P-03: Csaba Kovago, Nora Meggyeshazi, Gabor Andocs, Andras Szasz (2012) Proposed investigation on the possible synergic effect between high dose ascorbic acid application and oncothermia treatment

Proposed investigation on the possible synergic effect between high dose ascorbic acid application and oncothermia treatment

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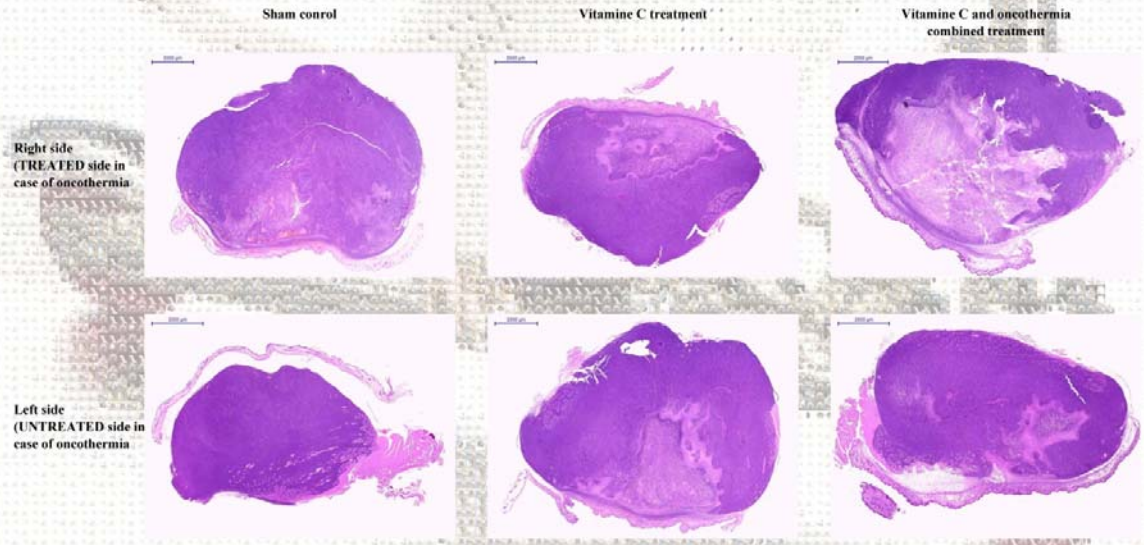
Introduction - According to recent investigations, the parenteral application of ascorbic acid (vitamin C) at high doses has significant antitumor activity in in vitro assays. This fact is a very important using ascorbic acid as complementary drug with standard antitumoral therapy or in cases where currently no other potent treatment is possible. Although the specific method of action is still unclear: high concentration of ascorbic acid produces oxidative shock by H_2O_2 lethal for tumor cells beyond a certain level, however healthy cells can survive the same stress effect.

Objective - The goal of our experiment will be to determine the possible potentiating effect of application of high dose pH-neutralized ascorbic acid to the normal oncothermia treatment method.

Method - The NMRI mice intended to inoculate with C26 Murine Colon Carcinoma cell line subcutaneously at both of their femoral regions and kept till the tumors reach symmetrically the 10 mm in diameter. We plan to create four experimental groups, containing 5 male and 5 female animals in each. The formed groups of animals will be: Gr1. no treatment (control), Gr2. only ascorbic acid treatment, Gr3. only oncothermia treatment, Gr4. both ascorbic acid and oncothermia treatment. Both vitamin-C and oncothermia treatment will be applied once ("single-shut" treatment regime), ascorbic acid will be pH-neutralized and applied intra peritoneal in dose of 2 g/kg bodyweight. Oncothermia treatment will be applied only to the right limb tumor, the other side will be used as internal control. Animals will be held in total anaethesia during the time period of the treatment using ketamine-xylazine combination intraperitonealy (100 mg/bwkg ketamine and 10 mg/bwkg xylazine dose). Oncothermia treatment will be carried out using LabEhy equipment (Oncotherm Ltd, Páty, Hungary), output power set between 5-10 W (to keep the treated tumor core temperarture around 42 °C), treatment time planed to be 30 minutes.
The animals will be sacrificed 48 hours after the treatment, all tumors will be removed and analyzed histopatologicaly. Slides will be stained with hematoxylin-eosin protocol, the slides will be scanned by Pannoramic Scan digital slide-scanner (3DHISTECH Ltd, Budapest, Hungary). The digital images will be analysed by HistoQuant module of the Pannoramic Viewer software (3DHISTECH Ltd, Budapest, Hungary).
The other organs will be routinely checked as well. Our main question centers on the comparison of the cell-destruction ratio of the various applied treatment regimes, and study the possible synergy or additive cross-potentiating of the methods.

Results from a pilot study - The following slides originated from a previously made experiment, to test the idea of the investigation. As it can be seen the combined treatment of vitamine C and oncothermia resulted much larger tumor-tissue death than the vitamine C application alone.



Conclusion - The results of this experiment can help us to plan regimes to potentiate the known effects of the oncothermia methods with fewer side effects than in case of standard complementary chemotherapeutic applications. Our future plan to study further chemical materials, and herbal drugs in the same way in order to determine their possible synergic effects with oncothermia.
Using the results and experiences geathered from this experiment, further investigations are planed targeting herbal and synthetic materials to check the compatibility of these compounds with the effects of the oncothermic treatment.