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COMPLEX EVALUATION OF CLINICAL AND INSTRUMENTAL DATA FOR JUSTIFICATION OF OPTIVE TREATMENT ACTIVITIES IN PATIENTS WITH RESISTANT FORMS OF EPILEPSY

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Abstract: The prevalence of epilepsy in the world, according to different authors, ranges from 0.4-0.8% to 0.3-2%. In 70% of patients, epilepsy responds well to medical correction, and in most of them it is possible to achieve remission or reduce the frequency of attacks. 30% with intractable pharmacoresistant forms of epilepsy require special attention in therapeutic and diagnostic terms."Intractable", "resistant", "unbreakable", intrastable forms of epilepsy are those in which the severity and frequency of seizures, associated neurological and mental symptoms and (or) side effects of anti-epileptic drugs are not amenable to satisfactory correction, are unacceptable for the patient and (or) his relatives.

Key words: epilepsy; seizures; pharmacoresistant; antiepileptic drugs; polytherapy of epilepsy.

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INTRODUCTION

The prevalence of epilepsy in the world, according to different authors, ranges from 0.4-0.8% [1] to 0.3-2% [2]. In 70% of patients, epilepsy responds well to medical correction, and in most of them it is possible to achieve remission or reduce the frequency of attacks. 30% with intractable pharmacoresistant forms of epilepsy require special attention in therapeutic and diagnostic terms [3-6, 8].

Intractable", "resistant", "uncurable", intrastable forms of epilepsy are those in which the severity and frequency of seizures, concomitant neurological and mental symptoms and / or side effects of anti-epileptic drugs are not

amenable to satisfactory correction, are unacceptable for the patient and (or) close ones [9]. True pharmacoresistance is defined as a failure in two attempts to use monotherapy and one additional AED (polytherapy), basic for this type of seizures, for 18 months [13, 14].

True pharmacoresistant epilepsy has a negative impact on the quality of life of both patients and their relatives. Frequent convulsive seizures and side effects of the drugs used have a negative effect on the cognitive functions of patients. In patients with uncontrolled epilepsy, mortality and depression are more common, and the need for medical care increases [7]. The main goal of treating such patients is to reduce not only the number of seizures, but also their severity, improve the quality of life, and social adaptation.

International standards for the treatment of refractory epilepsy, in addition to medical treatment, include surgical treatment, stimulation n. Vagus and ketogenic diet [11].

Numerous studies of recent years have shown that the surgical treatment of some forms of pharmacoresistant epilepsy improves the course of the disease and improves the quality of life of patients, and the result depends on the duration of the disease before surgery [9]. Currently, surgery is considered effective in non-replaceable forms of focal epilepsy, and in case of complete removal of the epileptogenic zone, it can relieve the patient from seizures and lifelong anticonvulsant therapy.

The fundamental principles of surgical treatment of epilepsyare accurate clinical and neurophysiological diagnosis of the epileptic focus and its radical removal under constant electrocorticogram(ECoG) and electrosubcorticographic (ESCG) control [7].

The main purpose of preoperative examination of patients is the most accurate determination of the localization of the epileptogenic zone.

This problem is solved by a thorough analysis of clinical anamnestic, electrophysiological and neuroimaging data. In case of proximity or coincidence of the epileptogenic zone and functionally significant areas of the cortex, additional examinations are carried out to determine the latter. Examination can be carried out using non-invasive techniques such as magnetic resonance therapy (MRI), functional MRI, positron emission tomography (PET), single photon emission computer-tomography (PEFT) and extracranial electrostimulation, and invasive - through direct electrical stimulation of the cortex [10].

The "gold standard" of preoperative examination todayday are subdural monitoring and direct electrical stimulation of the cortex [16]. However, the disadvantages of these types of invasive studies can be considered a high risk of complications and a rather high cost.

In the work carried out a clinical method was used, which is based

on the study of the neurological status of the patient and the analysis of attacks. EEG is a non-invasive method for studying the functional state of the brain, including the total recording of the bioelectric activity of individual zones, areas, brain lobes. According to the recommendations of the Internationalantiepileptic league, in the initial diagnosis of epilepsy, it is mandatory to conduct a magnetic resonancebrain graphs (with the exception of idiopathic forms of epilepsy with a clearly defined clinic and EEG picture).

This is due to the fact that in more than 60% of cases, epilepsy develops against the background of morphological changes in brain tissue that can be detected during MRI [9]. Changes in the structure of the brain in epilepsy are diverse. In children of early age, malformations of the brain, the consequences of intrauterine infections and hemorrhages are detected. In adults, the cause of epileptic seizuresthere may be brain tumors, injuries, strokes, infectious and inflammatory diseases and their consequences, vascular malformations, parasitosis, acute and chronic intoxication [14].

These pathological processes are related to macrostructural lesions of the brain, but the cause of pharmacoresistant epilepsy can be minimal morphological changes in the brain, such as, for example, focal cortical dysgenesis and dysplasia, heterotopies, hamartomas. Cortical dysgenesis is a violation neuronal migration at the stages of intrauterine development, when microscopic areas of the cerebral cortex (gray matter) find in an atypical place, for example, among the layers of neuroglia (in the white matter of the brain), where they acquire epileptogenic properties. Routine MRI provides information on structural abnormalities also in all cases. In this regard, at the present stage, it became necessary to carry out functional methods of neuroimaging, which allow not only to study the pathological changes in various brain structures in vivo, but also to clarify some mechanisms of epileptogenesis. Such methods include diffusion tensor MRI with tractography, which is a modern technology for morphological images [10, 12].

Diffusion-weighted magnetic resonance imaging (DWMRI) is based on measuring the diffusion of water in each volume element (bill) of the image. As a result, a diffusion matrix is formed, from which it is possible to obtain three numerical values and three vectors describing the strength and direction of diffusion at the selected point. In pathological processes, there is a violation of the linear organization of the pathways, since the membranes of axons are an obstacle to its diffusion in other directions. The diffusion tensor is determined by the magnitude andthe direction of diffusion of water molecules in three-dimensional space, allowing to obtain data on the magnitude of the anisotropy and the direction of

diffusion in each bill with three-dimensional coordinates. From the values of the tensor, some scalar indices are calculated (the average diffusion capacity is MD; fractional anisotropy is FA). These tensor values may reflect structural breakdowns and specific pathological processes [11].Thus, the use of a complex of structural and functional methods of neuroimaging allows non-invasively detecting the cause of the formation and dynamics of epileptogenesis, assessing the effectiveness of the treatment.

The purpose of the study is to assess the significance of instrumental neuroimaging examination methods in the diagnosis of pharmacoresistant epilepsy for determining tactical surgical treatment.

MATERIAL AND METHODS

The study included 43 patients aged from 18 to 68 years old who were admitted for treatment with a diagnosis of pharmacoresistant epilepsy. Disease duration averaged 16.5 (ё 0.3) years. The study involved 15 (35%) women and 28 (65%) men, respectively.

The social and labor status is as follows: working patients - 14 (33%) people and persons with disabilities of groups II and III - 29 (67%) person.

The etiological factors of the disease were cranial brain injury - in 16 (37%) cases, the effects of perinatal pathology - in 6 (14%), pathological formations of the brain - in 12 (28%) and neuroinfection - in 4 (9%). In the preoperative period, all patients were examined according to the standard diagnostic program for management of patients with epilepsy [12]. When confirming the epileptic natureof attacks on EEG, additional research was conducted to clarify the morphological substrate of the disease: MRI, CT, PET, MR-tractography. In the intraoperative period, in order to clearly establish the epileptic focus and establish its boundaries on the open brain, neurophysiological monitoring of cortical and deep structures was performed according to ECOG and ECGC through corticographic and deep-seated electrodes.

The following types of surgical interventions were performed: temporal lobectomy with resection of the anterior 2/3 of the temporal lobe, subpial resection of epileptic foci, amyglohali pocamppectomy, subpial transsections were performed in functionally significant areas of the brain. When selecting patients

The generally accepted criteria of resistance P. Kwan, MJ Brodie were taken into account, according to which the duration of the active course of the disease should be at least two years, during which the use of two or more relevant, in an adequate dose and well tolerated AED in the "monotherapy", " monotherapy-combination "had no effect. The frequency and severity of the attacks were also taken into account, although these criteria are not stringent. Evaluation of the results of surgical treatment was carried out using a modified scale J. Engel [7]

RESEARCH AND DISCUSSION

An analysis of the data obtained from a comprehensive survey allowed us to diagnose a multifocal, single-hemispheric form of temporal epilepsy in all patients. According to the results of dynamic EEG monitoring, all 43 patients were diagnosed with an extensive stable area of focal pathological paroxysmal activity, localized in the temporal lobe region - 29 patients, in the temporal central - 9 people, in the temporal light - 5 patients.

In the examined patients, the following forms of epilepsy were diagnosed: symptomatic focal - 11 patients (25.5%), cryptogenic focal - 2 (4.7%) patients, symptomatic generalized - 18 (41.9%) patients, cryptogenic generalized - 10 (23 , 2%) patients, unclassifiable form of epilepsy -2 (4.7%) of the patient. Seizures occurred during sleep deprivation in 9 (20.9%) patients, in hyperventilation in 11 (25.6%), associated with the onset of menstruation in 2 (4.5%). The greatest number of seizures, in 21 people, 49% It spontaneously arose. Auras of various nature were diagnosed in 38 (88.4%) patients, of whom cephalgic was observed in 18 patients (47.3%), visceral in 13 (34.2%) patients, visual in 3 (7.9%) patients and emotional in 4 (10.6%) cases. Generalized convulsive seizures were more often observed, in 22 people (51.2%), less often - complex partial with secondary generalization -in 15 (34.9%) cases, and rarely the remaining types of paroxysms.

Table 1. Types of epileptic seizures

Epileptic seizures	Number of patients	
	abs	%
Simple partial	6	13.9
Complex partial with secondary generalization	15	34.9
Generalized convulsive (tonic-clonic, tonic, clonic, static)	22	51.2
Total	43	100.0

The study of the neurological status revealed lesions of the cranial nerves in 15 patients (35%), anisoreflexia in 11 (25.5%) cases,hemiparesis in 10 (23%) and speech disorders in 10 (23%) cases. Intellectually mental disorders were detected in 25 (34.9%) patients.Options for epileptic seizures in patients are given in Table. 1.

The main electrographic changes in the form of pathological foci on the EEG are: sharp waves, peak wave complexes, acute - slow wave complexes, alternating with a group of slow waves d - to the range.

Focal changes in biopotentials were recorded against the background of widespread dysarrhythmia (usually bradyar-rhythmias) and, as a rule, were

accompanied by bilateral high-amplitude outbreaks of paroxysmal activity. In 12 (28%) patients with hyperventilation, changes in EEG in the form of an increase in epileptiform activity were detected.

In 12 (28%) patients, hyperventilation revealed changes in the EEG in the form of an increase in epileptiform activity. During MRI, 24 (55.5%) people showed structural changes in the temporal and frontal lobes of the brain in the form of subarachnoid and intra? Brain cysts, 11 (14.5%) parencephalic cysts were detected. In 10 (23%) patients, MRI showed signs of unilateral (usually left) and bilateral atrophy of the hippocampus (mesial temporal sclerosis), hydrocephalus occurred in 9% of cases. Asymmetry of the lateral ventricles was found in 5 (12%) patients, and changes in the left lateral ventricle prevailed. In addition to sclerotic transformations in the hippocampus, 4.5% of patients had atrophic changes in the cerebellum.

Table 2. Surgical intervention

Typeofsurgery	Numberofpatients	
	abs	%
Anteriortemporallobectomy	17	47.9
Anterior temporal lobectomy with sub-branch transsections	6	16.2
Resection of cortical epileptic foci	7	19
Transcorticalamygdalogoppocampectomy	5	13.5
Subpialtranssection in functionally significant areas of the brain	2	5.4
Total	37	100

Table 3. Results of surgical treatment of multifocal temporal epilepsy on a modified scale J. Engle.

	Multifocal temporal epilepsy form			
	temporal frontal	temporal central	temporal parietal	
I	4 (45 %)	3 (16 %)	3 (33 %)	10 (27 %)
II	3 (33 %)	8 (42 %)	3 (33 %)	14 (38 %)
III	2 (22 %)	6 (31 %)	2 (22 %)	10 (27 %)
IV	-	2 (11 %)	1 (12 %)	3 (8 %)

PET was performed in 21% of the examined patients. In all cases, glucose metabolism was observed in the affected area, which coincided with epileptiform activity on EEG. When comparing MRI images and tractographic research (11 people) in 65% of cases, the results were the same. An MRI picture of the depletion of white matter tracts at the level of the parietal? Occipital region was established in 35% of cases. The following FA values were obtained: 0.54 for the frontal sections of the brain, 0.52 for the back. The average diffusion capacity for the anterior brain regions was 0.87, for the posterior parts - 0.85.

Visual assessment of the symmetry of the tracts revealed that a decrease in their representation on the foci side is typical for patients with cortical dysplasia. In the case of the presence of mesial temporal sclerosis, there was a "impoverishment" of the tractographic picture in the opposite hemisphere, which can be explained by the phenomenon of hypocampaldeafferentation. The list of surgical interventions is given in table. 2

Anterior temporal lobectomy was performed on the largest number of patients - 23 cases (62%), of which anterior temporal lobectomy with subfiatranssections - in 6 (16.2%) patients. 5 (13.5%) patients underwent trans cortical amygdal ogoppocampectomy, resection of cortical epiocides -7 (19%), subpialtranssection in functionally important areas of the brain - 2 (5.4%) patients. intracranial complications. In the postoperative period, we did not have noted any significant neurological disorders in operated patients, with the exception of mild cerebral symptomatology,the regression of which occurred during the first few days after surgery. Evaluation of the results of surgical treatmentwas carried out on a modified scale J. Engle.

In 37 operated patients, the absence of clinical seizures was observed in 10 (27%) cases; the presence of seizures that do not change the quality of life of patients - in 14 (38%), a decrease in the frequency of seizures by more than 50% was observed in 10 (27%), in 3 (8%) patients there was no significant clinical improvement. The lack of effectiveness of surgical interventions, in our opinion, is due to the presence patients have a sufficiently long epileptic history of the disease, the spread of epileptic activity to functionally significant areas of the cortex, repeated craniocerebral injuries, as well as the patients' disruption of the treatment and treatment regimen of anticonvulsants in the immediate and late postoperative periods.

CONCLUSION

The findings of a comprehensive examination of clinico-electrophysiological and neurovascular studies (including CT, MRI, PET, and tractography) of patients with pharmacoresistant epilepsy can clarify the mechanisms of formation of the epileptic system and use them to substantiate adequate approaches to surgical treatment.

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