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Research Article

Modern Problems of Diagnosis and Treatment of Neonatal Seizures

Elena A Morozova[1]*, Rimma R Sergeeva[2] and Dmitry V Morozov[3]

[1]Professor at the Department of Pediatric Neurology, Kazan State Medical Academy, Kazan, Russia

[2]State Autonomous Health Care Institution "Children's City Hospital number 8", Kazan, Russia

[3]Assistant Professor at the Department of Pediatric Neurology, Kazan State Medical Academy, Kazan, Russia

***Corresponding Author:** Elena A Morozova, Professor at the Department of Pediatric Neurology, Kazan State Medical Academy, Kazan, Russia.

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Abstract

Aim: Analyze the current practice of management in patients with neonatal seizures and perinatal brain disorders and determine the ways to prevent long-term neurological complications.

Materials and Methods: The study group included 140 children (aged from 2 weeks to 18 months) with neonatal seizures and perinatal brain abnormalities. In these cases, the obstetric and early postnatal history was analyzed; all patients underwent video-EEG monitoring, cervical spine X-ray, neuroimaging, and a Doppler ultrasound test.

Results: We found a number of reliable ante- and intra- partum predictors of neonatal seizures. According to the medical documentation from the neonatal pathology departments, local neonatologists have difficulties in diagnosing and verifying the type and duration of seizures. In most patients with neonatal seizures, we detected epileptiform EEG activity, signs of birth defects (according to X-ray) and marked changes (according to neuroimaging) in the cervical spine.

Conclusion: The results confirm that neonatal seizures are one of the first symptoms of severe brain damage, including intra-natal damage. Evolution of neonatal seizures into drug-resistant epilepsy and further disability is associated with insufficient knowledge of neonatal seizures, standards for their diagnosis, therapy and multidisciplinary observation.

Keywords: *Neonatal Seizures; Newborn Infants; Epilepsy; Cerebral Ischemia*

Introduction

The relevance of the study of neonatal seizures (NA) is due to many reasons and, above all, the lack of alertness of the practitioner in relation to NA. Late diagnosis leads to such adverse neurological outcomes as pharmacoresistant epilepsy, cerebral palsy (CP) and cognitive impairment [1-4].

Neonatal convulsions (NA) is a reliable sign of severe brain damage to the newborn that occurs in the first four weeks of life [5,6].

Neonatal convulsions, according to various specialists, are observed in 0.7 - 16% per 1,000 live births [5]. More often, NS are found in premature babies, especially with a mass of less than 1500g [7].

Among all the causes of neonatal seizures worldwide, 50 - 75% in the first place remains hypoxic-ischemic encephalopathy (HIE) [5,8]. In Europe, HIE is on the 3rd place among the causes of neonatal mortality [9]. The second most common cause of seizures in newborns is perinatal ischemic stroke, with a frequency of 7.5 - 20% [13,14].

It is obvious that HIE and neonatal stroke can be the result of the use of different terminology by the authors in the interpretation of perinatal ischemia-hypoxia as the cause of the appearance of NA. The vagueness of terminological concepts leads, among other things, to large statistical errors. An analysis of world statistics shows a significant difference in the number of newborns with NA in different countries and regions within one country. Probably, this fact is also due to the depth of studying the problem in this particular region.

Studies of the last 10 years show that the score is below 5 on the Apgar scale after 5 minutes, PH < 7, the need for resuscitation and seizures for more than 30 minutes. are early predictors of the development of NA [11].

Diagnosing NA is challenging. The complexity of the diagnosis is due to the frequent absence of seizure correlates on the electroencephalogram (EEG) due to the anatomical and physiological features of the brain of the newborn. At the moment, special instrumental methods allow differential diagnosis of neonatal seizures with other paroxysmal conditions of the neonatal period. Video EEG monitoring (VEM) - Golden standard for diagnosing neonatal seizures and monitoring the effectiveness of antiepileptic therapy [13,14].

According to many researchers, VEM is best done in tandem with magnetic resonance imaging (MRI) [15,16]. The method of MRI and the detection of certain structural disorders in 87% is the most important prognostic factor of an unfavorable outcome [15].

Treatment of NA causes the most controversy. A number of authors consider it necessary to prescribe an anti-epileptic drug (AEP) only after confirming epileptiform activity on EEG [7,17], others recommend to refrain from early treatment of NA with anti-epileptic drugs due to the lack of evidence of the effectiveness of this tactic with regard to remote consequences [10,18]. Phenobarbital remains the drug of first choice, which is a priority in the neonatal pathology departments (ARF), despite evidence in the literature about its adverse effects on the developing brain.

Purpose of the Study

The purpose of the study is to analyze the management of patients with neonatal convulsions and perinatal brain pathology and to determine ways to prevent their long-term effects.

Materials and Methods

Our work was based on the study of 140 patients aged from two weeks to 18 months with a diagnosis of neonatal seizures, on the background of reliable perinatal CNS pathology, with the exception of children with idiopathic NS. The comparison group consisted of 40 patients representative of age and sex, without NS. AT The study examined obstetric and early postnatal history, conducted a neurological examination of children, neurosonography (NSG), evaluated the parameters of cerebral blood flow (ultrasound and transcranial dopplerography of the cerebral vessels), all patients were evaluated for brain bioelectrical activity (standard electroencephalography and video-EEG, standard electroencephalography and video-EEG were assessed (standard electroencephalography and video-EEG were evaluated by standard electroencephalography and video-EEG), radiography of the cervical spine, neuroimaging techniques were used (X-ray computer and magnetic brain scan), ophthalmoscopy.

Results and Discussion

When studying children with neonatal convulsions, it was found that in 125 newborns (89%) convulsions debuted during the first 72 hours of life against the background of cerebral ischemia II-III degree. Among antenatal risk factors, both acute and chronic intrauterine hypoxia of the fetus, resulting from anemia (45%), ARVI (32%), prolonged toxicosis (32%), late gestosis (28%), chronic placental failure (21%), threatened abortion at an early stage in 60 pregnant women (43%), premature %.

The onset of labor activity (20%) (Figure 1). Drug treatment, including hormonal and antibacterial therapy, received significantly more pregnant women in the study group ($p < 0.001$). One of the most significant causes of the development of NA is the pathology of labor [19,20]. An analysis of obstetric history showed that 42 of the pregnant groups in the study (30%) used generostimulation.

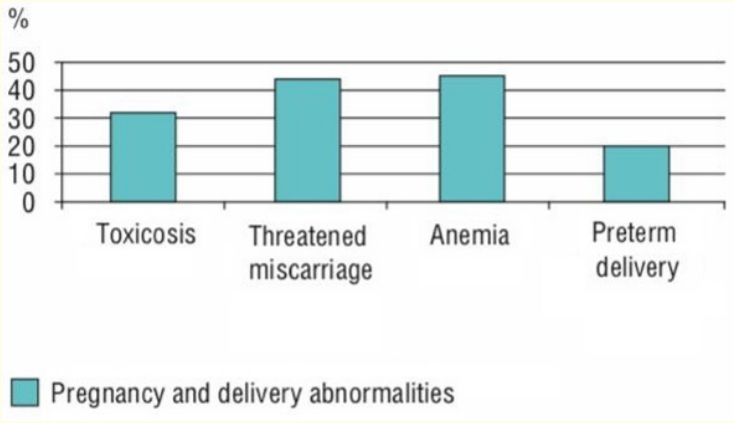

Figure 1: *Risk factors for cerebral ischemia.*

It is important to emphasize that birth stimulation in most maternity hospitals is used without objective reasons and can be regarded as inadequate obstetric activity. The same applies to the methods of pain relief during childbirth. For example, in 64 women in labor (46%) epidural anesthesia was used during natural childbirth. Active maternity stimulation (23 patients - 62.2%), use of obstetric benefits (12 patients - 17%), "extrusion of the fetus" equipment (45 studied - 32%) with "stuck" head and shoulder dystocia (22 patients - 31%) significantly more common in the main group ($p < 0.002$).

From the first days of life, 102 newborns (73%) were on artificial lung ventilation (ALV), of which 21 (15%) - for a long time: 7 - 10 days. The Apgar score of less than 5 points in the 5th minute of life was noted in 88 children (63%). Analysis of documentation obtained at discharge from maternity hospitals and acute renal failure, showed that the classification of neonatal seizures according to international standards was not carried out in any case, and no one noted the duration of attacks, their the duration of therapy for the relief of attacks and reactions to it. Each of the above factors should have been extremely important for a multidisciplinary team of doctors who would monitor a newborn with an NS in the future: a pediatrician, a pediatric neurologist, and an epileptologist in the event of the development of epilepsy.

In 112 patients (80%) with NA in the final diagnosis when the child is discharged from the ARF, "convulsive syndrome" sounds in the capacity of an additional diagnosis; These terms, in our opinion, are not able to reflect the correct phenomenology of seizures, since they imply the presence of motor manifestations in the structure of the seizure, which are absent in non-convulsive seizures in newborns.

At the same time, visually, many movements often do not differ from motor phenomena characteristic of a child with severe brain damage without seizures, such as dystonic paroxysms. 122 patients (87%) with indication of convulsive syndrome were given phenobarbital, without reasoned confirmation of the epileptic nature of attacks on EEG, only on the basis of clinical manifestations. In 49 patients with NS (35%), nootropic drugs were included in the AEP treatment regimen. It is known that nootropic therapy in the presence of epileptic seizures is considered very controversial [6,13].

VEM and MRI were performed only in two patients diagnosed with Otahara syndrome (early epileptic encephalopathy). In the recommendations for the discharge of a child from OPN, 7 (5%) patients were recommended to undergo a routine EEG followed by a consultation with a neurologist and none - monitoring VEM.

Formation of the effects of perinatal CNS pathology is clearly observed at the age of 12-18 months. According to the data obtained, the formation of persistent neurological disorders (variants of spastic tetra- or hemiparesis in combination with a gross delay of psychomotor development) by the age of 12 months was revealed. in 129 patients (Table 1). At the age of 18 months 73 patients (52%) with the presence of neonatal seizures had a diagnosis of "epilepsy".

Neurological condition	Occurrence in this study, %
Spastic teraparesis	64
Hemiparesis	28
Diffuse muscle hypotonia combined with hydrocephalus, hyperkinesis, and hyperreflexia	8
Delayed development of higher cortical functions	86

Table 1: *Types of neurological disorders in the studied patients.*

Anatomical neuroimaging techniques (MRI, CT) are an integral part of the diagnostic algorithm for children with NA all over the world. Among the children of the main group in 100% of cases there were marked changes according to MRI data. The most frequent of these were signs of external hydrocephalus and cystic-atrophic process in the brain.

Neurosonography (NSG) was performed for all children of the main group. The most frequent changes during NSG were cysts in the periventricular areas (56%), hemorrhages in the stomachs (45%), periventricular leukomalacia (54%) and hydrocephalus of varying severity (42%).

In order to determine the effect of cerebro-vascular discirculation on the formation of NS, all patients underwent the following informative research method, such as USDG. In the majority of infants in the study group, according to the results of the UZDG, the following were observed: a decrease in BFV in 88 (62.8%) patients, asymmetry of blood flow over standard age values - in 109 (77.8%) children, signs of and moderate violations of venous outflow from the cavity skulls in 120 (85.7%) patients (Table 2).

	Study group		Control group		P
Major parameters of USDT	Абс./Abs	**%**	Абс./Abs	**%**	
Reduced linear flow velocity	88	62,8	3	7,5	P < 0,001
Flow asymmetry in the spine arteries	109	77,8	28	70	P = 0,0955
Moderate venous dystonia	82	58,57	11	27,5	P < 0,001
Pronounced venous dystonia	38	27,14	4	10	P < 0,001

Table 2: *Occurrence of abnormalities detected with ultrasound vascular Doppler test (USDT).*

As can be seen from table 2, such indicators as a decrease in the linear velocity of blood flow (p <0.001) and signs of moderate and severe discirculation (p ≤ 0.001) were significantly more frequently observed in children in the main group.

The phenomena of optic atrophy were found in 39 (28%) patients, signs of retinal angiopathy were found in 102 (73%) children. In our opinion, the above-described data of the ophthalmoscopy reflect the phenomena of cerebro-vascular insufficiency.

One of the most dramatic statistical anomalies can safely be called the indicators of generic injuries in general and the cervical spine, in particular, and contradictory ideas about birth injuries are inherent in both foreign and Russian scientists [18,20,21]. Obviously, in such marginal representations, the main role is played by the qualifications of the doctor in understanding the symptoms of birth trauma and its origin, that is, knowledge of the problem as a whole.

Statistics of birth trauma in Russia, as reflected in guidelines on pediatric neurology and components.

The current 4%, in our opinion, is far from reality [5,6]. Birth injuries at the level of the cervical spine in newborns with NA and perinatal CNS pathology were found in 121 patients (86.5%) and had significant differences in the frequency of occurrence and severity in the study and comparison groups ($p < 0.001$). Radiography of the cervical spine revealed such signs of instability of the vertebrae as a displacement of the vertebrae relative to each other - 92 (66%) patients, asymmetry of the lateral masses of the atlas with respect to the denticular process of the II cervical vertebra - 34 (24%) patient, increase in the joint gap Cruveiller - 18 (13%) patients (Figure 2). For correct verification of the diagnosis of "epilepsy", video EEG monitoring is currently required. With the help of the continued EEG recording, numerous specific EEG patterns characteristic of full-term and premature babies were identified. The most unfavorable phenomena of the neonatal EEG are the isoelectric pattern (background activity amplitude less than 10 μV), the flash-suppression pattern, especially when persisting in the structure of the study record. Continued monitoring of EEG with video fixation registered epileptiform activity in 129 patients with NS (92%) at the age of 2 weeks of life: the pattern of "outbreak-oppression" - 36 (28%) patients, "acute-slow wave" - 45 (35%) patients, "Peak-slow wave" - 36 (29%) patients, "polyspayk-pattern" - 23 (18%) patients, gypsarhythmia - 15 (12%) people (Figure 3). During the periodic evaluation of the electroencephlogram of patients of the main group, evolucine epileptiform patterns as patients mature. The transformation of the "flash-suppression" pattern into multifocal epileptiform activity was noted with the subsequent formation of classical and modified gypsarhythmia in 38 (27%) patients.

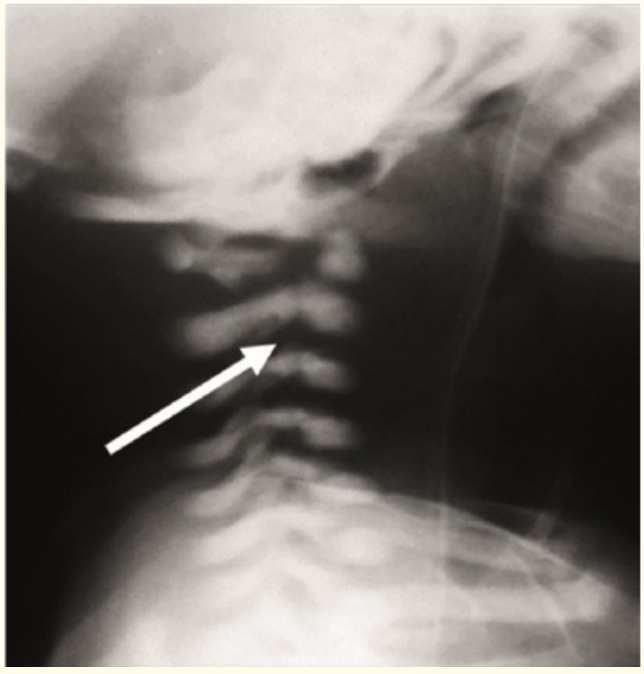

Figure 2: *Patient S., One month old. Cervical spine X-ray (lateral view). C1-C2 dislocation towards the anterior segment.*

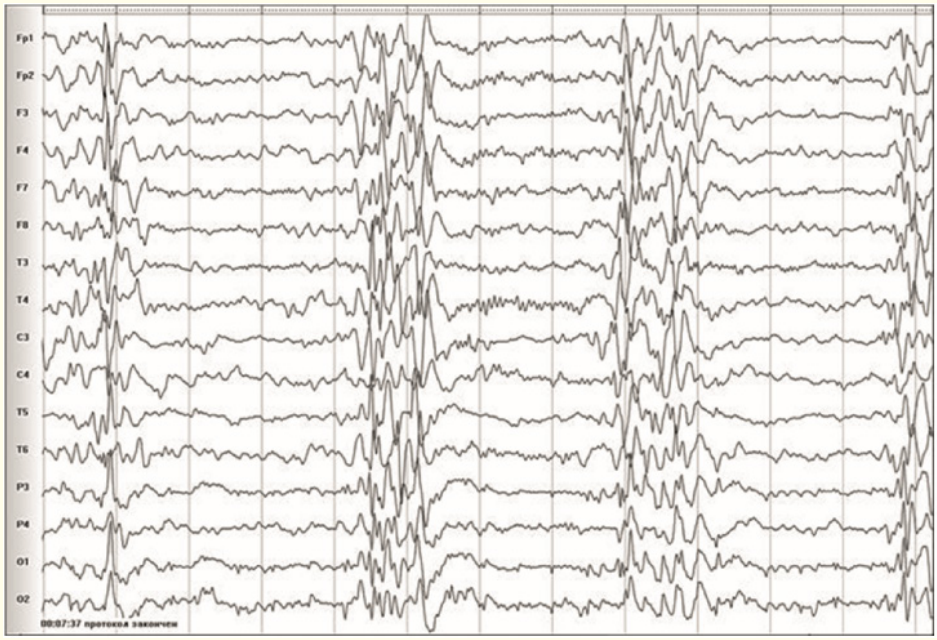

Figure 3: *Electroencephalogram of patient G., 6 months old. The "excitation-inhibition" pattern.*

In 87 patients (62%), changes on the EEG were observed, followed by normalization in the absence of recurrent seizures, 49 (35%) of the subjects studied showed negative dynamics of the EEG pattern and by the age of 18 months. various forms of epilepsy were formed: symptomatic focal - 15 (30.6%) patients and multifocal epilepsy - 8 (16%) patients, symptomatic West syndrome - 17 (34.7%) patients (Figure 4). In 9 (18%) of the 49 patients studied, there was a negative trend not only according to EEG data, but also according to the clinical response to taking AED, and subsequently a pharmacoresistant form of epilepsy was formed.

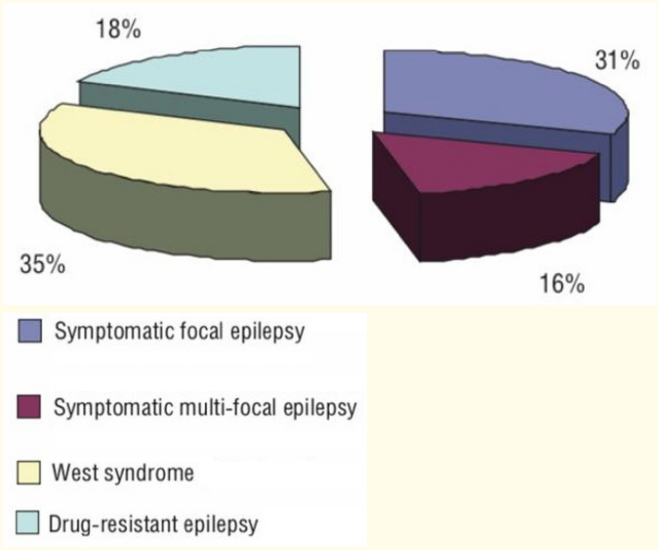

Figure 4: *Transformation of neonatal seizures into various forms of epilepsy.*

Clinical example

Patient S., 6 months old, was admitted to the State Autonomous Educational Institution "Children's City Hospital №8" with complaints of isolated paroxysms in the form of propulsive contractions from 3 to 5 times a day, startles with sharp sounds, twitching of the right corner of the mouth and right hand, restless and short sleep.

Anamnesis: Pregnancy 2nd, proceeded against the background of ARVI for a period of 20 weeks. (use of antibiotic therapy), threatened abortion for a period of 35 weeks. against the background of late gestosis. Birth 2nd, premature, for a period of 35 weeks., By emergency caesarean section. Apgar score - 1 - 4 points. On a ventilator for 7 days in the neonatal intensive care unit (ORN). Diagnosis in acute renal failure: "cerebral ischemia of the 3rd degree: hypertensive syndrome (pre-brainwave), neuroendocrine syndrome, motor impairment syndrome".

In the extract from the arrester there are indications of clonic twitching in the right limbs, which were stopped by themselves. A routine EEG was performed - epileptiform activity was not detected. Repeated EEG at 3 mo. - without pathology.

Neurological status at the time of admission (6 months): head of microcephalic form; FMN: convergent squint, a look fixes briefly; muscle hypertonus along the pyramidal type in the flexors of the arms and legs; tendon reflexes from the arms and legs spastic, equal; elements of athetosis in the hands; reliance on the hands is reduced, reliance on the legs on the "socks" with a cross, holding his head uncertainly.

VEM: Multiregional epileptiform discharges from peak-to-polyped-slow wave complexes registered in morphology resembling a pattern of modified hypsarrhythmia. Diagnosis: Symptomatic infantile spasms. Perinatal pathology of the brain in the form of spastic tetraparesis, athetosis, psychomotor retardation.

Treatment: Valproic acid in drops in the initial dose of 10 mg/kg/day. Recommended: MRI of the brain (Figure 5), titration of the dose of anti-epileptic drug, consultation of the epileptologist in a month, HEM after 3 months (Figure 6).

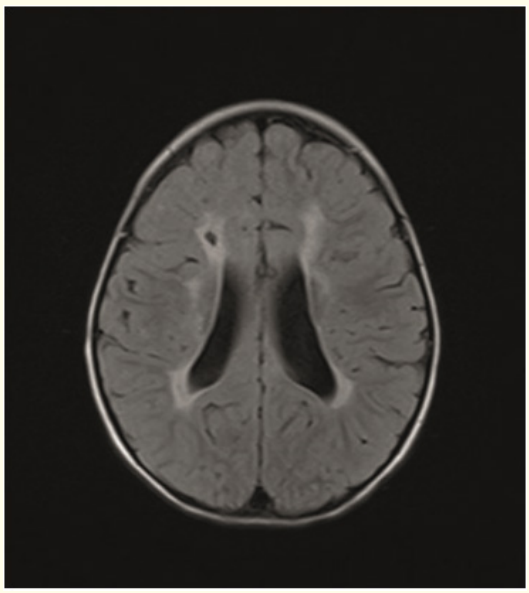

Figure 5: *MRI of the brain. Patient S., 8 months old. Atrophic changes in the frontal lobes of the cerebral hemisphere.*

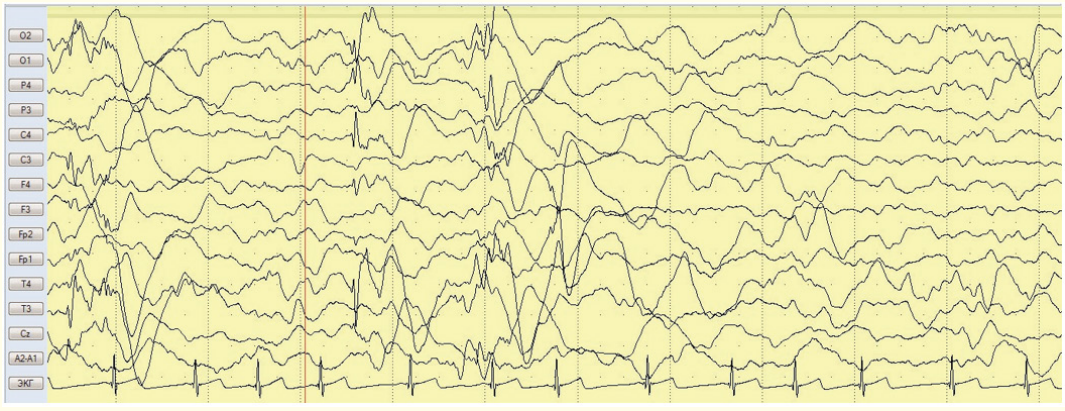

Figure 6: *Video-EGG. Patient S., 9 months old. Modified hypsarrhythmia.*

This clinical example is a convincing argument for the absence of an algorithm for managing patients with NS, which is typical for most medical institutions in Russia. First of all, the description of a clear clinical correlate of a paroxysmal event is not presented. That is, one of the most important rules of medical diagnosis is not observed: "the diagnosis is as accurate as the history is." The duration of the attack is not known, the complex of necessary studies, including the registration of paroxysm with the help of a continuous EEG study, has not been carried out. The discharge summary also does not reflect the patient's response to the therapy being conducted, which is extremely important in trying to understand which drugs or procedures help the patient. The logical consequence was the evolution of NA in symptomatic epileptic encephalopathy by the age of 6 months. It can be assumed that this evolution as a whole is typical of NA. The lack of a clear diagnostic and therapeutic algorithm for children with perinatal pathology and neonatal convulsions undoubtedly contributes greatly to the development of delayed epilepsy in this category of children.

Conclusion

The data obtained as a result of the research show that NS are one of the first symptoms of severe brain damage, including intrapartum. Moreover, part of the intranatal damage can be reduced by limiting inadequate obstetric participation in the birth certificate. Neonatal convulsions are characterized by transformation into various forms of epilepsy, including pharmacoresistant. With greater severity of perinatal pathology and persistent epileptiform activity, the formation of cerebral palsy and cognitive impairment are typical. The main problem of the evolution of neonatal seizures and the growth of disability is associated with the lack of a multidisciplinary step-by-step algorithm for the management of newborns with NA. In addition, the analysis of discharge epicrises from the neonatal pathology departments shows a lack of understanding by the clinician of the problem of neonatal seizures, including the conditions under which the prescription of AED is appropriate.

It is important to understand that the problem of NA is determined not only by the effects of the attacks on the developing brain, but also by neuronal apoptosis, which develops as a result of perinatal brain damage. The search for the algorithm of medical tactics in children with neonatal convulsions should take into account all the components of pathomorphogenesis, starting from the first hours of a child's life.

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