

EFFICACY OF THERMOCHEMOTHERAPY AGAINST MURINE LUNG CARCINOMA

Andronova N.V.¹, Treshalina H.M.¹, Filonenko D.V.¹, Nikolaev A. L.², Gopin A.V.²,
Bozevolnov V.E.², Kogan B.Ya.³, Butenin A.V.³, Vorozhtsov G.N.³

¹ *Blokhin Russian Cancer Research Center of RAMS, 115478 Moscow, Russia*

² *Moscow State University, 119992 Moscow, Russia*

³ *FGUP GNC NOIPIK, 123995 Moscow, Russia.*

Introduction. Significance of thermochemotherapy of different tumor types is well-known. It was interesting to investigate influence of this therapeutic approach for lung cancer using local laser (LH), water (WH) or ultrasound (USH) hyperthermia.

Methods. Mice C₅₇BL₆ with i.m. transplanted Lewis lung carcinoma were used. Treatment was started on 6-9th day after tumor inoculation into leg when tumor volume achieved 0.6-1.6 cm³. Tumors were heated up to 43-45°C during 5-10 min with LH or USH, and 20-30 min with WH. LH was performed with $\lambda=810$ nm. USH was performed using two frequencies simultaneously (2.64 and 0.88 MHz with 1 and 2 W/cm² correspondingly). WH was performed with thermal water in thermostat. The cytostatics (cisplatin, doxorubicin, cycliphosphamide, etoposide and others, their double or triple combinations) with the therapeutic doses were administrated to mice single i.v. or i.p. to be followed by hyperthermia at 0.5 – 5 h interval. There was 1 or 2 courses of thermochemotherapy with 48 or 72 h interval. Groups of comparison received only hyperthermia or chemotherapy. Control groups of mice received injections of saline (did not treat anything). Double time (Dt) of tumor volume was calculated, and it was used for tumor growth evaluation. As a criterion of efficacy coefficient «C»=Dt_{exp}/Dt_{control} was used. Simultaneously during 2-3 weeks local and system side effects were registered after all kinds of treatment.

Results. Control groups had Dt=1.5-2 days. LH groups had Dt=2 days and «C»=1.3. Group WH had Dt=4 days and «C»=2.0. Group USH had Dt=4 days and «C»=2. Group USH with 2 courses of treatment s Dt=12 days and «C»=6. Groups receiving any kind of chemotherapy had Dt=3-9 days and «C»=1.5-6. Thermochemotherapy groups with 1 course of treatment had Dt=9-12 days and «C»=6-8. Thermochemotherapy groups with 2 courses of treatment had Dt=14-16 days and «C»=7-8. The highest activity was demonstrated by the 1 courses of LH thermochemotherapy with cyclophosphamide 200 mg/kg or 2 courses of USH thermo- chemotherapy with doxorubicin 4 mg/kg + cisplatin 3 mg/kg. Side effects of hyperthermia were revealed as a local toxicity with edema just after application and during 3-4 days. If the schedule of treatment included 2 course of hyperthermia alone >43°C such effects were more intensive up to the necrosis of soft tissue. Only after 1 course of thermochemotherapy with high dose of cyclophosphamide application the decrease of body weight in treated mice without death from toxicity was observed. After the 2nd course of thermochemotherapy with other cytostatics local side effects were the same.

Conclusion. The group with hyperthermia only demonstrated Dt>2.0-4.0 time as compared to the control group. All treated groups demonstrated Dt>1.3-5.8 time in comparison with hyperthermia alone, or Dt>2-3 time in comparison with chemotherapy alone. Thus, local water, laser or ultrasound hyperthermia together with chemotherapy including cisplatin, doxorubicin, etoposid, cycliphosphamide or their combinations in therapeutical doses inhibit tumor growth more significantly than chemotherapy or hyperthermia alone. Two courses of USH thermochemotherapy with cisplatin led to increase of efficacy without any side effects or other types of toxicity.

Acknowledgement. This work supported by Moscow Government (Russia).