cell lung cancer

Yu Jiang ¹, Gang Liu ¹, Li Zhang ², Sheng Cheng ¹, Chun Luo ¹, Yang Liao ¹, Shuliang Guo ³

Affiliations

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Abstract

The aim of the present study was to investigate the effects of combination therapy of LY294002, a specific inhibitor of phosphatidylinositol 3-kinase (PI3K), with hydrogen-rich saline on the proliferation and apoptosis of the non-small cell lung cancer (NSCLC) A549 cell line and the mechanisms underpinning this. Excessive production of reactive oxygen species (ROS) may induce DNA mutations, DNA damage, genomic instability and cell proliferation, and ROS are involved in several types of cancer, particularly lung cancer. In a previous study, hydrogen was recognized as an antioxidant in preventive and therapeutic applications. The PI3K/protein kinase B (Akt) pathway is an important signaling pathway that may activate downstream of a series of extracellular signals and impact on cellular processes including cell proliferation, apoptosis and survival. To date, the PI3K/Akt signaling pathway has been indicated as a feasible target for novel antineoplastic drugs. Different strategies combining the two treatment modalities have been used in cancer therapy in order to achieve an improved therapeutic response and longer control of tumor modalities control. The present study investigated the effect of hydrogen-rich saline alone and in combination with the PI3K inhibitor, LY294002, on the proliferation, oxidative stress and apoptosis of NSCLC A549 cells. This combination therapy may be more effective than separate drug treatment; it decreased the malondialdehyde level and increased the superoxide dismutase activity. The combination therapy also enhanced the efficacy of anti-proliferation and apoptosis. Similarly, the results of the present study demonstrated that administration of the two agents in combination may inhibit phospho-Akt activity, and reduce expression of heme oxygenase-1 and nuclear factor- κ B p65. The results further suggested that the combination therapy may reduce cell proliferation and promote cell apoptosis by downregulating Akt phosphorylation and inhibiting the PI3K pathway in NSCLC cell lines. Therefore, the present study provided evidence that combined therapy may be a novel therapeutic option for patients with NSCLC.

Figures

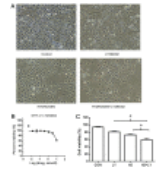


Figure 1. Effects of hydrogen-rich saline and...

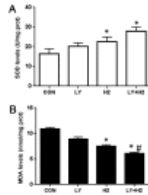


Figure 2. Effects of hydrogen-rich saline and...

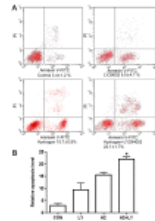


Figure 3. Effects of hydrogen-rich saline and...

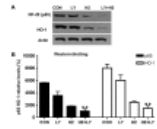


Figure 4. Western blotting analysis of A549...

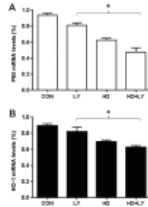


Figure 5. (A and B) Reverse transcription-quantitative...

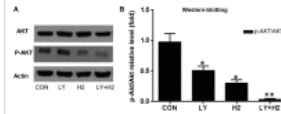


Figure 6. (A and B) Effects of...

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