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Neuroprotection in intrauterine herpesvirus infection

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The aim of the study is to assess the effectiveness of the neuroprotection complex in intrauterine herpesvirus infection.

Materials and methods. To test the effectiveness of the developed neuroprotection complex (erythropoietin, early use of sensory integration techniques), 60 children with intrauterine herpesvirus infection, who were classified as high-risk for significant central nervous system disorders, were examined from birth to 1 year of age: the main group was 30 newborns who were additionally treated with a new complex of neuroprotection, and the comparison group — 30 children, whose medical support was carried out in accordance with the protocols of the Ministry of Health of Ukraine. The obtained data were processed by the methods of variational statistics accepted in medicine, using the Student's t-test for numerical indicators and Fisher's angular transformation for indicators represented by frequencies, with a critical significance level of $p<0.05$.

The results. According to the static and motor development of children at the age of 12 months by the Denver scale, the vast majority of children (70.0%) of the comparison group were delayed in development by 2–4 months, while in the main group only 6 (20.0%) remained slight delay of 1–2 months. Accordingly, the assessment of psychomotor development according to the Griffiths scale was significantly reduced relative to the main group (112.7±7.6 points vs. 156.4±7.1 points, respectively). There were no cases of infant death in the examined children. Perinatal disorders of the central nervous system led to the disability of 2 (6.7%) children of the comparison group. Side effects or complications of the proposed therapy were not observed.

Conclusion. The use of a complex of therapeutic and preventive measures aimed at neuroprotection in newborns with intrauterine infection with herpesviruses (prediction of the risk of central nervous system disorders at birth, in children at high risk — early neuroprotective treatment with low doses of recombinant erythropoietin and early use of sensory-motor integration) allows to improve neurocognitive and psychomotor abilities of children up to 1 year of age. The effectiveness of the neuroprotective complex was 80.0%.

The research was carried out in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by the Local Ethics Committee of the specified institution. Informed consent of the children's parents was obtained for the research.

The authors declare no conflict of interest.

Keywords: newborn, herpesvirus infection, central nervous system disorders neuroprotection, erythropoietin, sensory integration.

Нейропротекція при внутрішньоутробному інфікуванні герпесвірусною інфекцією

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Мета дослідження — оцінити ефективність комплексу нейропротекції при внутрішньоутробному інфікуванні герпесвірусною інфекцією.

Матеріали та методи. Для перевірки ефективності застосування розробленого комплексу нейропротекції (еритропоетин, раннє застосування методик сенсорної інтеграції) обстежено від народження до 1 року життя 60 дітей з внутрішньоутробним інфікуванням герпесвірусами, які віднесені у групу високого ризику суттєвих порушень центральної нервової системи (ЦНС): основна група — 30 новонароджених, яким додатково застосовували новий комплекс нейропротекції, і група порівняння — 30 дітей, медичний супровід яких здійснювався у відповідності до протоколів МОЗ України. Отримані дані оброблено методами варіаційної статистики, прийнятими в медицині, з використанням t-критерію Стьюдента для числових показників та кутового перетворення Фішера для показників, представлених частотами, з критичним рівнем значущості $p<0,05$.

Результати. За статикою та моторним розвитком дітей у віці 12 місяців згідно Денверської шкали на відставання у розвитку на 2–4 місяці встановлено переважної більшості дітей (70,0%) групи порівняння, тоді як у основній групі лише у 6 (20,0%) лишилась незначна затримка на 1–2 місяці. Відповідно суттєво зниженою відносно основної групи була і оцінка психомоторного розвитку за шкалою Гріффітс (112,7±7,6 балу проти 156,4±7,1 балу відповідно). Випадків малюкової смерті у обстежених дітей не відмічено. Перинатальні порушення ЦНС призвели до інвалідизації 2 (6,7%) дітей групи порівняння. Побічних ефектів або ускладнень запропонованої терапії не спостерігали.

Висновок. Застосування комплексу лікувально-профілактичних заходів з метою нейропротекції у новонароджених з внутрішньоутробним інфікуванням герпесвірусами (проведення при народженні дитини прогнозування ризику порушень ЦНС, у дітей з високим ризиком — нейропротективне раннє лікування низькими дозами рекомбінантного еритропоетину та раннє застосування сенсорно-моторної інтеграції) дозоляє покращити нейрокогнітивні та психомоторні здібності дітей до 1 року життя. Ефективність нейропротективного комплексу склала 80,0%.

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом зазначеної установи. На проведення досліджень отримано інформовану згоду батьків дітей.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: новонароджений, герпесвірусна інфекція, центральна нервова система нейропротекція, еритропоетин, сенсорна інтеграція.

The problem of intrauterine infection (IU) is one of the leading ones in obstetric practice and perinatology due to the high level of infection of pregnant women, the danger of impaired fetal development, morbidity of newborns and health problems. The presence of infection in the mother is a risk factor for IU of the fetus, but does not always mean its disease [9]. Intrauterine infection is understood as the process of penetration of microorganisms into the fetus, in which there are no signs of an infectious disease of the fetus, often developing placentitis, chorioamnionitis, etc. [14].

Herpes infection is one of the most common viral infections in the world, mostly caused by herpes simplex virus (HSV) types 1 and 2. Usually, these pathogens persist in the central nervous system (CNS), maintaining a latent infection, which is manifested by periodic diseases [7,20].

Fetal development in conditions of maternal infection is recognized to be associated with impaired cognitive development, poor intellectual abilities, as well as impaired development of the CNS and mental problems in childhood and old age [16].

There is accumulated evidence that infectious and inflammatory processes during pregnancy negatively affect the fetal brain and neuropsychiatric consequences for the children in later life [1].

The further development of methods of neuroprotection in newborns does not lose its relevance, which is due to the high frequency of CNS pathology in newborns due to prematurity, hypoxic-ischemic damage, intrauterine infection, in particular herpesvirus. Various methods of neuroprotection in newborns and young children are proposed, both drug-based and various physical effects (protective mode in case of prematurity, hypothermia in case of severe hypoxia/asphyxia, early use of sensory integration techniques, etc.).

Neonatal brain damage is a complex, multifactorial process that is influenced by genetic, epigenetic, metabolic, prenatal, perinatal, and postnatal factors [17]. This complexity makes it impossible to develop a monotherapy because it is unlikely that a single intervention will be effective in all cases [13]. There is growing interest in a complex approach with several interventions [11].

Many different treatment strategies have been suggested as complementary strategies. These include allopurinol, azithromycin, ascorbic acid, ibuprofen, magnesium sulfate, vitamin D, xenon gas treatment, and sildenafil. Melatonin, erythropoietin, and mesenchymal stromal cells are now being evaluated in clinical trials [11,19].

Erythropoietin is a 30.4 kDa glycoprotein that is mainly produced in the fetal liver and in the kidney and liver of the child after the neonatal period. Erythropoietin and its receptor are expressed by many types of brain cells. In animal models, erythropoietin can modulate inflammation, angiogenesis, and neurogenesis and promotes white matter development [5].

In humans, erythropoietin monotherapy for neonatal encephalopathy has been tested in small clinical trials. These studies suggest a short-term neurodevelopmental benefit with high-dose erythropoietin for the first 5 days of life or three times a week for 2 to 4 weeks, or a long-term benefit with every other day for 2 weeks. No safety issues were reported, but small sample sizes do not allow erythropoietin to be recommended for widespread clinical use [10].

Studies of combined erythropoietin and hypothermic therapy have demonstrated the safety of high-dose erythropoietin, at a dose of 1000 units/kg intravenously, achieving serum concentrations that most closely approximate optimal neuroprotective levels in preclinical models. Studies of bolus administration of erythropoietin at 1, 2, 3, 5, and 7 days of age may provide additional benefit as reflected by motor responses at 12 months of age [18].

Erythropoietin exerts intracellular protective effects after ischemic injury, such as reducing apoptosis, oxidative stress, and blood-brain barrier damage. In addition, it has been proven that erythropoietin is able to stimulate angiogenesis, neurogenesis and neuron plasticity. Both in animal models and in newborns, erythropoietin has demonstrated anti-apoptotic, antioxidant and anti-inflammatory properties. Additional studies of individual regimens that take into account risk stratification of brain damage in newborns are needed [15].

Today, sensory integration methods in the context of early intervention in accordance with the Concept of creation and development of the early intervention system (order of the Cabinet of Ministers of Ukraine dated September 15, 2021 No. 1117) attract more attention. Early intervention is understood as a set of actions to identify children with existing developmental and cognitive disorders or a high risk of such disorders and providing assistance to such children and their

families by a team of specialists of various profiles. The target group of early intervention is children from birth to three years (in some countries — up to seven years) with the presence or risk of developmental delay, disability, behavioral or mental disorders [2,12].

The first years of life are crucial for laying the foundation for a child's healthy development. The health benefits of early intervention for children with intellectual and developmental disabilities have been well established, albeit with varying levels of evidence for effectiveness. Medical and social and corrective-targeted rehabilitation of children with perinatal pathology provides compensation for pathological changes under the condition of natural plasticity of the organism and realizes the reserve and adaptive capabilities of children during ontogenesis, which has a beneficial effect on the correction and sanogenetic guidance of compensatory and adaptive reactions. Starting from the early period of the child's development (from 3 months of life), in order to ensure proper sensorimotor, cognitive, functional-emotional development, it is recommended to use the methods of sensory integration, neurocorrection, the method of substitute ontogenesis (provided there are previously detected motor disorders or the detection of incorrect formation of priority passive movement patterns) [3].

The founder of the direction of sensory integration (SI) is A. Jean Ayres (USA). The theory and practice of SI continues to evolve as a deeper understanding of the neurobiology of human behavior emerges. Modern research tests and refines the proposals of A. Jean Ayres, describing the functions of the vestibular, proprioceptive and tactile sensory systems and investigating their relationship with ocular, postural, bilateral integration, praxis and sensory modulation. neuroplasticity is the mechanism that underlies changes as a result of SI intervention [8].

The aim of the study is to assess the effectiveness of the neuroprotection complex in intrauterine herpesvirus infection (HVI)

Materials and methods of the research

The conducted complex studies created a theoretical basis for the development of a pathogenetically justified three-stage (preconceptional stage — before pregnancy, antenatal stage — during pregnancy, postnatal — from birth to one year) complex of neuroprotection for newborns with intrauterine infection with HVI, differentiated according to the severity of the detected violations, including forecasting. The proposed complex consists of the following:

— at the preconception stage, when planning a pregnancy, women should be examined for infections of the torch group, in the presence of HVI, antiviral and anti-recurrence treatment, remediation of foci of genitourinary infection;

— during pregnancy, monitoring of the condition of the fetus, detection of markers of placental disorders, remediation of foci of infection, prevention of premature birth (taking into account the neuroprotective properties of magnesium preparations);

— at the birth of a child — to assess the degree of risk of the CNS damage: taking a woman's history, assessing the child's clinical condition, conducting examinations of the newborn: neurosonographic (NSG) examination of brain structures, dopplerometric examination of cerebral hemodynamics, assessment of the state of cellular immunity and cytokine profile, identification of risk factors and prognosis.

When determining a high risk, start early prevention (within the first 48 hours of life, taking into account the presence of a therapeutic window) of CNS disorders by prescribing low doses of recombinant human erythropoietin 400 IU subcutaneously every day of 7 injections, if the NSG picture improves and there are no clinical signs of disorders on the second examinations (5–7 days of life) — stopping treatment with erythropoietin. With a predicted low risk – assessment of the clinical condition and NSG for 5–7 days, in case of detection of violations – 3 injections of erythropoietin every other day. For all children with intrauterine infection, it is desirable to repeat the NSG examination at the age of one month and six months, dynamic assessment of psychomotor development. When psychomotor development abnormalities are detected, early (from three months) application of sensory integration techniques.

Children who have undergone intrauterine infection with herpesviruses should be classified as a high-risk group for perinatal disorders of the central nervous system, infectious-inflammatory diseases, allergies, and should be monitored by a pediatrician, neurologist, and immunologist.

To check the effectiveness of the application of the developed complex of neuroprotection at the postnatal stage, 60 newborns with intrauterine infection with HVI were selected, who, after the

Table 1

Clinical manifestations of neurological disorders, abs.n. (%)

Indicator	Main group, n=30		Comparison group, n=30	
	abs. n.	%	abs. n.	%
Changes in muscle tone	23	76.7	21	70.0
Unstable physiological reflexes	22	73.3	24	80.0
Disorders of motor activity	16	53.3	14	46.7
Neuro-reflex excitability syndrome	17	56.7	17	56.7
Depression syndrome	8	26.7	10	33.3
Convulsions	3	10.0	2	6.7

Note. No statistical difference was found in the indicators in the groups of children (p>0.05).

prognosis, were assigned to the group of high risk of significant disorders of the central nervous system. Children with severe disorders of brain structures were not included in the study. By the method of randomization (randomly), the children were divided into 2 groups: the main group — 30 newborns who, in addition to treatment according to the protocols of the Ministry of Health of Ukraine, were given a new complex of neuroprotection, and the comparison group — 30 children whose medical support was carried out in accordance with the protocols of the Ministry of Health of Ukraine. The study was conducted on the basis of the Kyiv City Center of Reproductive and Perinatal Medicine. Observation of children continued until 1 year of life.

A neurosonographic (NSG) examination of brain structures was carried out using the Sono Scape P15 device. Psychomotor development was assessed according to the scales of the Denver developmental screening test (from birth to 6 years) [4] and the Griffiths scale of mental development (from 0 to 8 years) [6].

The study was carried out in accordance with the main provisions of GCP ICH and the Declaration of Helsinki, agreed with the Local Ethics Committee of the institution mentioned in the work. All studies were performed after obtaining informed consent from parents/guardians for diagnosis and treatment.

The obtained data were processed by the methods of variational statistics accepted in medicine, using the Student's t-test for numerical indicators and Fisher's angular transformation for indicators represented by frequencies, with a critical significance level of $p<0.05$. The Microsoft Excel statistical analysis package was used.

Results of the research and discussion

Clinical manifestations of neurological disorders occurred in the vast majority of newborns of both groups and were characterized by polymorphism (Table 1). Changes in muscle tone, unstable physiological reflexes were observed in the vast majority of children of both groups. High frequency of motor activity disorders and neuro-reflex excitability syndrome (about 50.0%). Seizures were noted in several children (3 children in the main group and 2 in the comparison group). Clinical manifestations of both groups did not differ before the start of treatment.

On the 1st day of life, a NSG examination revealed a high frequency of ultrasound signs of brain structure disorders in children of both groups (Table 2). The presence of liquid in the cavity of the transparent membrane in half of the newborns indicates disorders on the part of the central nervous system caused by cerebral edema, which is confirmed by higher ventriculometry indicators. Intraventricular hemorrhage (IVH) of the 1st degree was found in half of the newborns, the frequency of more severe ones (II degree) was about 10.0%. 3 children of each group had 3rd degree IVH. Periventricular leukomalacia was noted in 16.7% and 20.0% of children in the main and the comparison group. Ultrasound signs of vasogenic cerebral edema were diagnosed in 73.3 and 70.0% of children, respectively. It should be especially noted the presence of cysts and calcifications in the brain structures of children of both groups, which, according to the literature, are considered signs of intrauterine HVI.

Therefore, before the start of treatment, the groups were compared both by clinical manifestations of neurological disorders and by the results of NSG examination of brain structures.

On the 5th–7th day of life (Table 3), the manifestations of cerebral edema remained in half of the examined children of both groups, in 10.0% and 6.7%, interventricular asymmetry was observed, expansion of the lateral ventricles, mainly the posterior horn (about 15 mm) remained.

Table 2

Indicators of neurosonography of examined newborns on 1–2 days of life

Indicator	Main group, n=30	Comparison group, n=30
Interventricular asymmetry, abs. n. (%)	2 (6.7)	1 (3.3)
Width of the third ventricle, mm	1.94±0.15	1.88±0.11
Lateral ventricles, mm:		
— front horn	8.13±0.34	7.98±0.28
— the body	5.42±0.40	5.52±0.36
— rear horn	12.54±0.52	11.93±0.25
Liquid in the cavity of the transparent membrane, abs. n. (%)	15 (50.0)	14 (46.7)
The width of the vascular plexus at the level of the body of the lateral ventricle, mm	8.21±0.25	8.11±0.42
Intraventricular hemorrhages by degrees, abs.n. (%):		
I	15 (50.0)	16 (53.3)
II	3 (10.0)	4 (13.3)
III	2 (6.7)	2 (6.7)
Periventricular leukomalacia, abs.n. (%)	5 (16.7)	6 (20.0)
Cysts	6 (20.0)	6 (20.0)
Calcifications	4 (13.3)	5 (16.7)
Vasogenic edema of the brain, abs.n. (%)	22 (73.3)	21 (70.0)

Note. No statistical difference was found in the indicators in the groups of children (p>0.05).

Table 3

Indicators of neurosonography of examined newborns on 5–7 days of life

Indicator	Main group, n=30	Comparison group, n=30
Interventricular asymmetry, %	3 (10.0)	2 (6.7)
Width of the third ventricle, mm	3.89±0.27	3.93±0.19
Lateral ventricles, mm:	8.30±0.26	8.18±0.31
— front horn		
— the body	8.43±0.25	8.37±0.26
— rear horn	15.11±0.62	14.83±0.51
Liquid in the cavity of the transparent membrane, abs. n. (%)	14 (46.7)	13 (43.3)
The width of the vascular plexus at the level of the body of the lateral ventricle, mm	8.87±0.22	8.91±0.18
Intraventricular hemorrhages by degrees, abs. n. (%):	14 (46.7)	15 (50.0)
I		
II	4 (13.3)	4 (13.3)
III	1 (3.3)	2 (6.7)
Periventricular leukomalacia, abs. n. (%)	5 (16.7)	5 (16.7)
Cysts	7 (23.3)	6 (20.0)
Calcifications	5 (16.7)	6 (20.0)
Vasogenic edema of the brain, abs. n. (%)	14 (46.7)	15 (50.0)

Note. No statistical difference was found in the indicators in the groups of children (p>0.05).

The frequency of detected cysts due to the reduction of swelling of brain structures increased slightly, the same applies to calcifications. In 63.3% of the children of the main group and 70.0% of the comparison group, signs of IVH remained, mostly of the 1st degree. Therefore, no significant improvement in NSG indicators was observed on the 5–7th day of life, therefore, erythropoietin therapy in the main group was continued.

At the age of 1 month, all children underwent NSG of the brain, ultrasound of internal organs, examination by a pediatrician, a neurologist, and an ophthalmologist.

In children, during the examination, an increase in muscle tone was noted (30.0% in both groups), a decrease in muscle tone in 13.3% and 23.3% in the main group and the comparison group, unstable physiological reflexes (20.0 and 23.3% respectively), decreased knee and abdominal reflexes, hand and chin tremors (16.7 and 20.0%, respectively). These changes were confirmed by signs of fluid-dynamic disorders detected in NSG (Table 4).

According to NSG data, some children have an expansion of the external cerebrospinal fluid spaces and local swelling of cerebral structures, interventricular asymmetry and ventriculodilatation.

Table 4

Indicators of neurosonography of examined newborns at the age of 1 month

Indicator	Main group, n=30	Comparison group, n=30
Local swelling of cerebral structures	5 (16.7)	6 (20.0)
The presence of interventricular asymmetry	3 (10.0)	5 (16.7)
Ventriculodilatation without peri- and intraventricular hemorrhages	5 (16.7)	7 (23.3)
The presence of cysts	6 (20.0)	6 (20.0)
Expansion of external CSF spaces	6 (20.0)	8 (26.7)

Note. No statistical difference was found in the indicators in the groups of children (p>0.05).

Against the background of fluid-dynamic disorders, cysts are quite often noted in children of both groups.

Along with this, 13.3% and 20.0% of children in the main group and the comparison group had gastrointestinal reactions in the form of regurgitation of milk, hiccups. Weak sucking was noted in 16.7 and 20.0% of children respectively.

The assessment of psychomotor development according to the Griffiths scale showed a slightly higher average score in the children of the main group (6.8±2.1 points vs. 5.3±2.1 points), especially in the «motor» and «eyes and hands» patterns.

From the age of 3 months, the children of the main group are included in the early intervention program using the methods of sensory integration, neurocorrection, the method of substitute ontogenesis (provided there are previously detected motor disorders or the detection of improper formation of primary passive motor patterns). Priority was given to work with the proprioceptive system (work with the body-muscles, joints, tendon-ligament apparatus) through deep compressions, vibration manipulations, tight wraps and, as early as possible, stimulating the child to active physical, motor-motor independent acts. Work with the vestibular system (by working out various vector movements) with the aim of improving spatial orientation strategies, coordination and feeling of one's own body as a whole. Working with the tactile system for sensory saturation in order to improve the perception of the surrounding world, the formation and development of bony praxis, body sensation and the establishment of correct olfactory, gustatory, visual and auditory perception of the surrounding world. The work is carried out according to the concept of «Tandem-partnership» — mutual cooperation of a doctor, parents and social educators, which includes early medical and socio-pedagogical rehabilitation, since the reparative capabilities of the nervous system are much higher in the first year of life.

In addition, traditional methods of rehabilitation were widely used, in particular, kinesiotherapy (massage, exercise therapy, use of parapodia, the method of dynamic proprioceptive correction using the Gravistat reflex-loading device), reflexology, hydrokinesiotherapy — balneotherapy (pearl baths, hydromassage), the «Swim before walking» program. Modern rehabilitation methods were used: Sherborn therapy, classes based on the principle of biological feedback using the Ambliokor apparatus.

Dynamic observations up to 6 months of age in children revealed a decrease in muscle tone and motor activity in 3 (10.0%) and 6 (20.0%) of the main group and the comparison group. In 2 (6.7%) and 6 (20.0%) and, respectively ($p < 0.05$), reduced abdominal, knee and tendon reflexes remained.

The assessment of static and motor development according to the Denver scale established that the lag in the development of most children of the comparison group: at the age of six months in 19 (63.3%) it corresponded to 3–4 months, while in the main group in 5 (16.7%) children were slightly delayed, their development corresponded to 4–5 months of age. The assessment of psychomotor development according to the Griffiths scale corresponded to these results (45.8±6.9 points in the children of the main group versus 68.4±5.7 points in the comparison group, p<0.05).

A high level of CNS lesions in 4 (6.7%) children of the comparison group was manifested by hydrocephalic and convulsive syndrome. 3 (10.0%) children required inpatient treatment in the neurological department: 2 children with increasing ventriculodilatation and 1 — with a convulsive syndrome.

According to the NSG data (Table 5), at the age of 6 months, against the background of the therapy, some improvement in the condition of the brain structures was noted in the children of the main group. In the children of the comparison group, 6.7% had signs of local edema of cerebral structures, they had a 5 times higher frequency of interventricular asymmetry and ventriculodi-

Table 5

Indicators of neurosonography of examined newborns at the age of 6 month

Indicator	Main group, n=30	Comparison group, n=30
Local swelling of cerebral structures	–	2 (6.7)
The presence of interventricular asymmetry	1 (3.3)*	5 (16.7)
Ventriculodilatation without peri- and intraventricular hemorrhages	1 (3.3)*	5 (16.7)
The presence of cysts	5 (16.7)	6 (20.0)
Expansion of external CSF spaces	5 (16.7)	7 (23.3)

Note. * — the difference is significant relative to the indicator of children of comparison group ($p<0.05$).

Table 6

Indicators of neurosonography of examined newborns at the age of 1 year

Indicator	Main group, n=30	Comparison group, n=30
Local swelling of cerebral structures	–	1 (3.3)
The presence of interventricular asymmetry	–	3 (10.0)
Ventriculodilatation without peri- and intraventricular hemorrhages (PIVH)	–	5 (16.7)
The presence of cysts	2 (6.7)	5 (16.7)
Expansion of external CSF spaces	1 (3.3)*	5 (16.7)

Note. * – the difference is significant relative to the indicator of children of comparison group ($p<0.05$).

latation (16.7 vs. 3.3% children of main group, $p<0.05$).

During dynamic observation up to 1 year, the general level of morbidity of the examined children remained high, which is indicated by the high frequency of additional (unplanned) referrals to narrow specialists. Most often, children needed referral to a neurologist, immunologist, and allergist. The frequency of visits to a neurologist in the comparison group exceeded that in the main group by more than 2 times and amounted to 2.6 per 1 child versus 1.1, respectively.

NSG signs of disorders of the structures of the brain remained only in 2 children of the main group in the form of cysts and expansion of the cerebrospinal fluid spaces (Table 6), while the NSG picture of the children of the comparison group almost did not change compared to that at 6 months (violations were noted in 26.7% of children).

According to the static and motor development of children at the age of 12 months according to the Denver scale, the vast majority of children (70.0%) of the comparison group were delayed in development by 2–4 months, while in the main group only 6 (20.0%) remained slight delay of 1–2 months. Accordingly, the assessment of psychomotor development according to the Griffiths scale was significantly reduced relative to the main group (112.7±7.6 points vs. 156.4±7.1 points, respectively, $p < 0.05$).

There were no cases of infant death in the examined children. Perinatal disorders of the central nervous system led to the disability of 2 (6.7%) children of the comparison group.

Side effects or complications of the proposed therapy were not observed.

The effectiveness of the neuroprotective complex was 80.0%.

Conclusions

The use of a complex of therapeutic and preventive measures aimed at neuroprotection in newborns with intrauterine infection with herpesviruses (prediction of the risk of central nervous system disorders at birth, in children at high risk — early neuroprotective treatment with low doses of recombinant erythropoietin and early use of sensory-motor integration) allows to improve neurocognitive and psychomotor abilities of children up to 1 year of age according to the Denver scale and the Griffiths scale. The effectiveness of the neuroprotective complex was 80.0%.

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