



EFFICACY OF ANTICONVULSANTS IN THE TREATMENT OF POSTOPERATIVE HEADACHE IN PATIENTS WITH BRAIN TUMORS

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Abstract. Headache is one of the most frequent symptoms in patients with brain tumors and often persists in the postoperative period, significantly impairing quality of life. This study aimed to evaluate the effectiveness of anticonvulsant therapy in the management of postoperative headaches in neuro-oncological patients. A total of 257 patients who underwent surgical removal of brain tumors were enrolled in the study. Among them, 88 patients received anticonvulsants (gabapentin, lamotrigine, and lamotrigine generic formulations), while 169 patients formed the control group without anticonvulsant therapy. Headache intensity, duration, and frequency were assessed using the Visual Analogue Pain Scale and dynamic clinical monitoring. Anticonvulsant therapy resulted in a significant reduction in headache intensity (53.5–57.0%), frequency (28.9–32.0%), and duration (27.3–31.2%) compared with the control group. The results indicate that anticonvulsants are effective and well-tolerated agents for postoperative headache management in patients with brain tumors.

Keywords: brain tumors, postoperative headache, anticonvulsants, gabapentin, lamotrigine, neuro-oncology, pain management.

ЭФФЕКТИВНОСТЬ ПРОТИВОСУДОРОЖНЫХ ПРЕПАРАТОВ В ЛЕЧЕНИИ ПОСЛЕОПЕРАЦИОННОЙ ГОЛОВНОЙ БОЛИ У ПАЦИЕНТОВ С ОПУХОЛЯМИ ГОЛОВНОГО МОЗГА

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Аннотация. Головная боль является одним из наиболее частых симптомов опухолей головного мозга и нередко сохраняется в послеоперационном периоде, значительно снижая качество жизни пациентов. Целью данного исследования была оценка эффективности противосудорожных препаратов в лечении послеоперационных головных болей у нейроонкологических больных. В исследование были включены 257 пациентов, перенесших хирургическое удаление опухолей головного мозга. Из них 88 пациентов получали противосудорожные препараты, а 169 пациентов составили контрольную группу. Интенсивность, частота и длительность головной боли оценивались с использованием визуальной аналоговой шкалы боли и динамического клинического наблюдения. Противосудорожная терапия достоверно снижала интенсивность головной боли (53,5–57,0%), частоту (28,9–32,0%) и длительность приступов (27,3–31,2%) по сравнению с контрольной группой. Полученные результаты свидетельствуют о высокой эффективности и хорошей переносимости противосудорожных препаратов в лечении послеоперационных головных болей у пациентов с опухолями головного мозга.

Ключевые слова: опухоли головного мозга, послеоперационная головная боль, противосудорожные препараты, габапентин, ламотриджин, нейроонкология, лечение боли.

BOSH MIYA O'SMALARI BILAN OG'RIGAN BEMORLARDA OPERATSIYADAN KEYINGI BOSH OG'RIG'INI DAVOLASHDA ANTIKONVULSANT PREPARATLARNING SAMARADORLIGI

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Ixtisoslashtirilgan ilmiy-amaliy neyroxirurgiya va neyroreabilitatsiya markazi

Annotatsiya. Bosh og'rig'i bosh miya o'smalarining eng ko'p uchraydigan simptomlaridan biri bo'lib, operatsiyadan keyingi davrda ham saqlanib qolishi mumkin va bemorlarning hayot sifatini sezilarli darajada pasaytiradi. Ushbu tadqiqotning maqsadi neyroonkologik bemorlarda operatsiyadan keyingi bosh og'rig'ini davolashda antikonvulsant terapiyaning samaradorligini baholashdan iborat edi. Tadqiqotga bosh miya o'smalari jarrohlik yo'li bilan olib tashlangan 257 bemor kiritildi. Ulardan 88 nafariga antikonvulsant preparatlar buyurildi, 169 nafar bemor esa nazorat guruhini tashkil etdi. Bosh og'rig'ining intensivligi, davomiyligi va tez-tezligi vizual analog og'riq shkalasi yordamida baholandi. Antikonvulsant terapiya bosh og'rig'i intensivligi, davomiyligi va chastotasini nazorat guruhiga nisbatan sezilarli darajada kamaytirdi. Natijalar antikonvulsant preparatlarning operatsiyadan keyingi bosh og'rig'ini davolashda samarali va yaxshi ko'tarilishini ko'rsatdi.

Kalit so'zlar: bosh miya o'smalari, operatsiyadan keyingi bosh og'rig'i, antikonvulsantlar, gabapentin, lamotrigin, neyroonkologiya, og'riq terapiyasi.

Introduction. Headache is one of the most common symptoms of brain tumors. According to various authors, they occur in an average of 78.5–92% of patients preoperatively [1, 4, 5, 7]. According to our data, they occur in 79.5% of patients. Headache regresses as a result of tumor treatment, as two pathogenic factors disappear or reduce their impact on the clinical picture: intracranial hypertension and tumor irritation of the dura mater. Increased intracranial pressure is treated with dehydration therapy, as well as tumor removal, bypass surgery, or decompressive trepanation. Complete or partial tumor removal relieves or reduces irritation of the dura mater by the tumor. However, headache in some cases persists in the postoperative period. Pain characteristics differ preoperatively and postoperatively. While preoperative headaches are most often attributed to intracranial hypertension and accompanied by corresponding symptoms (worsening in the morning or during coughing, vomiting at the onset of headache), postoperative headaches resemble tension-type headaches. However, there are also differences: headaches in neuro-oncological patients differ from tension-type headaches in that they are often accompanied by more or less significant signs of intracranial hypertension, are associated with tumor location, and are aggravated by physical exertion [2, 4, 5, 9, 11–16]. Headaches, like any pain, reduce the patient's quality of life, acting in conjunction with other symptoms, and lead to emotional disturbances and dissatisfaction with treatment. Furthermore, patients often bring pain to the attention of their physician, if not more often, then at least no less often than other manifestations of the tumor, especially if the other symptoms are mild. Anticonvulsants have proven effective in treating pain of various locations and origins, including headaches, as evidenced by numerous studies [3, 6, 8, 10, 17]. Modern anticonvulsants are quite effective with moderate severity and frequency of side effects.

Purpose of the study consisted of assessing the effectiveness of anticonvulsants in the treatment of headaches in patients with brain tumors in the postoperative period.

Materials and methods. The study involved 257 people who had undergone surgery for brain tumors. The patients' age ranged from 19 to 69 years, with an average of 50.1 years. The following were the criteria for inclusion of a patient in the study: 1. A brain tumor was diagnosed in the patient, for which surgical intervention (tumor removal) was performed. 2. Pathological histological verification of the diagnosis. 3. The presence in the patient of a headache in the postoperative period, consistent with the clinical picture of a brain tumor, developing in close temporal relationship with the neoplasm and not related to the types of headache described in the sections G43 ("Migraine") and G44 ("Other headache syndromes") according to ICD-10. 4. The

absence of disorders in the patient that prevent him from adequately communicating with the doctor.

5. Informed consent of the patient to the study. The following were the criteria for exclusion of a patient from the study: 1. The patient's refusal to participate in the study. 2. Taking psychotropic drugs (other than anticonvulsants) that can change the severity, frequency, and duration of headache attacks. Headache severity was assessed using the Visual Analogue Pain Scale (VAPS). The severity, duration, and frequency of headache attacks were assessed for 3–4 weeks after surgery (beginning of treatment) and then every 2 weeks (a total of 6 studies). For the treatment of headaches, 88 patients took the following drugs: Tebantin, Lamictal, and Lamolep. The drugs were dosed according to the following regimens: 1. Tebantin: day 1 — 300 mg/day, day 2 — 600 mg/day, day 3 — 900 mg/day. Then the dose was selected individually and ranged from 900 to 1800 mg/day. 2. Lamictal: 1-2 weeks — 25-50 mg/day, 3-4 weeks — 50-100 mg/day, then the dose was selected individually and amounted to 100-300 mg/day. 3. Lamolep: 1-2 weeks — 25-50 mg/day, 3-4 weeks — 50-100 mg/day, then the dose was selected individually and amounted to 100-300 mg/day. The control group was formed of patients who refused to take anticonvulsants, but agreed to the examination (169 people). All patients in this group were diagnosed with headache in the postoperative period. The characteristics of the patient groups are presented in Table 1. Statistical processing of the obtained results was performed using nonparametric methods. To compare two independent samples, the Mann-Whitney test was used. To compare one group of patients at different periods of time, the Wilcoxon test was used. The Kruskal-Wallis test was used to compare one sample with several.

Table 1. Characteristics of patient groups included in the study

Study drug	Number of patients	Mean age (years)	Sex distribution of the group	Mean VAS score at baseline	Attack frequency (per week)	Attack duration (hours)
Tebantin	41	54.2	41.5% men (17) / 58.5% women (24)	7.2	0.76	12.5
Lamictal	21	49.9	33.3% men (7) / 66.7% women (14)	7.4	0.84	12.8
Lamolep	26	52.3	38.5% men (10) / 61.5% women (16)	7.1	0.79	12.1
Patients not receiving anticonvulsants	169	50.0	45.0% men (76) / 55.0% women (93)	7.3	0.78	11.9
Total	257	50.9	42.8% men (110) / 57.2% women (147)	7.3	0.78	12.1

Results of the survey and their discussion. Patients noted the subjective effect of Tebantin after 1–2 weeks of treatment. Most often (63.4%), patients initially noted a decrease in headache intensity, followed by a reduction in attack duration. Attack frequency decreased less significantly (as a percentage of the initial value). Minimum headache intensity values were achieved within 6–8 weeks of treatment (subsequently, a very slow decrease was noted, which showed a statistically insignificant difference from the 6–8 week values). Attack duration had a similar trend—minimum values were achieved within 6–8 weeks of treatment. Attack frequency decreased throughout the entire treatment period. Adherence to Tebantin treatment was quite high. Only 7.3% of patients discontinued treatment (all cases of withdrawal occurred no earlier than 8 weeks of therapy), and another 12.1% expressed a desire to change the medication after completing the course of treatment. In 4.9% of cases, the reason for discontinuing or switching medications was price; in the remaining cases, it was dissatisfaction with the severity of side effects or a desire to use a more effective medication. Patients taking Lamictal reported a reduction in headache intensity as early as the first

week of treatment. Furthermore, patients noted subjective sensations such as improved thinking and memory (at the end of the second week and thereafter). At the end of the fourth week of therapy, patients noted a decrease in the duration of headache attacks, and at the end of the eighth week, a decrease in the frequency of headache attacks. Minimal headache intensity values were reached within 6-8 weeks of therapy (then a very slow decline was noted, showing statistically insignificant differences from the values for 6-8 weeks). Attack duration showed a similar trend, with its minimum values reached within 8 weeks of treatment. Attack frequency decreased throughout the entire treatment period. Adherence to Lamictal treatment was comparable to that in the Tebantin group. A total of 9.5% of patients discontinued the drug early (2 cases – at 8 and 10 weeks of treatment). After completing the course, the same number of patients chose to change the drug. In all cases, the reason for discontinuation and switching was the price of Lamictal. The dynamics of parameters in the Lamolep group were similar to those in the Lamictal group. Within 1-2 weeks of therapy, patients noted a decrease in headache intensity and improvement in thinking and memory. At the end of 4-6 weeks of treatment, patients noted a decrease in the duration, and at the end of 8 weeks, a decrease in the frequency of headache attacks. Minimum values of headache intensity were reached within 6-8 weeks of therapy (then a very slow decrease was noted, which showed a statistically insignificant difference from the values for 6-8 weeks). Similar dynamics were observed for attack duration – its minimum values were reached within 8 weeks of treatment. Attack frequency decreased throughout the entire treatment period. Adherence to Lamolep treatment was similar to that in the two groups described above. 11.6% of patients discontinued the drug early (2 cases at week 8 and 1 case at week 10 of therapy). The same number of patients chose to change medications during treatment (3.8% at week 8) and thereafter (7.8%). Reasons for discontinuation and change included high cost (in 15.4% of cases) and the desire to use a more effective medication (in 7.8% of cases). It should be noted that a slight reduction in headache intensity, duration, and frequency was also observed in the group not taking anticonvulsants. The dynamics of headache intensity (according to the VAS) in different groups of patients is presented in Table 2. The dynamics of the average frequency of headache attacks in different groups of patients is presented in Table 3. The dynamics of the average duration of headache attacks in four groups of patients is presented in Table 4.

Table 2. Dynamics of the mean VAS score during treatment with different anticonvulsants

Drug	Baseline	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12
Tebantin	7.2	6.7	5.8	4.6	3.3	3.1	3.1
Lamictal	7.4	6.1	5.9	4.8	3.5	3.3	3.2
Lamolep	7.1	6.6	5.8	4.8	3.6	3.4	3.3
Patients not receiving anticonvulsants	7.3	7.1	7.0	6.8	6.5	6.4	6.5

Table 3. Dynamics of the mean frequency of headache attacks during treatment with different anticonvulsants

Drug	Baseline	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12
Tebantin	0.76	0.73	0.70	0.66	0.60	0.56	0.54
Lamictal	0.84	0.86	0.81	0.74	0.67	0.62	0.57
Lamolep	0.79	0.80	0.75	0.70	0.68	0.63	0.56
Patients not receiving anticonvulsants	0.78	0.82	0.77	0.73	0.74	0.70	0.69

Table 4. Dynamics of the mean duration of headache attacks during treatment with different anticonvulsants (hours)

Drug	Baseline	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12
Tebantin	12.5	12.3	11.4	10.4	9.0	8.8	8.6

Lamictal	12.8	12.5	11.7	10.6	9.2	9.0	8.9
Lamolep	12.1	12.0	11.7	10.7	9.3	9.0	8.8
Patients not receiving anticonvulsants	11.9	11.7	11.8	11.5	11.7	11.4	11.1

Taking into account the percentage reduction in different headache characteristics in patients taking anticonvulsants, it can be said that the most significant dynamics is noted in the decrease in headache intensity. This indicator decreased during treatment by 53.5-57.0% depending on the group. In the group of patients not taking anticonvulsants, this indicator decreased by only 11.0%. The frequency of headache attacks decreased in different groups taking anticonvulsants by 28.9-32% of the initial value. In the group of patients not taking anticonvulsants, this indicator decreased by 11.5%. Headache duration in the groups of patients taking anticonvulsants decreased by 27.3-31.2%, while in the group of patients not taking these medications, this figure decreased by only 6.7%. Treatment adherence was similar across all three groups. Approximately 80% of patients considered the treatment results satisfactory. During treatment, this indicator decreased by 53.5-57.0% depending on the group. In the group of patients not taking anticonvulsants, this indicator decreased by only 11.0%. The frequency of headache attacks decreased in different groups taking anticonvulsants by 28.9-32% of the initial value. In the group of patients not taking anticonvulsants, this indicator decreased by 11.5%. The duration of headache attacks in the groups of patients taking anticonvulsants decreased by 27.3-31.2%, while in the group of patients not taking these drugs, the above-mentioned indicator decreased by only 6.7%. Adherence to treatment was similar in patients of all three groups. About 80% of patients considered the treatment results satisfactory. During treatment, this indicator decreased by 53.5-57.0% depending on the group. In the group of patients not taking anticonvulsants, this indicator decreased by only 11.0%. The frequency of headache attacks decreased in different groups taking anticonvulsants by 28.9-32% of the initial value. In the group of patients not taking anticonvulsants, this indicator decreased by 11.5%. The duration of headache attacks in the groups of patients taking anticonvulsants decreased by 27.3-31.2%, while in the group of patients not taking these drugs, the above-mentioned indicator decreased by only 6.7%. Adherence to treatment was similar in patients of all three groups. About 80% of patients considered the treatment results satisfactory.

Conclusions. Anticonvulsants are effective in treating headache in neuro-oncology patients in the postoperative period. Headache intensity is reduced most rapidly and significantly, while attack frequency and duration are reduced to a lesser extent. Despite this, the degree of regression of all three parameters is significantly higher than that of similar parameters in the group of patients not taking anticonvulsants.

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