Accelerator-based boron neutron capture therapy on human glioblastoma U87 - in vitro, in vivo experiments.

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Introduction

Preclinical investigations of BNCT were carried out at an accelerator source of epithermal neutrons at the Budker Institute of Nuclear Physics. The purpose of this work is to determine the effects of BNCT on U87 human glioblastoma cell line in vitro and U87 heterotopic subcutaneous transplant model of SCID mice in vivo.

Materials and Methods

Firstly, cytotoxic effects of boron-containing drugs in various concentrations were evaluated. U87 cells were incubated with boronophenylalanine (BPA) and sodium borocaptate (BSH) in concentrations ranging from 0 to 1280 μg^{10}B/ml for 1, 2 and 10 days. Secondly, cells were incubated with effective and safe concentration of ^{10}B in the growth medium for 24 hours with following neutron irradiation for 25 minutes with 2.05 MeV proton energy. The colony forming assay was used to investigate the changes in proliferative activity of cells.

In vivo BNCT experiments were conducted on the SCID mice model with subcutaneously implantated glioblastoma cell suspension in the right paw. BPA at a dose of 350 mg / kg and BSH at a dose of 100 mg / kg and pegylated liposomes with encapsulated BSH at a dose of 100 mg / kg were used as boron carriers. The drugs were injected intravenously into the retroorbital sinus. Irradiation was performed 3 weeks after tumor inoculation once for 90 minutes with 2.05 MeV proton energy. According to the calculations tumor absorbed dose was about 6 Gy-Eq, whole body absorbed dose was about 2 Gy-Eq.

Results

Dose- and time-dependent cytotoxic effects of both boron containing drugs were shown. The concentration higher than 80 μg^{10}B/ml showed significant reduction in cell viability, so 40 μg^{10}B/ml was considered to be effective and safe. Survival fraction of U87 after BNCT in the presence of BPA was 18 ± 2%, and in the presence of BSH was 13 ± 2%.

Irradiation of tumors in animals after administration of boron drugs resulted in a significant ($P < 0.05$) decrease of tumor volume compared with the control group irradiated without boron.

Liposomal form of BSH and BPA during BNCT showed the best long-term results. However, significant advantage in therapeutic effect of liposomal BSH compared with BPA was not observed. Further research is needed on various modifications of liposomes to improve treatment outcomes.

Conclusion

The study showed the safety and efficacy of the neutron beam, confirming the possibility of its use in the treatment of malignant glioma.

Acknowledgments

The investigations were carried out on the base of the laboratory of biomedical problems of BNCT, NSU, supported by the grant from the Russian Foundation for Basic Research (project No. 18-29-01007) using the equipment of the Center for Genetic Resources of Laboratory Animals, supported by the Ministry of Education and Science of Russia (The unique identifier of the project RFMEFI62117X0015). The authors are grateful to A. Makarov, D. Kasatov, I. Schudlo, I. Kolesnikov, E. Sokolova, A. Koshkarev, T. Bykov for neutron generation.