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Pulsed high-intensity focused ultrasound enhances apoptosis of pancreatic cancer xenograft with Gemcitabine

Eun Sun Lee, Jae Young Lee, Harry Kim, Yoon Seok Choi, Jisuk Park, Joon Koo Han, Byung Ihn Choi
Seoul National University Hospital, Korea.
leejy4u@gmail.com

PURPOSE: To investigate whether combining pulsed high-intensity focused ultrasound (HIFU) with the chemotherapeutic drug Gemcitabine could enhance tumor apoptosis of pancreatic cancer.
MATERIALS AND METHODS: All experiments were conducted with our institutional animal care and use committee approval. Human pancreatic cancer cells were inoculated subcutaneously in BALB/c Nude mice at bilateral flank. When tumors reached an approximate (± 20%) size of 500 mm^3,mice were randomly assigned to one of two groups; 1) the mice were divided into 5 subgroups (4 mice in each group) by the dosage of Gemcitabine from 0 to 200 mg/kg, 2) the mice were divided into also 5 subgroups (4 mice in each group) by the therapeutic time interval between Gemcitabine injection and HIFU therapy from immediate to 24 hours. In group 1, HIFU was performed immediately after Gemcitabine injection and in group 2, the dosage of Gemcitabine was fixed to 150 mg/kg. All administration of Gemcitabine was given by intraperitoneal injection and the mice were sacrificed 3 days after HIFU therapy in order to guarantee the time for cell apoptosis. Tumors were stained with Harris Hematoxylin Solution and Eosin Y and apoptotic cells were measured by terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay by quantification. Statistical analysis was performed by grouping in each group; 1) 100 mg/kg or less vs. more than 100 mg/kg of Gemcitabine, 2) 2 hours or less vs. more than 2 hours of therapeutic time interval.
RESULTS: The median values of apoptotic cell percentage were higher in all concurrent groups than Gemcitabine alone groups regardless Gemcitabine dosage and therapeutic time interval. The highest median value of apoptotic cell percentage was 46.90% in more than 100 mg/kg of Gemcitabine group. The lowest p value was obtained in the 150 mg/kg of Gemcitabine with 2 hours or less interval group ($p = 0.0781$). Gross tumor necrosis was not significantly different in all therapeutic groups.
CONCLUSION: Treatment with concurrent HIFU and Gemcitabine therapy can enhance the cell apoptosis of pancreatic carcinoma.