

Effect of Hyperbaric Oxygen Treatment and Gemcitabine on Apoptosis in Pancreatic Ductal Adenocarcinoma Cells

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Context Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive human malignancies with dismal prognosis. Gemcitabine is one of first-line therapies for locally advanced PDAC; however, severe resistance is responsible for poor survival and response rate. There is evidence that administration of HBOT can enhance the delivery of oxygen to hypoxic tumor cells and increase their susceptibility to the cytotoxic effects of chemotherapy. We hypothesized that the anticancer activity of gemcitabine may be enhanced if tumor cells were placed in oxygen rich environment. **Objective** This study was designed to evaluate the effects of gemcitabine, hyperbaric oxygen treatment (HBOT) and their combination on apoptosis of tumor cells. **Materials and methods** PANC-1 and AsPc-1 tumor cell lines were used because they are sensitive to gemcitabine. Cultured tumor cells were treated with gemcitabine at its growth-inhibitory concentration (IC₅₀) value for the cell line PANC-1: 3.25x10⁻⁸ M and AsPc-1: 1.27x10⁻⁷ M, and HBOT at

2.5 ATA for 90 minutes or combination of both. Twenty-four hours after treatment, the apoptotic cells in each group were analyzed and apoptotic index (AI) was calculated. **Results** PANC-1 cell line: HBOT alone had no effect on AI: 6.5±0.03 vs. 5.9±0.01. HBOT before and after gemcitabine did not increase AI in comparison to gemcitabine alone: AI: 8.2±0.02, 8.5±0.02 vs. 8.1±0.02. Combination of HBOT and gemcitabine significantly increased AI 10.7±0.02 (P<0.001 vs. all groups). AsPc-1 cell line: HBOT alone had no effect on AI: 5.9±0.03 vs. 5.9±0.01. HBOT before and after gemcitabine did not increase AI in comparison to gemcitabine alone: 8.2±0.02, 8.4±0.02 vs. 8.0±0.01. Combination of HBOT and gemcitabine significantly increased AI 9.7±0.02 (P<0.001 vs. all groups). **Conclusion** Our data show that HBOT alone, or administered before and after gemcitabine has no effect on apoptosis in PDAC cells *in vitro*. HBOT significantly increased apoptosis when administered with gemcitabine.