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Sono-Photodynamic Therapy in the Treatment of Glioblastomas Alterative or Traditional Treatment?

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Abstract

In the presented short article the authors consider the method of sono-photodynamic therapy as an effective option for treating patients with recurrent glioblastomas. According to our data, the inclusion of sono-photodynamic therapy in the scheme of combined treatment of glioblastomas, allows to achieve median overall survival of patients in 20.9 months and median survival after recurrence of disease in 9.4 months.

Keywords: Glioblastoma; Sono-photodynamic therapy; Photosensitizer

Introduction

Glioblastoma (GBM) is one of the most aggressive and malignant brain tumors in humans [1]. Traditional methods of treatment of this severe pathology are surgical intervention with adjuvant chemoradiotherapy [2,3]. Despite the obvious achievements of modern medical science, the prognosis for patients with GBM remains unsatisfactory. According to epidemiological studies, the median overall survival from the time of histological verification varies from 12.6 to 14 month and the percentage of patients alive at 2 years increases from 10.4% to 26.5% [4].

Unsatisfactory results of treatment of this severe pathology make it necessary to search for and develop new methods of treatment. The main requirement for them is the improvement of patient survival rates and a positive impact on the quality of life.

One of such methods is Sono-PhotoDynamic Therapy (SPDT). SPDT is a treatment method based on the significant increase of the cytotoxicity of drugs combined with ultrasound and photoirradiation of the tumor tissue. According to numerous studies of sono-photochemical reactions include a direct interaction of excited molecules with the help of ultrasonic radiation, the Photosensitizer (PS) on the substrate and forming transient radicals that react with oxygen. Interaction initiates a complex cascade of free radicals, such as singlet oxygen, hydroxyl radical, hydrogen peroxide and superoxide anion radical, causing the development of oxidative stress syndrome. As a result, SPDT effectively induced glioma-cell apoptosis and necrosis [5]. At the moment, experimental studies devoted to the study of Sono Dynamic Therapy (SDT) and SPDT are conducted in the scientific centers of South Korea, China and Japan. As photosensitizing agents, the authors use photofrin II, hematoporphyrin, radachlorin and 5-aminolevulinic acid [6-10]. All trials devoted to the study of the effectiveness of methods and SDT and SPDT of malignant gliomas are experimental [5].

In our opinion, the main indications for the use of SPDT in clinical neuro-oncology are:

- GBM (grade IV, WHO), primary and recurrence form.
- Anaplastic astrocytoma (grade III, WHO), primary and recurrence form.
- Anaplastic astrocytoma with transformation into GBM.
- Refusal of patients from the use of traditional methods of treatment (systemic chemotherapy, immunotherapy, etc.)

The treatment regimen for treatment of patients with GBM includes:

- Performing the operation in the volume of complete or partial resection of the tumor.

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- Intravenous infusion of PS.
- Local ultrasound irradiation of the postoperative cavity.
- Photoirradiation of the postoperative cavity.

The pilot study included 18 patients with verified recurrence form of GBM. The study was approved by local ethic committee. Patients signed informed consent to procedure in compliance with Helsinki declaration of 1964 (revised 2013).

After the introduction of patients with anesthesia, the removal of the recurrent tumor was performed in the volume of complete or partial resection. After that, intravenous infusion of the chlorine-based PS «Photolon®» (RUE «Belmedpreparaty», Republic Belarus; 2 mg/kg) was performed for 30 minutes. After the end of infusion local ultrasonic irradiation was performed at a frequency of 1.04 MHz with intensity of radiation 0.7 W/cm^2 for 10 minutes. Photoirradiation of the bed and walls of the removed tumors was performed at the exposure doses of 75 mJ/cm^2 -100 J/cm^2 for 9-30 minutes. One month after the treatment, the patients received chemotherapy (lomustin40 mg (orally) and/or carmustin 2 mg (intravenously).

The complications and adverse reactions of the applied methods of treatment were headache, convulsive syndrome (n=2) and cerebral edema (n=1). According to our own data, the use of SPDT in combined and complex treatment with recurrence forms of GBM allows to achivea median overall survival of patients in 20.9 months and a median survival after the recurrence of the disease in 9.4 months.

Conclusion

In our opinion, the SPDT can be recommended as an alternative treatment option for patients with a recurrence of GBM. The received results testify to good tolerability and antitumor efficacy of the developed method. At the moment, a randomized controlled trial has been started in our research center aimed at studying the antitumor efficacy of SPDT in patients with primary forms of GBM.

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