Transcranial laser treatment of rat brain glioblastoma without photosensitizers

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Glioblastoma (GBM) is the most lethal form of brain cancer, which remains incurable despite advances in neuroscience. Phototherapy with photosensitizers (PS) is considered as a promising, non-pharmacological and safe method of treating GBM. However, this method has side effects due to PS, which can cause allergies, photophobia, and even disruption of the blood-brain barrier. This study investigated the effect of transcranial phototherapy of GBM in rats without PS using a 1267 nm laser, which stimulates the formation of singlet oxygen directly in the GBM cells. For the assessment of effectiveness of a 30-day course of phototherapy in rats with GBM, tumor progression, animal survival, and cellular mechanisms of apoptosis were evaluated.

To optimize parameters of phototherapy, the experiments were conducted to select an effective and safe of laser radiation. This included temperature monitoring using an A-K3 type thermocouple (Ellab, Hillerød, Denmark) on the skull surface and brain cortex, as well as survival analysis (using the Kaplan-Meier method) of male Wistar rats (age 6 months, weight 350-380 g) and tumor volume assessment (using the magnetic resonance imaging, MRI) at different laser doses (8.7, 12.6, and 16.3 kJ/cm²).

The results revealed that a course of phototherapy with a power of 100 mW, providing a total dose of 12.6 kJ/cm², is optimal as it does not cause critical heating of brain tissue and shows the best therapeutic outcomes.

After establishing the effective dose, experiments were conducted to study the effect of phototherapy on the GBM growth. The MRI and histological analysis results showed that a course of phototherapy (12.6 kJ/cm²) led to significant suppression of tumor growth (the GBM volume decreased 1.5 times compared to the control group); to the changes in the nature of tumor growth (after phototherapy the diffuse GBM growth transformed into tumor encapsulation). A key result was the increase in animal survival from 34% in the control group to 64% after the therapy course, i.e., resistance to GBM progression doubled following a course of phototherapy.

In sum, the obtained data indicate that a course of phototherapy with a wavelength of 1267 nm and a total dose of 12.6 kJ/cm² effectively suppresses glioblastoma growth in the rat brain, induces apoptosis, and reduces the proliferation of tumor cells, which critically increases rat survival.

Keywords: glioblastoma, phototherapy, 1267 nm laser, lymphatic system.

Acknowledgements: The research was supported by the Russian Science Foundation (project No. 25-45-20004).