

Results on complex treatment of patients with glial tumors of brain with local chemotherapy

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Aim. For the purpose of local chemotherapy in patients with malignant brain tumors after partial or total removal of tumors we used biodegradable film with methotrexate. The film, due to its properties, is firmly attached to the wound surface. With its composition of chemotherapeutic agents over specified time, the dosed film immediately affects diseased tissue, playing the role of a local chemotherapy depo. **Methods.** Results of treatment of 74 patients with low differentiated gliomas of the brain, which have undergone a comprehensive treatment that includes surgical removal of tumor and implantation of methotrexate depo in the wall of postoperative cerebral injury followed by radiotherapy in the pig on a bed of the tumor removed. **Results.** A retrospective analysis of the results of complex treatment of patients with glial brain tumors with local chemotherapy showed a significant increase in disease-free period in patients who have undergone, consistently, surgery, chemotherapy and adjuvant local radiation therapy. **Conclusions.** Our research has shown that the use of local chemotherapy greatly improves the results of treatment of patients not only for total removal of intracerebral tumors, but also for subtotal removal, as well as in patients with prolonged tumor growth, when there is no possibility of radiation treatment.

Keywords: glial tumors, local chemotherapy, methotrexate, polymeric film.

Introduction. Intracerebral or glial tumors account for 50 % of all tumors of the central nervous system. Despite diagnostics improvement, a mortality of patients with intracerebral tumors remains high, and results of treatment are unsatisfactory. A role of adjuvant chemotherapy up to date has not been fully clarified.

We attempted to solve the problem of developing the most optimal way to deliver chemotherapeutic agents to partially resected tumor, or to the areas of previously removed brain tumor. Our studies on experimental animals indicated the preferred activation mechanisms of apoptosis in the drugs implanted films with methotrexate, compared to the drugs with a depot effect of cisplatin.

Low grade glioma (LGG) is a group of malignant brain tumors of neuroectodermal origin. According to the WHO classification, they include: anaplastic glioma (anaplastic astrocytoma, oligodendrogliomas and oligoastrocytomas) and glioblastoma multiforme.

Treatment of patients with low grade gliomas remains today one of the most pressing problems of neurosurgery and oncology. Despite using practically entire arsenal of anticancer therapies and surgical techniques, the average life of patients with LGG usually does not exceed 12 months.

From biological viewpoint on tumoral growth, LGG represents the local process that affords a possibility of wide application of local methods of anticancer therapy at this disease. The local chemotherapy is the most perspective in this respect.

The studied and control groups

Histological structure of tumor	All patients	Disease-free period		
		Less than 6 months	Less than 1 year	More than 1 year
<i>The studied group</i>				
Anaplastic astrocytoma	30	6	7	17
Anaplastic oligoastrocytomas	14	1	2	11
Anaplastic oligodendrogliomas	9	–	–	9
Glioblastoma	21	1	2	18
Total	74	8 (10.8 %)	11 (14.86 %)	55 (74.3 %)
<i>The control group</i>				
Anaplastic astrocytoma	36	12	17	7
Anaplastic oligoastrocytomas	14	4	8	2
Anaplastic oligodendrogliomas	10	2	4	4
Glioblastoma	20	6	10	4
Total	80	24 (30 %)	39 (48.7 %)	17 (21.3 %)

In both domestic and foreign literature there are numerous publications regarding clinical experience with solutions of various anticancer drugs for local chemotherapy, but the results were not very comforting. In recent years, some investigators attempted to use the brain-polymer formulations of cytotoxic drugs deposited in resorbable polymers for local chemotherapy of non-differentiated gliomas.

Materials and methods. For local chemotherapy of patients with glial brain tumors after partial or total removal of tumors we used self-resolving film with methotrexate. One option for the localization of anticancer drugs may be their deposition in the polymer matrix (biodegradable), and the tool itself realized in the form of a multilayer polymeric film, affixed to the affected area.

Successful application of a polymer adhesive self-resolving film of «diplén» in medical practice allowed us to use the latter as a basis for creating anticancer drug depot with the cytostatic methotrexate.

The films, due to their properties, are firmly attached to the wound surface. With the composition of chemotherapeutic agents over a specified time, the films being resolvable and dosed, directly affect the diseased tissue, playing the role of a depot chemotherapy.

74 patients with the brain LGG had undergone a comprehensive treatment that included surgical removal of the tumor within the intact brain tissue, or after subtotal removal, with implantation in the wall of the postoperative brain injury depot methotrexate followed by radiotherapy in the total focal dose in resected tumor bed of 60 Gy.

80 patients in the control group had undergone a standard combination therapy consisting of similar surgery and radiation therapy on ODS in the removed tumor region (60 Gy).

For histological classification the tumors were assigned to the following groups: anaplastic astrocytoma – 30; anaplastic oligoastrocytomas – 14; anaplastic oligodendrogliomas – 9; glioblastoma – 21. The pa-

tients' age from 10 to 78 years. The median age was 50 years. There were 38 men, 36 women.

In the group studied 48 patients received complex treatment: surgery with total or subtotal resection of tumor and implantation of the polymer film with methotrexate for the local chemotherapy and adjuvant radiation therapy.

The remaining 26 patients underwent only surgery with implantation of the polymer film with methotrexate, and postoperative radiation therapy was performed. Of the 74 patients studied, 23 with continuing growth of the previously removed malignant brain tumor were operated on. This group consisted mostly of the patients who did not receive postoperative radiation therapy, as they completed the full course of radiation treatment after the first operation. The remaining 3 patients, for various reasons, refused radiotherapy.

An assessment of the overall condition of the patients on admission was made on a scale of Karnofsky and ranged from 40 % to 80 %.

As accompanying diseases 5 patients had diabetes, 4 – hypertension, 4 – varicose veins of the lower extremities, 2 – hepatitis C, 1 – calculous cholecystitis, and 1 – syphilis.

The operations were performed under general anesthesia. Of 74 patients in 61 the tumor was removed within a macroscopically visible healthy tissue, in 13 – subtotally.

Results and discussion. Our study showed that the patients with glial structures of the brain consist 50 % of the total number of neuro-oncology patients. The most aggressive in terms of recurrence of the tumor is anaplastic astrocytoma.

A comparative analysis of relapse-free period between the studied and control groups is presented in the Table.

A retrospective analysis of the results of complex treatment of patients with glial brain tumors with local chemotherapy showed a significant increase in disease-free period in the patients who have undergone, consistently, surgery, chemotherapy and adjuvant local radiation therapy.

Our research has shown that the use of local chemotherapy greatly improves the results of treatment of patients not only for total removal of intracerebral tumors, but also for subtotal removal, as well as in patients

with prolonged tumor growth, when there is no possibility of radiation treatment.

Thus, we examined the results of complex treatment of patients with glial brain tumors using the method of local chemotherapy. Given these results, we believe further research is very promising in this regard.

Л. Р. Арутюнян

Результати комплексного лікування хворих гліальними пухлинами головного мозку із застосуванням локальної хіміотерапії

Резюме

Мета. Для проведення локальної хіміотерапії у хворих злоякісними пухлинами головного мозку після часткового або тотального видалення пухлин нами використано плівку з метотрексатом, здатну саморозсмоктуватися. Завдяки своїм властивостям плівка міцно приклеюється до поверхні рани. Маючи у своєму складі хіміопрепарат, протягом заданого часу плівка, розсмоктуючися, безпосередньо і дозовано впливає на пошкоджені тканини, виконуючи роль своєрідного депо хіміопрепарату. **Методи.** Проаналізовано результати комплексного лікування 74 хворих низькодиференційованими гліомами головного мозку, яким хірургічним шляхом видалено пухлину з імплантацією на стінки післяопераційної мозкової рани депонованої форми метотрексату, з наступною променевою терапією в СОД на місці видаленої пухлини. **Результати.** Ретроспективний аналіз результатів комплексного лікування хворих гліальними пухлинами головного мозку із застосуванням локальної хіміотерапії виявив значне збільшення безрецидивного періоду у хворих, яким послідовно здійснили хірургічне втручання, локальну хіміотерапію та ад'ювантний курс променевої терапії. **Висновки.** Наші дослідження показали, що використання локальної хіміотерапії набагато покращує результати комплексного лікування хворих не лише за тотального, але й субтотального видалення внутрішньомозкової пухлини, а також у хворих з подовженим ростом пухлини, коли немає можливості променевого лікування.

Ключові слова: гліальні пухлини, локальна хіміотерапія, метотрексат, полімерна плівка.

Л. Р. Арутюнян

Результаты комплексного лечения больных глиальными опухолями головного мозга с применением локальной химиотерапии

Резюме

Цель. Для проведения локальной химиотерапии у больных злокачественными опухолями головного мозга после частичного или тотального удаления опухолей нами использована саморассасывающаяся пленка с метотрексатом. Благодаря своим свойствам пленка прочно приклеивается к раневой поверхности. Имея в своем составе химиопрепарат, с течением заданного времени пленка, рассасываясь, непосредственно и дозированно влияет на пораженные ткани, играя роль своеобразного депо химиопрепарата. **Методы.** Проанализированы результаты комплексного лечения 74 больных низкодифференцированными глиомами головного мозга, которым было проведено хирургическое удаление опухоли с им-

плантацией на стенки послеоперационной мозговой раны депонированной формы метотрексата, с последующей лучевой терапией в СОД на ложе удаленной опухоли. **Результаты.** Ретроспективный анализ результатов комплексного лечения больных глиальными опухолями головного мозга с использованием локальной химиотерапии выявил значительное увеличение безрецидивного периода у больных, подвергшихся последовательно хирургическому вмешательству, локальной химиотерапии и адъювантному курсу лучевой терапии. **Выводы.** Наши исследования показали, что применение локальной химиотерапии намного улучшает результаты комплексного лечения больных не только при тотальном, но и субтотальном удалении внутримозговой опухоли, а также у больных с продолженным ростом опухоли, когда нет возможности лучевого лечения.

Ключевые слова: глиальные опухоли, локальная химиотерапия, метотрексат, полимерная пленка.

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