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

Andrea Casarotto¹, Claudio Bosio¹, Gerardo Bosco², Luca Guizzon², Zhongjin Yang³, Aram Megighian², Marta Cannato², LuanaToniolo², Emanuele Nasole², Enrico Camporesi³, Carlo Reggiani², Giacomo Garetto², Claudio Bassi¹

¹Department of Surgery and Laboratory of Translational Surgery (LURM), University of Verona, “Policlinico GB Rossi”. Verona, Italy. ²Department of Biomedical Sciences, Environmental Physiology, University of Padua. Padua, Italy. ³Department of Anesthesiology, SUNY Upstate Medical University. Syracuse, NY, USA

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, 8.4±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.