



RESULTS OF A STUDY OF CLINICAL AND NEUROPHYSIOLOGICAL CHANGES IN PATIENTS WITH POST-TRAUMATIC EPILEPSY WITH CONCOMITANT SOMATIC DISEASES ON THE BASIS OF COMPLEX DRUG THERAPY

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Article history:	Abstract:
<p>Received: March 11th 2022 Accepted: April 20th 2022 Published: May 30th 2022</p>	<p>The etiological role of mild traumatic brain injury in the genesis of the disease has not been definitively established; the prognosis of posttraumatic epilepsy after trauma and the feasibility of preventive therapy with antiepileptic drugs (AEDs) in these patients to reduce the risk of the disease remain unresolved. The informative value of new highly sensitive electrophysiological (video-eEG monitoring) and neuroimaging (magnetic resonance spectroscopy and positron emission tomography) instrumental studies in diagnosing the disease and indications for their use have not been established. The efficacy of combination therapy with antiepileptic and neuroprotective drugs has not been studied. This is the cause of late diagnosis and untimely treatment in patients with post-traumatic epilepsy. As a result, the number of patients with pharmacoresistant course of the disease, personality changes, intellectual and mental disorders, social disadaptation, sharp deterioration in quality of life increases significantly. All of the above suggests. the relevance of this study, which provides for the improvement of diagnosis and drug treatment of post-traumatic epilepsy.</p>

Keywords: Epilepsy, seizures, epileptic status, trauma, EEG, paroxysmal index, MRI

INTRODUCTION.

Posttraumatic epilepsy can be characterized as a variant of the consequences of craniocerebral trauma (CMT) with a leading epileptic syndrome, which is manifested, respectively, by systematically repeated epileptic seizures, most often of convulsive nature. The leading etiological factor of symptomatic epilepsy of young age is craniocerebral trauma, which takes 30-50% of all types of injuries in peace time. The incidence of post-traumatic epilepsy in cases of previously suffered traumatic brain injury ranges from 5 to 50%, according to numerous studies, and its course is often progredient. The problem of diagnosis and drug treatment of posttraumatic epilepsy remains one of the most difficult tasks of clinical neurology [1,3,5].

In spite of the successes of modern neurology, many issues are still relevant, in particular, the problem in the course of the disease in people with posttraumatic epilepsies, suffering from concomitant cardiovascular pathology is insufficiently studied.

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definitively established; the prognosis of posttraumatic epilepsy after trauma and the feasibility of preventive therapy with antiepileptic drugs (AEDs) in these patients to reduce the risk of the disease remain unresolved. The informative value of new highly sensitive electrophysiological (video-eEG monitoring) and neuroimaging (magnetic resonance spectroscopy and positron emission tomography) instrumental studies in diagnosing the disease and indications for their use have not been established. The efficacy of combination therapy with antiepileptic and neuroprotective drugs has not been studied. This is the cause of late diagnosis and untimely treatment in patients with post-traumatic epilepsy. As a result, the number of patients with pharmacoresistant course of the disease, personality changes, intellectual and mental disorders, social disadaptation, sharp deterioration in quality of life increases significantly. All of the above suggests. the relevance of this study, which provides for the improvement of diagnosis and drug treatment of post-traumatic epilepsy.



PURPOSE OF THE STUDY:

To study the dynamics of clinical and neurophysiological changes against the background of complex medical therapy in patients with posttraumatic epilepsy with concomitant somatic diseases.

MATERIAL AND METHODS:

We examined 110 patients with posttraumatic epilepsy who were under observation in the Department of Neurology 1 of the SamMI clinic. The duration of disease ranged from 6 to 10 years, men 74%, women 26%, as well as 48 patients in whom posttraumatic epilepsy was not detected (comparison group).

The main group consisted of 110 patients with posttraumatic epilepsy in whom the diagnosis was established or confirmed on the basis of repeated (at least two) unprovoked epileptic seizures that they had already had. The control group consisted of 48 patients with epilepsy in whom posttraumatic epilepsy was not diagnosed during follow-up.

All patients underwent a comprehensive examination including neurological status, EEG, MRI (MSCT), transcranial Doppler sonography of cerebral vessels and neuropsychological examination, laboratory tests (blood biochemistry), and consultations with narrow specialists. The diagnosis of forms of epilepsy and types of epileptic seizures was made according to the International Classification of Diseases.

RESULTS AND DISCUSSION:

In the majority of patients with posttraumatic epilepsy we examined, seizures were partial with secondary generalization (60.0%), and the clinical picture of the partial component predominantly corresponded to temporal mediobasal localization of the epileptic focus (temporal pseudoabsences, vegeto-visceral, and automorphisms). In addition, a significant proportion of patients had only generalized seizures without a partial component (29.3%) or polymorphic seizures (16.0%). As for the frequency of seizures, in the majority of cases, it was high - more than 3 times a year to once a month and more than once a month (30.7% and 20.0% of cases, respectively).

All patients underwent brachiocephalic artery (BCA) CTDG during the interictal period (at least 3 days after the attack). Velocity and resistive indices were analyzed, features of cerebrovascular reserve were studied using functional tests. The obtained indices of cerebral blood flow in patients with different forms of posttraumatic epilepsy were compared with

each other, with indices in patients with posttraumatic epilepsy in the presence of hemodynamically significant changes of the bca and with control indices.

When examining patients with posttraumatic epilepsy, we found that the most informative parameter, valuable in prognostic terms, was the level of cerebrovascular reactivity and decreased blood flow velocity in the intracranial segments of the vas on the side of the lesion. Cerebrovascular reactivity serves as a quantitative characteristic of the system of cerebral circulation regulation and reflects the state of perfusion reserves. In the 1st group of patients with posttraumatic epilepsy and concomitant somatic diseases, cerebrovascular reactivity in carotid basins was assessed in 57 patients and in vertebro-basilar basin - in 52 patients.

In Group 2, the state of perfusion reserves in the carotid system was studied in 38 patients and in the vertebro-basilar basin - in 37 patients. Normal or reduced (less than 25%) indices of cerebrovascular reactivity were observed in all groups of the examined patients. No individuals with increased cerebrovascular reactivity were detected.

No significant differences in decreased perfusion reserves in carotid pools were found in patients with different pathogenetic subtypes of stroke ($\chi^2=2.64$; $p=0.44$): in the atherothrombotic stroke subtype, decreased responsiveness to hypercapnia was found in 54 (49.1%) patients, in the cardioembolic subtype in 23 (20.9%), in the lacunar subtype in 8(7.3%), and in stroke of unspecified genesis in 5 (4.5%) patients. In the group of patients with early attacks, there was also no correlation of decreased vascular reactivity in the carotid basins in patients with only acute symptomatic attacks in 18 (16.3%) patients and in patients in whom attacks recurred and a week after stroke onset in 18 (16.3%) patients ($\chi^2=0.66$; $p=0.41$). Cerebrovascular reactivity serves as a quantitative characteristic of the system of cerebral circulation regulation and reflects the state of perfusion reserves. In the 1st group of patients with posttraumatic epilepsy and concomitant somatic diseases, cerebrovascular reactivity in carotid basins was assessed in 57 patients and in vertebro-basilar basin - in 52 patients.

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In patients with posttraumatic epilepsy and concomitant somatic diseases with the development of epileptic seizures with decreased hypercapnia reactivity values, focal pathological changes on EEG were registered more frequently in 44 (67.7%) patients than in patients with normal carotid basin reactivity values in 27 (41.5%), ($\chi^2=8.8$; $p=0.003$). At the same time, pathological activity on EEG was registered predominantly when hypercapnia reactivity was lower than 19% in 49 (75.4%) patients, while pathological activity was found in 29 (44.6%) patients with normal or slightly decreased (up to 20%) reactivity values ($\chi^2=14.7$; $p=0.00013$).

A comparative analysis of cerebrovascular reactivity in patients who suffered a CHT with the development of epileptic seizures showed that impaired perfusion reserve in the vertebrobasilar basin predominated in 94 (85.45%) patients compared to the carotid basin in 67 (60.9%) patients, $p<0.001$, with clearer differences observed among patients with grossly reduced perfusion reserves: Cerebrovascular reactivity reduction of less than 10% in the vertebrobasilar basin was observed in 37 (33.6%) observations and in the carotid basin in 9 (8.2%, $p<0.001$).

In the control group of patients, there was no significant difference in the changes of cerebrovascular reactivity in the carotid system and in the vertebrobasilar basin in 32 (66.7%) patients, respectively. In assessing the state of hemodynamic indices, we note that pulse indices in the left carotid basin were more frequently changed in patients with ischemic stroke with the development of epileptic seizures (in 23 (48%) observations increased, in 3 (6.2%) decreased, and in 21 (43.7%) normal). Similarly, no differences in pulse indexes values in the right carotid pool were found for both sexes in the main and comparison groups ($\chi^2=3.2$; $p=0.20$): increased pulse indexes were registered in 60 (54,5%)

patients in the main, and 22 (45,8%) in comparison groups, reduced - in 8 (7,3%) main, and 2 (4,2%) comparison groups, normal values - in 42 (38,2%) main, and 23 (47,9%) comparison group patients.

After functional tests we have revealed that autoregulation on the right side was changed more often in patients with posttraumatic epilepsy and concomitant somatic diseases of the main group (29 (44,6%) patients, than in comparison group patients (8 (16,7%), $p<0,01$). Assessment of autoregulation state on the left side also revealed predominance of changes in the indicators in patients of the main group in 46 (41,8%) patients compared to comparison group patients (12 (25%), $p<0,05$). Among the patients studied, 104 patients received two antiepileptic drugs, and 45 patients received monotherapy. The course included the following neuroprotective drugs: cytoflavin intravenously drip 10 ml per day and Dinar 4 ml intramuscularly for 10 days, then Dinar in tablet 250 mg 3 times a day for 6 weeks, then Espa-Lipon in capsules 600 mg 3 times a day for 4 weeks. In parallel with neuroprotection, AED therapy was continued according to the scheme previously performed in this patient.

The effectiveness of corrective therapy was evaluated by the positive dynamics of clinical, hemodynamic and tcdg and eeg parameters in patients with posttraumatic epilepsy at different periods after corrective treatment (1, 3, 6 months).

A positive clinical dynamics was revealed: a decrease in the frequency of seizures by 50% or more was registered in 92.5% of patients ($p<0.05$), including complete control of seizures in 23.1 and 57.1% of posttraumatic epilepsy patients and a decrease in their number by more than 75% in 44.9 and 33.3% of observations, respectively. The percentage of complete seizure control prevailed in LVE patients ($p<0.05$). Six months after the therapy, seizure frequency returned to the initial data.

A reduction in subjective and objective neurological symptoms ($p<0.05$). The percentage of patients with regression of headache, dizziness, and positive neurological dynamics was higher among patients with posttraumatic epilepsy and comorbid somatic diseases ($p<0.05$), and positive dynamics of reflex sphere and coordinator disorders was higher among patients with posttraumatic epilepsy ($p<0.05$). This may be associated with an improvement in cerebral hemodynamics.

Doppler-physical examination with functional tests performed one month after corrective therapy in all patients with posttraumatic epilepsy revealed positive dynamics of ivmr ($p<0.05$) due to increased



vasodilator reserve (hypercapnic kp+ test) ($p < 0.05$). However, in patients with posttraumatic epilepsy i group, despite their positive dynamics, kp+ values didn't reach control values ($p < 0.05$). In patients with GH pathology of BCA no dynamics of hypercapnic test values were observed, which indicated a deficit of vasodilator reserve ($p < 0.05$). The increase of hypocapnic coefficient (Kr-), reflecting increased constrictor reserve, was seen in LVE patients and in patients with GZ pathology of BCA ($p < 0.05$). The absence of its dynamics in MVE patients suggested that the vasoconstrictor effect was depleted. The overdrive coefficient statistically significantly increased in posttraumatic epilepsy patients of all studied groups, which could indicate an increased vasodilatation reserve after the course of corrective therapy. The data obtained 3 months after corrective therapy were similar; after 6 months, the resistive indices were closer to the initial data.

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CONCLUSION:

Thus, integrated therapy with AEDs and neuroprotective drugs significantly increases the efficacy of drug treatment of posttraumatic epilepsy in its pharmacoresistant course, which is objectively confirmed by the results of clinical and instrumental high-sensitivity research methods.

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