

BIOMEDICAL EVALUATION OF THE SIMULTANEOUS APPLICATION OF RADIATION AND LOCAL HYPERTHERMIA INDUCED BY NEW MICROSTRIP APPLICATOR OPERATING AT 434 MHZ: PRELIMINARY RESULTS

Osinsky S.*¹, Bubnovskaya L.¹, Kovelskaya A.¹, Mazokhin V.², Gelvich E.²

¹Inst. exp. Pathol. Oncol. Radiobiol., NASU, Kiev, Ukraine

²State Res. Product. Co., “Istok”, Fryazino, Russia

Purpose

To evaluate the tumor response to simultaneous application of radiation (RT) and local hyperthermia (LHT) applied with a new microstrip applicator in experiments in vivo.

Materials & Methods

Female rats (strain IEPOR bred, with a body weight of 175-200g) bearing subcutaneous Guerin carcinoma were used. Tumors were transplanted into the right flank. Animals were kept in Makrolon cages bedded with dust free wood granulate, and had free access to a standard diet and tap water. All experiments had been approved by the regional animal ethics committee. A treatment was initiated when the tumors were approximately 1.0-1.2 m³ in volume (day 7-8 after tumor transplantation). LHT was administered using a new device with special designed microstrip applicator (19x16 mm) operating at 434 MHz. Tumor temperature was measured by means of semiconductor thermoprobes (0.7 mm diameter). Hyperthermic treatment was as a single (43⁰C, 60 min). Irradiation was carried out using a 190 kV (current 10 mA, HVL = 0.5 mm Cu + 1.0 mm Al) X-ray machine (RUM-17, Russia). The dose rate was 1.23 Gy/min. Total doses of RT were 5, 10 and 15 Gy. Tumors were treated in a single exposure. RT was commenced on the 15th min of LHT (temperature under tumor 43⁰C as usually). The antitumor effect of TRT will be evaluated by means of the following criterias: inhibition of tumor growth (ITG, %); the number of tumor complete regression (CR, %); the number of cured rats [(the number of animals with tumor complete regression without recurrence over 120 days after regression (%)]. The bioenergetic status of tumor was assessed by ³¹P NMR spectroscopy (NMS), tumor choline-containing substances were registered using ¹H NMRS. Correlation between the parameters were evaluated by Spearman-*rho* coefficient or *chi*-squared test. Differences between values were assessed by Mann-Whitney test. Statistical significance was considered if $P < 0.05$.

Results

The required tumor temperature (43⁰C) was reached rather quickly (10-15 min) and maintained on the same level during 1-1.5 h with minimal deviations ($\pm 0.3^{\circ}\text{C}$) in a case of using the new applicator. The combined RT and LHT treatment was feasible, any kind of serious complications were not registered. It was obtained only that the combined treatment (LHT+RT, 10 Gy) resulted in the skin response in one-third of animals (moderate erythema) and in 10% of animals – severe erythema, radiation alone (10 Gy) did not result in any skin reaction.

It was found increases in Pi and decreases in ATP and PDE levels radiation with a dose of 15 Gy (24 and 48 h after RT). Radiation (5, 10 and 15 Gy) combined with LHT resulted in the more strength effect on tumor metabolism.

The evaluation of antitumor efficacy of the simultaneous application of RT and LHT has been performed in the two experimental groups: 1) LHT (43⁰C, 45 min), RT was started on the 15th

min of heating (5 Gy or 10 Gy, as a single fraction). 2) RT (5 Gy or 10 Gy) 1.5 hr before heating (43°C, 45 min). It was shown that the value of ITG and the number of CR were the same after application of RT (5 Gy) combined with LHT in simultaneous regime and after RT (10 Gy) supplemented with LHT in consequent regime. The number of cured rats was increased by a factor of 1.5 in group “RT + simultaneous LHT” in comparison with such in group “RT + consequent LHT” for both radiation doses. Simultaneous radiation and heat gave tumor thermal enhancement ratio of approximately 1.7-2.0.

Conclusion

A new system for LHT is feasible and convenient for exploitation in the experimental studies; the simultaneous application of RT and LHT provided by means of a new HT system resulted in an improved tumor response: the inhibition of tumor bioenergetic status was found to be more profoundly, the increase of the numbers of tumor complete response and cured rats were observed, the enhancement of skin response to radiation was not registered under simultaneous using of RT and heating. The evaluation of tumor responses to RT using in other doses in combination with simultaneous LHT to assess the therapeutic gain factor is under investigation.

Acknowledgement

This study is supported by the ISTC grant, project 2221.