

REPUBLIC OF AZERBAIJAN

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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

**THE PREVALENCE RATE, CLINICAL FEATURES, RISK
FACTORS, TREATMENT AND PREVENTION OPPORTU-
NITIES OF NEONATAL SEIZURES**

Specialty: 3223.01 – Neurological disease

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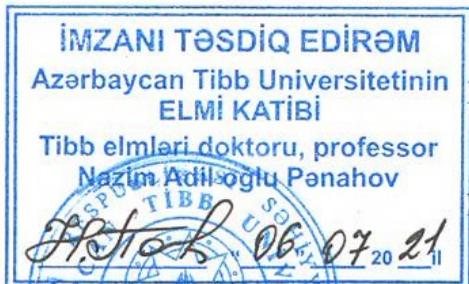
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INTRODUCTION

Relevance and development rate of the topic. Neonatal seizures causes severe medical and social consequences, such as hypoxia and ischemia of the central nervous system, infectious damage, metabolic imbalance, seizure syndrome associated with congenital anomalies in the first month (0-27 days) of life in a term infant.^{1;2;3} Data about prevalence reate of this syndrome given by different clinics and hospitals significantly doffers from each-other: nearly 5 cases of neonatal seizure have been recorded per 1000 full-term newborns (gestation age >37 full weeks, body mass at birth >2500 gram), but the frequency of neonatal seizures among early term newborns is more than 130% , depending on body mass and degree of asphyxia. There are many reasons.^{4;5;6;7;8} for neonatal seizures: ischemic encephalopathy due to hypoxia of the central nervous system, traumatic brain injury, inflammatory processes of infectious origin, glycemic and micronutrient imbalance, etc. Most of theses reasons depends on the quality of maternity care service due to reional development rate. That is why interregional differences on prevalence rate of neonatal seizures

¹ Zavadenko, A.N. i dr. Neonatal'nye sudorogi: osobennosti klinicheskoy diagnostiki // Detskaja bol'nica, - 2013. № 4, - s. 41 – 48

² Glass, H.C. Seizures in preterm neonates: a multi – center observational cohort study // *Pediatr. Neurol.*, - 2017. 72, - p.19 – 24

³ Al – Momen, H., Muhammed, M.K., Alshaheen, A.A. Neonatal seizures in Iraq: cause and outcome // *Tohoku J. Exp. Med.*, - 2018. 246, - p.245 – 249.

⁴ Myrzaliev, B.D. Neonatal'nye sudorogi. Jetiologicheskie aspekty i voprosy terapii // *Vestnik AGIUV, special'nyj vypusk*, - 2011. - s. 24-25.

⁵ Glass, H.C. Neonatal seizures: advances in modernisms and management // *Clin. Perinatal.*, - 2014. 41(1), - p.177 – 190.

⁶ Bateman, B.T. et al. Calcium channel blocker exposure in late pregnancy and the risk of neonatal seizures // *Obstet Gynecol.*, - 2015. 126 (2), - p. 271 – 278.

⁷ Li, Q. et al. Recording of neonatal seizures in birth certificates, maternal interviews, and hospital discharge abstracts in a cerebral palsy. Case – control study in Michigan // *J Child neurol.*, - 2016. 31 (7), - p. 817 – 823.

⁸ Andrade, E. et al. Tramiento de las convulsions neonatales / [et al.] // *Medicina, suplemento*, - 2018. Vol.78, - p.30 – 35.

are significant: the prevalence rate of the pathology is relatively low in developed countries and relatively high in countries with weak economies.^{9;2;3} The Republic of Azerbaijan has a special position on the availability and quality of maternity care, the country applies the international standard of live birth, a three-stage perinatal care network has been established. Therefore, in a country with such a medical, social and economic situation, it is important to assess the prevalence of neonatal seizures and the role of the factors that forms this level. In addition, the organization of treatment for neonatal seizures is currently in complete.^{10;11;12} First of all, it is necessary to ensure the availability of a specialized neurological hospital for the treatment of neonatal seizures, the transfer of newborns from maternity hospitals to the special hospital.

The options of specialized units for the treatment of neonatal seizures are different: in 3 specialized neonatal centers in Baghdad³, in numerous pediatric neurological clinics in the United², in the Scientific Research Institute of Pediatrics named after K. Farajova in Azerbaijan¹³. Therefore, it is realistic that the results of treatment are different.

Finally, the transition to the international standard of live births in Azerbaijan leads to an increase in the number of newborns weighing 500-1000 grams. This, in turn, may lead to the peculiarities of the

⁹ Saliba, R.M. et al. Risk factors for neonatal seizures: a population based study, Harris country, Texas, 1992 – 1994 // American journal of epidemiology, - 2001. № 1, vol .154, - p. 14 – 20

¹⁰ Jensen, F.E. Neonatal seizures: an update on mechanisms and management // Clinic Perinatal, - 2009, 36 (4), - p.881.

¹¹ Chapman, K.E., Raol, Y.H., Brooks-Kayal, A. Neonatal seizures: controversies and challenges in translating new therapies from the lab to the isolette // Eur J Neurosci, - 2012. 35(12), - p.1857 – 1865.

¹² Okumara, A. The diagnosis and treatment of neonatal seizures // Chang Gung Med J, - 2012. 35, - p.365 – 372.

¹³ Jefendieva, M.Z., Kulieva, K.A., Gusejnova, G.I., Mamedova, T.A. Kliniko – funksional'naja karakteristika neonatal'nyh sudorog // V.Y.Axundovun 100 illik yubileyinə həsr edilmiş elmi – praktik konfransının tezisləri toplusu. – Bakı: - 2016. - s.163

epidemiological characteristics of neonatal seizures. All of the above mentioned facts make the study of the prevalence rate, risk factors and features of the treatment of neonatal seizures in Azerbaijan necessary. Therefore, the topic of the scientific research work is relevant.

The object and subject of the study. The object of study are newborns aged 0 - 28 days with the diagnosis of neonatal seizures confirmed by clinical, instrumental and laboratory methods, and his nervous system and metabolism were selected as the subject of the study.

The purpose of the study. To substantiate the prevalence rate, risk factors and risk level and effectiveness predictors of treatment of neonatal seizures in condition of the transition to the international standard of live birth in Azerbaijan.

Research objectives.

1. Assess the anamnesis and clinical features of neonates with a diagnosis of neonatal seizures at the Perinatal Center.
2. To determine the prevalence of neonatal seizures, risk factors and risk levels in newborns.
3. Outcomes of treatment of neonatal seizures, their predictors and prognostic significance.

The methods of the study:

- Methods of clinical neurological examination;
- Laboratory diagnostic methods (determination of potassium, sodium, calcium, magnesium, glucose in the blood);
- Instrumental-diagnostic methods (electroencephalography, magnetic resonance imaging);
- Statistical methods (descriptive statistical methods of qualitative and quantitative characteristics, correlation, variance analysis, xi-square).

The main thesis to be defended:

- To assess the anamnesis and clinical features of newborns diagnosed with neonatal seizures at the Perinatal Center;
- To determine the prevalence rate, risk factors and the level of risk of neonatal seizures among newborns;

- The treatment results of neonatal seizures, their predictors and prognostic significance.

Scientific innovation of the study results:

- For the first time, the prevalence rate, etiological causes of neonatal seizures, structure of clinical forms of convulsions have been determined in the sample of newborns in the Perinatal Center;
- Antenatal and postnatal risk factors affecting the prevalence of neonatal seizures were identified, and the role of these factors was substantiated according to the level of relative and attributive risk;
- Outcomes of inpatient treatment of neonatal seizures, medical organization influencing the results, the role of antenatal, intranatal and postnatal factors were determined; the methodology of classification according to the specificity, sensitivity and prognostic significance of risk factors was substantiated.

Theoretical and practical significance of the study:

– Information on the prevalence rate, etiological causes and structure of clinical forms of neonatal seizures is important for the planning and organization of neonatal neurological care in perinatal centers of the country;

– The results that determine the role of risk factors for neonatal seizures provide an opportunity to implement targeted preventive measures in the antenatal, intranatal and postnatal periods;

– The obtained information on the factors influencing the outcome of the treatment of neonatal seizures is useful for planning positive outcomes;

– The methodology for detecting risk factors for neonatal seizures, predictors of treatment outcomes, can be used for study of the relevant characteristics of other pathologies.

Approbation and application of achieved results of the study.

The results of the study was reported at the Scientific Council of the Department of Therapy of the State Advanced Training Institute for Doctors named after A.Aliyev, at the meetings of the Association of Neurologists of Azerbaijan, VI International Scientific-Practical

Conference in Moscow (2018), Bukhara III Congress of World Turkic-speaking countries (2018), All-Russian scientific-practical conference in Penza (2018), Scientific-practical conference at the Azerbaijan Perinatal Center (Baku, 2018), at the scientific-practical conference of the National Association of Neuropathologists (2018), at the International Congress of European Pediatric Neurologists and Neurologists of Turkic-speaking countries (Baku, 2019).

The results of the dissertation have been published in 7 scientific-practical journals (including Scopus indexing database) on the relevant list of the Higher Attestation Commission for the last five years, including 1 article in a Kazakh journal. 3 theses and 4 reports were published in the collections of scientific conferences.

Results of the scientific research work is being applied in neonatal hospitals, and in postgraduate education in the State Advanced Training Institute for Doctors named after A.Aliyev.

The organization where the scientific research work has been conducted: the State Advanced Training Institute for Doctors named after A.Aliyev.

The structure and volume of the dissertation:

- Introduction – 7913 symbols;
- Chapter I. Prevalence of neonatal seizures, risk factors and modern features of treatment (literature review) – 43673 symbols;
- Chapter II. Materials and methods of the study – 18881 symbols;
- Chapter III. Clinical and anamnestic features of newborns with a diagnosis of neonatal seizures – 29829 symbols;
- Chapter IV. Prevalence of neonatal seizures, risk factors and risk level – 28594 symbols;
- Chapter V. Outcomes and predictors of outcomes of treatment of neonatal seizures – 43381 symbols;
- Chapter VI. Discussion of achieved results – 24065 symbols;
- Achieved results – 2365 symbols;
- Practical recommendations – 1548 symbols;

The total volume of the dissertation with a sign – 200249 (excluding the table of contents, bibliography, tables and diagrams) - consists of a sign.

MATERIALS AND METHODS OF THE STUDY

According to aim and objectives of the study its materials have been collected in to institutes - “Republican Perinatal Center” of the Ministry of Health of the Republic of Azerbaijan and Scientific Research Institute of Pediatrics named after K. Farajova.

24472 live born infants have been registered in the Republican Perinatal Center during 2012 – 2017 years, neonatal seizures was diagnosed in 73 of them. The standard volume of information per each newborn included: mother's age at the pregnancy period; number of pregnancies and births; chronic diseases of mother during pregnancy (diabetes, hypertension, anemia, etc.); pregnancy complications (preeclampsia, eclampsia, infections, etc.); complications of child-birth (anomalies of birth process, complicated births, etc.) birth options (abdominal, abdominal-night shift, vaginal-without intervention, vaginal-with medical intervention); body weight at birth, status on the Apgar scale 5 minutes after birth. The diagnosis of neonatal seizures is based on the confirmation of the seizure symptoms by a neonatologist. Convulsions are thought to be involuntary contractions of muscles in any form. Commonly accepted guidelines have been used to classify seizures.

Serum tests to determine the amount of calcium, glucose, magnesium and sodium was conducted for all infants with neonatal seizures diagnosis. The following results have been achieved according to these tests:

- Hypocalcemia (serum calcium <7.0 mg / dl);
- Hypoglycemia (serum glucose <40 mg / dl);
- Hypomagnesaemia (serum magnesium content <1.5 mg / dl);
- Hyponatremia (serum sodium <130 mg-eco / l).

The patient was diagnosed with asphyxia on the Apgar scale within 5 minutes of birth and on the background of metabolic acido-

sis ($\text{PH} < 7$). The diagnosis of neonatal infection (meningitis, sepsis, etc.) was made on the basis of microbiological examination of urine, blood, cerebrospinal fluid. Neuroimaging method was used to confirm the diagnosis of intracranial hemorrhage.

Efficiency and predictors of efficiency of the treatment of neonatal seizures was studied on basis of Scientific Research Institute of Pediatrics named after K. Farajova. The medical histories of 250 newborns with a diagnosis of neonatal seizures admitted to the hospital by the method of massive covering were analyzed. The age of the children was 0-27 days, and the gestational age was 23-41 weeks. Their complex clinical examination was accompanied by EEG and MRI examination methods.

The children's EEG results were classified according to the existing (Lyderes) classification: type of background activity (intermittent or constant), maximum and minimum amplitude, cyclical changes in background activity (sleep - wakefulness), the presence of seizure patterns. The results of EEG monitoring were assessed in accordance with the protocol approved in the Russian Federation.

Three factors have been used for assessment of treatment outcomes:

- Mortality (complete failure of treatment of neonatal seizures and perinatal pathologies, their main cause);
- Improvement (disappearance of neonatal convulsions against the background of medication, the patient's ability to write home, provided that he takes anti-convulsive drugs);
- Recovery (cessation of neonatal convulsions, reduction of the role of perinatal pathologies as a cause of convulsions).

Grouping of patients according to their characteristic features (clinical, anamnestic, EEG and MRI) and variants of symptoms, assessment of the level of lethality, probability of improvement and recovery in each group and 95% reliability interval, determination of accuracy of intergroup differences with χ^2 criterion was carried out.

The following features have been considered as predictors of all symptoms affecting treatment outcomes:

- Sensitivity of the symptom (Se): the probability of association of the symptom in cases when the treatment results in lethality, healing and recovery;
- Specificity of the symptom (Se): the probability of non-association of the symptom when the treatment does not result in lethality, healing or recovery;
- Prognostic significance of symptom positivity (PV+): probability of lethality, healing or recovery against the background of symptom positivity;
- Prognostic significance of symptom negativity (PV-): the probability of lethality, healing or absence of recovery against the background of symptom negativity.

CLINICAL AND ANAMNESTIC FEATURES OF NEWBORNS WITH A DIAGNOSIS OF NEONATAL SEIZURES

Hypoxia of the central nervous system is the main etiologic reason for of neonatal seizures (43,8±5,8% as the sole cause, combined with 12,3±3,8% intracranial hematoma), share of other reasons is not significant: 16,4±4,3% metabolic imbalance, 5,5±2,6% intracranial hemorrhage, 5,5±2,6% sepsis, 11,0±3,6% meningitis, 5,5±2,6% idiopathic.

The first manifestation of neonatal seizures is usually observed on the first day after birth (79,5±4,7%), in 12,3±3,8% of cases on the second day, 4,1±2,3% on the third day, 4,1±2, 3% on the IV and subsequent days.

Neonatal seizures are mostly clonic (32,9±5,4% focal; 16,4±4,3% multifocal), 24,7±5,0% of cases are tonic, the specific gravity of other forms of seizures is 26,0±5,1%.

Against the background of neonatal seizures, metabolic imbalance in 30,1±5,4% of cases, hypoxia and ischemia of the central nervous system in 49,3±5,8% of cases (19,2±4,6% of them combined), 13,7±4,0% Infections of the central nervous system (sepsis and meningitis) in of cases are recorded.

61,6±5,6% of children with a diagnosis of neonatal seizures were boys, 38,4±5,6% had a gestational age <37 weeks, and 42,5±5,7% had a birth weight of <2500 grams. 21,9±4,8% of body weight was below the normal for gestational age (SGA), and 43,8±5,8% had a condition <7 on the Apgar scale within 5 minutes after birth.

Full-term (gestational age >37 weeks, body weight ≥2500 grams) and not full-term (gestational age <37 weeks, body weight <2500 grams) newborns with a diagnosis of neonatal seizures have different antenatal and intranatal characteristics, statistically significant difference there is between mothers with chronic diseases (31,0±7,1 and 58,1±8,8%), those born by the abdominal route (23,8±6,5 and 51,6±8,9%), especially those born at night by the abdominal route (4,8±3,2 and 29,0±8,1%), those with a score of <7 on the Apgar scale (23,8±6,5 and 71,0±8,1%), those in need of resuscitation at birth (23,8±6,5 and 80,7±7,0%), respectively.

PREVALENCE OF NEONATAL SEIZURES, RISK FACTORS AND RISK LEVEL

In the Republican Prenatal Center where we have conducted our observations during 2012-2017 years 73 of 24472 live-born infants have been registered as neonatal seizures diagnosed newborns. 3,0±0,1 neonatal seizures cases was registered per 1000 live-born infants (95% confidence interval 2,8 – 3,2‰).

The frequency of neonatal seizures cases among newborns with gestation age <37 and ≥37 full weeks correspondingly was 5,1±0,96‰ (95% confidence interval 3,17 – 7,01‰) and 2,4±0,35‰ (95% confidence interval 1,66 – 3,07‰) and the data statistically differed from each other. In comparison with newborns with gestation age ≥37 full weeks newborns with gestation age <37 full weeks the probability of neonatal seizures is 2,2 times higher, the attributive risk is 2,7 per 1000 children.

The body mass of 10,2% of newborns was less from normal measurements of gestational age (small for gestational age – SGA),

and of 7% was more than normal measurements (large for gestational age – LGA), 82,8% was corresponding (AGA – appropriate for gestational age). The frequency of neonatal seizures cases in these groups (SGA, LGA, AGA) correspondingly was: $6,4 \pm 1,60$ ‰ (95% confidence interval 3,21 – 9,59‰), $2,5 \pm 0,35$ ‰ (95% confidence interval 1,81 – 3,22 ‰) & $3,5 \pm 1,43$ ‰ (95% confidence interval 0,65 – 6,37 ‰). Differences between groups were statistically reliable ($\chi^2=13,5$; $\nu = 2$; $P < 0,01$). The mean level of the indicator was relatively small in newborns whose body weight corresponded to the age of gestation (AGA). If we consider this group as a control group (referent), the risk of neonatal seizures was higher in the other two groups compared to it. Relative and attributive risk levels were respectively: 2,5 and 3,9‰ in the group with a body weight less than the normative age of gestation (SGA), 1,4 and 1,0‰ in the group with a body weight greater than the normative level of gestation age (LGA) in the group.

The highest rate of neonatal seizures was registered among children with body mass <1500 gram ($11,8 \pm 2,76$ ‰; 95% confidence interval 6,26 – 17,30‰). In comparison with this group the frequency of neonatal seizures in other groups was statistically less (body mass 1500 – 1999; 2000 – 2499; 2500 – 4000; 4000 gram and more). It is noticeable that the frequency of neonatal seizures doesn't change proportionally (11,8; 3,5; 2,7; 2,1 vs 4,1‰) in groups ordering due to the body mass.

Health condition of newborns was assessed according to the Apgar scale during the first 5 minutes after birth. Condition of 6,5% of newborns (1580 infants) was <3 points; 7,7% (1895 infants) 3 – 5 points; 14,2% (3475 infants) <5; 22,9% (5600 infants) 5 – 7 bal; 37,1% (9075 infants) <7; 62,9% (15397 infants) ≥ 7 points. Four groups have been detected according to these featured (<3, <5, <7 and ≥ 7 points). In the groups where the condition of newborns was <3 (children was born with severe asphyxia) the frequency of neonatal seizures was $12,0 \pm 2,74$ ‰ (95% confidence interval 6,52 – 17,48‰). In comparison with this group in all other groups the frequency of neonatal seizures was $6,0 \pm 1,31$ ‰ (95% confidence inter-

val 3,38 – 8,62‰) and only in one group (infants with ≥ 7 points) was comparatively statistically more ($2,7 \pm 0,41$ ‰; 95% confidence interval 1,83 – 3,49‰).

The frequency of neonatal seizures was $2,0 \pm 0,46$ ‰ when the maternity age was 20 – 24 years (95% confidence interval 1,09 – 2,93‰). The frequency depending on age of mother is the smallest in this age group. When age of mother is 25 – 29 years, the frequency of neonatal seizures among newborns increased ($2,4 \pm 0,48$ ‰; 95% confidence interval 1,40 – 3,33‰) but not significantly more than in the group with maternity age 20 – 24 years ($P > 0,05$). The maternity age group where the frequency of neonatal seizures was relatively little (in comparison with 20-24 years age group) was the group with maternity age < 20 ($4,1 \pm 1,82$ ‰; 95% confidence interval 0,44 – 7,75‰), but the frequency of neonatal seizures was high among children of mother with ages 30 – 34 years ($4,9 \pm 1,41$ ‰; 95% confidence interval 2,08 – 7,74‰), ≥ 35 years ($10,6 \pm 2,92$ ‰; 95% confidence interval 4,74 – 16,42‰).

The incidence of neonatal seizures in neonates with gestational hypertension and anemia was $3,3 \pm 1,63$ ‰ (95% confidence interval 0.1 - 6.54‰) and $3,0 \pm 0,59$ ‰ (95% confidence interval, respectively 1,84 – 4,22‰) and did not differ statistically ($P < 0,05$). The incidence of neonatal seizures ($7,3 \pm 7,22$ ‰; 95% confidence interval 0 – 21,68‰) in statistically diabetic pregnancies compared with this group of newborns was not statistically significant ($\chi^2 = 1,3$; $\eta = 1,0$; $P > 0,05$).

The frequency of neonatal seizures among infants born after pregnancies on the background of preeclampsia and eclampsia and without any complications respectively was $5,2 \pm 0,92$ ‰ (95% confidence interval 3,30 – 6,99‰) and $2,3 \pm 0,35$ ‰ (95% confidence interval 1,6 – 3,0‰) and statistically accurately differed from each other ($P < 0,01$).

The frequency of neonatal seizures among infants born after pregnancies on the background of infections and without infections respectively was $3,9 \pm 1,75$ ‰ (95% confidence interval 0,42 – 7,46‰)

and $2,9 \pm 0,35\%$ (95% confidence interval 2,2 – 3,6%) and didn't statistically accurately differ from each other ($P > 0,05$).

The frequency of neonatal seizures among infants born on the background of abnormal and normal birth activity respectively was $4,3 \pm 1,73\%$ (95% confidence interval 0,78 – 7,71%) and $2,9 \pm 0,35\%$ (95% confidence interval 2,2 – 3,6%) and didn't statistically accurately differ from each other ($P > 0,05$).

The frequency of neonatal seizures among infants born on the background of complicate and non-complicate birth activity also didn't statistically accurately differ from each other and respectively was: $4,4 \pm 1,55\%$ (95% confidence interval 1,30 – 7,52%) and $2,9 \pm 0,35\%$ (95% confidence interval 2,2 – 3,6%).

The frequency of neonatal seizures among infants born at vaginal and abdominal birth was nearly similar: $2,9 \pm 0,40\%$ (95% confidence interval 2,14 – 4,54%) and $3,1 \pm 0,71\%$ (95% confidence interval 1,68 – 4,54%). A comparison of these figures does not disprove the hypothesis of zero ($P > 0,05$).

OUTCOMES AND PREDICTORS OF OUTCOMES OF TREATMENT OF NEONATAL SEIZURES

Observations for assessment of outcomes of treatment of neonatal seizures were conducted at the Scientific Research Institute of Pediatrics named after K. Farajova. By the full coverage method the data base of 250 patients younger than 28 days have been collected.

The first place among etiologic reasons of neonatal seizures was occupied by hypoxia (hypoxia-ischemic encephalopathy) ($51,2 \pm 3,2\%$), intracranial hematoma and cerebral hypoxia was detected at $12,0 \pm 2,1\%$ of patients.

The percentage of neonatal seizures associated with metabolic disorders was $14,0 \pm 2,2\%$. The percentage of neonatal seizures associated with intracranial hemorrhage, sepsis, meningitis and other causes respectively was $4,8 \pm 1,4$; $10,0 \pm 1,9$; $4,0 \pm 1,2$ and $4,0 \pm 1,2\%$.

As the result of assessment of trace elements and glucose disbalance among observed patients the following variations of disbalance were determined:

- 32,0±2,9% hypoglycemia;
- 30,0±2,9% hypocalcemia;
- 10,0±1,9% hypomagnesemia;
- 13,2±2,1% hyponatremia;
- 4,8±1,3% hypernatremia;
- 6,4±1,5% hypokalemia;
- 3,2±1,1% hyperkalemia.

Results of MRI imaging of newborns with signs of neonatal seizures showed that cystic encephalomalacia is a mostly observed complication (35,2±3,0%). Ischemic damage of the gray matter of the cerebral cortex was observed at 25,6±2,8% of all cases. Relatively common symptoms of mixed atrophy were hydrocephalus signs (37,6±3,1%). Hemorrhagic lesions of the basal ganglia was observed at 12,8±2,1% of infants.

The main rhythm amplitude during continuous activity changed within the interval 20 – 30 mkB. In the mostly observed was the main rhythm in δ - θ diapason (32,0±2,9%), the main rhythm in α – β diapason was detected in 7,2±1,6% of patients. Interruption of the main rhythm, including to the "suppression-burst" pattern correspondingly was characteristic for 32,4±3,0 and 12,8 ±2,1% of patients.

The sharp-slow waves complex was detected in 16,8±2,4% of cases. Sharp wavy ignition within the θ rhythm diapason was observed in 19,2±2,5% of cases, sharp wavy ignition in α – β rhythm diapason was observed in 7,2±1,6% of cases. The frequency of other signs was relatively rare: 8,0±1,7% - polyspike, 7,2±1,6% - ictal epileptic activity, 5,6±1,5% - focal monorhythmic pattern in α diapason, 9,6±1,9% - focal rhythmic activity in a form of "sharp-slow waves" complex.

Besides the drugs for treatment of etiopathogenetic problems of patients, phenobarbital was used as the main specific drug. This drug was prescribed to 29,2±3,0% of patients. Hydantoins and levetirace-

tam are relatively low ($20,0\pm 2,5\%$ and $15,2\pm 2,3\%$), while other drugs such as valproates – $4,8\pm 1,4\%$; carbamezepine – $4,8\pm 1,4\%$; lamotrigine – $4,0\pm 1,2\%$; succinamides – $4,0\pm 1,2\%$; benzodiazepine – $4,0\pm 1,2\%$; topiramate – $4,0\pm 1,2\%$ are prescribed more rarely ($\leq 4,3\pm 1,4\%$).

The most negative outcome of treatment - lethality was recorded in $11,2\pm 2,9\%$ of cases. Counting (cessation of convulsions and home treatment without the need for medication) occurred in $40,4\pm 3,1\%$ of cases. In the majority of patients ($48,4\pm 3,2\%$), the frequency of seizures was significantly reduced and patients were discharged home on condition of continuing specific drug treatment in an outpatient setting.

Mortality cases ($13,4\pm 4,0$ and $7,0\pm 3,0\%$, respectively) among children aged 8-17 and 18-27 days, treated from perinatal pathologies on the background of neonatal seizures did not differ statistically. The proportion of those discharged home with recovery varied in the respective age groups ($55,5\pm 5,8$ and $34,9\pm 5,6\%$; $p<0,01$). Children hospitalized at an early age (8-17 days) have a higher risk of recovery (relative risk – 1,6; attributive risk – 20,6%).

Among patients aged 8-17, 18-27 days, improvement (elimination of convulsions against the background of medication) was observed at $31,1\pm 5,4$ and $58,1\pm 5,8\%$ of patients, respectively, and differed statistically significantly ($p<0,01$). This effect is more common in newborns aged 18 to 27 days.

Lethality in inpatient treatment of newborns with perinatal pathologies on the background of neonatal seizures, among newborns with gestation age $42,9\pm 5,8$; $23,3\pm 4,9$ and $2,6\pm 1,8\%$ full weeks respectively was 100; $42,9\pm 5,8$; $23,3\pm 4,9$ and $2,6\pm 1,8\%$ and differed statistically significantly from each other ($p<0,05$).

The probability of survival among newborns with gestation age <28 , 28-32, 32-37 and >37 weeks respectively was 0; $14,2\pm 4,1$; $33,3\pm 5,5$ and $45,4\pm 5,8\%$ and differed statistically significantly from each other.

Positive outcomes of treatment among newborns with gestation age <28 , 28-32, 32-37, >37 weeks respectively was registered in 0; $42,9\pm 5,8$; $43,4\pm 5,8$ and $52,0\pm 5,8\%$ of cases, the difference in indica-

tors is statistically accurate only in comparison with the group of newborns with gestation age <28 weeks.

Outcomes of treatment of perinatal pathologies on the background of neonatal convulsive syndrome, among newborns with body mass 1500-1999, 2000-2499 and ≥ 2500 gram respectively in $45,0 \pm 5,8$; $53,1 \pm 5,8$ and $51,7 \pm 5,8\%$ of cases was positive (cessation of convulsions by continuing drug treatment) and the level of this indicator depended on body mass options.

Outcomes of treatment of prenatal pathologies on the background of neonatal seizures, among newborns with body mass 1500-1999, 2000-2499 and ≥ 2500 gram respectively in $45,0 \pm 5,8$; $53,1 \pm 5,8$ and $51,7 \pm 5,8\%$ of cases was positive (cessation of convulsions by continuing drug treatment) and the level of this indicator depended on body mass options.

Resulting of treatment of prenatal pathologies on the background of neonatal seizures with improvement of health condition of the patient (possibility of drug control of convulsive syndrome in an outpatient setting) was recorded respectively at $33,4 \pm 5,5$; $49,4 \pm 5,8$ and $72,8 \pm 5,2\%$ of patients in SGA, AGA and LGA groups.

The efficiency of treatment of prenatal pathologies on the background of neonatal seizures depends on condition of newborn. The mortality rate among children according to the Apgar scale, allowing to assess the health condition of newborn objectively, as ≤ 3 , 4-6, 7 and more respectively was $30,4 \pm 5,4$; $13,3 \pm 3,9$ and $1,8 \pm 1,5\%$ and differed statistically significantly differed from each other.

When the etiologic factors of neonatal seizures (prenatal pathologies on the background of convulsions) are hypoxia (intracranial hematoma and hemorrhage), metabolic imbalance, sepsis and meningitis lethality as the result of treatment respectively was $7,0 \pm 3,0$; $5,7 \pm 2,7$ and $42,9 \pm 5,7\%$ and statistically significantly differed from each other ($p < 0,01$).

Treatment of neonatal seizures caused by hypoxia, metabolic imbalance, sepsis and meningitis, and other reasons, in $45,6 \pm 5,8$; $34,3 \pm 5,5$; $14,2 \pm 4,1$ and $54,5 \pm 5,8\%$ of cases, resulted in recovery ($p < 0,05$).

Dependence of positive outcomes of treatment of neonatal seizures on etiologic factors is statistically accurate ($p < 0,05$) and the level of indicator was $47,4 \pm 5,8\%$ against hypoxia, $60,0 \pm 5,7\%$ against metabolic imbalance, $42,9 \pm 5,7\%$ against sepsis and meningitis, and $45,5 \pm 5,8\%$ against other causes.

In case with and without hypoglycemia the lethality as the result of treatment of prenatal pathologies on the background of neonatal seizures respectively was $17,5 \pm 4,4$ and $8,2 \pm 2,1\%$ and statistically significantly differed from each other ($p < 0,05$).

Probability of recovery as the result of treatment of prenatal pathologies on the background of neonatal seizures in case with and without hypoglycemia respectively was $23,8 \pm 5,0$ and $60,0 \pm 3,8\%$ and statistically significantly differed from each other ($p < 0,010$).

Probability of improvement of health condition of the patient as the result of treatment of prenatal pathologies on the background of neonatal seizures in case with and without hypoglycemia respectively was recorded at $58,7 \pm 5,7$ and $43,5 \pm 3,8\%$ of patients ($p < 0,05$).

The lethality as the result of treatment of prenatal pathologies on the background of hypocalcemia and normocalcemia respectively was $20,0 \pm 4,6$ and $7,4 \pm 2,0\%$ and statistically significantly differed from each other.

Probability of resulting of treatment of neonatal seizures on the background of hypocalcemia and normocalcemia in recovery respectively was $28,0 \pm 5,2$ and $57,1 \pm 3,7\%$ and statistically significantly differed from each other ($p < 0,01$).

Probability of resulting of treatment of neonatal seizures on the background of hypocalcemia and normocalcemia in improvement respectively was $52,0 \pm 5,8$ and $46,9 \pm 3,8\%$ and didn't statistically significantly differ from each other.

Probability of resulting of treatment of neonatal seizures on the background of hypo and normomagnesemia in recovery respectively was recorded at $32,0 \pm 5,5\%$ and $41,3 \pm 3,3\%$ of cases ($p > 0,05$). In this group resulting of treatment in improvement respectively was observed at $44,0 \pm 5,8$ and $40,0 \pm 4,2\%$ cases ($p > 0,05$). The closeness of

the indicators does not justify the assessment of hypermagnesemia as a predictor of treatment.

One of the most notable MRI symptoms is cystic encephalomalasic. Treatment of neonatal seizures in groups with and without this symptom resulted in lethality respectively in $18,4 \pm 4,5$ and $9,9 \pm 3,5\%$ cases. Although the difference in indicators is significant, the null hypothesis cannot be ruled out ($p > 0,05$). In these groups, treatment was completed respectively in $23,7 \pm 5,0$ and $43,4 \pm 5,8\%$ of patients. Against the background of cystic encephalomalasic, the probability of resulting of treatment in recovery is 1,8 times less.

Mortality rate among patients with and without mixed atrophy-type hydrocephalus respectively was $16,7 \pm 4,3$ and $9,5 \pm 3,4\%$, and did not differ statistically significantly ($p > 0,05$). However, the difference in the probability of ending treatment with recovery ($26,7 \pm 5,1$ and $44,7 \pm 5,8\%$) was statistically significant. Against the background of mixed atrophic hydrocephalus, neonatal convulsions are 1,7 times less.

The probability of lethality in children with and without ischemic injury of the cerebral cortex is statistically significant ($24,4 \pm 2,7$ and $9,8 \pm 1,6\%$; $p < 0,05$).

The probability of improvement of health condition of infants with neonatal seizures, depending on the presence or absence of ischemic injury of the cerebral cortex, is not statistically significant ($56,0 \pm 3,1$ and $47,5 \pm 3,1\%$; $p > 0,05$).

The probability of lethality was observed in $18,5 \pm 2,4$ and $7,7 \pm 1,6\%$ of patients with and without a pattern of major arrhythmias on the EEG, respectively, and were statistically significant ($p < 0,05$).

The presence of the main rhythm in the δ - θ range differs statistically from the background of the pattern and without it, the probability of neonatal convulsions resulting in lethality ($16,3 \pm 2,3$ and $8,8 \pm 1,8\%$).

In the presence or absence of the main rhythm in the δ - θ range, the probability of ending treatment with recovery was $23,8 \pm 2,7$ and $48,2 \pm 3,1\%$, respectively, and the difference was statistically significant ($p < 0,01$).

In the presence or absence of the main rhythm in the δ - θ range, the probability of improvement of neonatal convulsions was $60,0\pm 3,1$ and $43,0\pm 3,1\%$ ($p < 0,01$), respectively.

Mortality was respectively $33,3\pm 3,0\%$ and $9,5\pm 1,9\%$ ($p < 0,010$) among patients with and without ictal epileptic activity.

Against the background of and without ictal epileptic activity, the proportion of patients who recovered respectively was $27,8\pm 2,8$ and $41,4\pm 3,1$ and the difference was statistically significant ($p < 0,01$).

The probability of discharge home with improvement among children with and without signs of ictal epileptic activity did not differ statistically ($38,9\pm 3,1$ and $49,1\pm 3,2\%$; $p > 0,05$).

In case of inpatient treatment of prenatal pathologies on the background of syndrome of neonatal seizures, the clinical characteristics of patients are different: age and sex, body mass and severity of hypoxia at birth, seizures, multiple variants of etiological factors, different microelement imbalances, MRI and EEG patterns, etc. The effect of these characteristics on the efficiency of treatment has been proven.

The followings affects the risk of death during inpatient treatment of prenatal pathologies with neonatal convulsive syndrome: gender of the child (high risk among boys), from where sent to the hospital (increased mortality due to untimely referral to clinics), gestation age at birth (age is inversely proportional to the risk of death), body mass at birth (body mass is inversely proportional to the risk of death), body weight gestation age inconsistency (body weight less than gestation age), condition of the child with Apgar scale at 5 minutes after birth (Apgar scale is inversely proportional to the risk of death), etiological factors (risk is high against the background of sepsis and meningitis), MRI (cystic encephalomalacia), mixed atrophy-type hydrocephalus, ischemic damage to the gray matter of the cerebral cortex) and EEG (interruption of the main rhythm, the presence of the main rhythm in the δ - θ range, sharp slow wave complex, sharp wave inflammation in the θ rhythm range, sharp wave inflammation in the α - β range, ictal epileptic activity, focal rhythmic activity in the form of a sharp slow wave complex) patterns.

ACHIEVED RESULTS

1. In prenatal center $3,0 \pm 0,1$ cases of neonatal seizures per 1000 newborns were recorded. Seizures are mainly observed during the first two days after birth ($79,5 \pm 4,7\%$ and $12,3 \pm 3,8\%$), in most cases clonic ($32,9 \pm 5,4\%$ focal clonic, $16,4 \pm 4,3\%$ multifocal clonic) and tonic ($24,7 \pm 5,0\%$) forms, among the etiological causes are hypoxia-ischemic damage of the central nervous system ($43,8 \pm 5,5\%$), metabolic imbalance ($30,1 \pm 5,4\%$), central nervous system infection ($13,7 \pm 4,0\%$) plays a priority role.
2. Factors statistically increasing the risk of neonatal seizures at newborns ($p < 0,05$) are the gestation age < 37 full weeks ($5,1 \pm 0,96\%$), body mass less than normal for gestational age ($6,4 \pm 1,60\%$), body mass at birth < 1500 gram ($11,8 \pm 2,76\%$) and < 2500 gram ($5,3 \pm 0,95\%$), condition at birth according the Apgar scale < 3 bal ($12,0 \pm 2,74\%$), < 5 points ($6,01 \pm 1,31\%$).
Antenatal and intranatal risk factors for neonatal seizures at newborns are: pregnancy age of the woman, complications of pregnancy with preeclampsia, number of births.
3. Important features of newborns in inpatient treatment with perinatal pathologies on the background of neonatal convulsive syndrome: share of boys among patients ($56,8 \pm 3,1\%$), age - 8-17 days ($65,6 \pm 3,0\%$), gestation age > 37 full weeks ($78,4 \pm 2,6\%$) and body mass ≥ 2500 gram ($60,4 \pm 3,1\%$) at birth, points on Apgar scale < 7 ($54,4 \pm 3,2\%$), relative majority of patients with hypoxia and ischemic damage of the central nervous system ($63,2 \pm 3,0\%$), cystic encephalomalacia in $35,2 \pm 3,0\%$, hemorrhagic lesions of the basal ganglia in $12,8 \pm 2,1\%$, ischemic damage to the gray matter of the cerebral cortex in $25,6 \pm 2,8\%$ and mixed atrophy-type hydrocephalus in $37,6 \pm 3,1\%$ of them were detected.
Cases of mortality in $11,2 \pm 2,0\%$, improvement in $48,4 \pm 3,2\%$ and recovery in $40,4 \pm 3,1\%$ were observed as the result of inpatient

treatment of prenatal pathologies on the background of neonatal seizures. The predictors of treatment efficiency are: delayed hospitalization, gestational age <37 full weeks, body mass <2500 g at birth, body mass at birth less than normal for gestational age, Apgar scale points ≤ 3 , onset of seizures on the background of sepsis and meningitis, MRI and EEG presence of pathological patterns. The maximum sensitivity of the predictors of the results of treatment of neonatal seizures was 87,5% (Apgar score ≤ 3 points), specificity 94.6% (against the background of epileptic activity), prognostic value of positivity 100% (age of hesitation <28 weeks), prognostic negativity Significance is 100% (gestational age <28 weeks, birth weight <1500 grams).

PRACTICAL RECOMMENDATIONS

1. To provide EEG examination of newborns (gestational age <37 full weeks, birth weight <2500 g) for early and complete detection of neonatal seizures.
2. To transfer the newborn to a children's hospital of the appropriate profile directly from the maternity hospital when it is not possible to permanently eliminate the symptoms of neonatal seizures.
3. Neurological examination, especially MRI and EEG examination of newborns should be performed taking into account the risk factors (gestation age <37 full weeks (5,1 \pm 0,96%), body mass less than normal for gestational age (6,4 \pm 1,60%), body mass at birth <1500 gram (11,8 \pm 2,76%) and <2500 gram (5,3 \pm 0,95%), condition at birth according the Apgar scale <3 bal (12,0 \pm 2,74%), <5 points (6,01 \pm 1,31%, pregnan-

cy age of the woman, complications of pregnancy with preeclampsia, number of births) for neonatal seizures.

4. The probable outcome of the treatment of neonatal seizures is predicted (delayed hospitalization, gestational age <37 full weeks, body mass <2500 g at birth, body mass at birth less than normal for gestational age, Apgar scale points ≤ 3 , onset of seizures on the background of sepsis and meningitis, MRI and EEG presence of pathological patterns.) taking into account the predicates.
5. Carrying out EEG examination of newborns with asphyxia, hypoxia, congenital traumas of the central nervous system.
6. Treatment tactics for neonatal seizures should be determined by neuroimaging and monitoring of electrobiological activity.

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