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PREDICTORS OF THE FORMATION OF NEUROLOGICAL DISORDERS IN PREMATURE INFANTS

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Abstract
Premature newborns requiring observation and examination and treatment in the intensive care unit are at high risk for the development of perinatal brain lesions. Congenital pneumonia and early neonatal sepsis are one of the most common causes of perinatal morbidity and mortality in premature infants. According to various authors, the incidence of congenital pneumonia and early neonatal sepsis in children ranges from 4 to 20 per 1,000 live births.

Keywords Predictors, neurological disorders, premature infants, cerebral palsy.

INTRODUCTION

According to the latest data from literary sources, there is a tendency to decrease infant mortality rates, but at the same time there is a steady increase in the frequency of premature births. According to WHO, preterm birth in various countries ranges from 5 to 12%, where premature babies account for 6-12% of all newborns. It is characteristic that the highest rates of perinatal morbidity and mortality are observed in children born with very low body weight (ONMT) and extremely low body weight (ENMT) at birth. Important, in a situation of premature birth (small children), is the susceptibility of babies to the development of complications that can have an

adverse effect on health, in general, and affect cognitive development in subsequent periods of life. In this regard, statistical indicators indicate evidence of adherence to disorders such as cerebral palsy (cerebral palsy), while the development of deeply premature infants in 21-28% of cases, blindness — in 2-8% of cases, hearing impairment — in 5% of cases. Therefore, the main and most important task of providing medical care to premature infants is the desire to minimize their disability and improve the quality of later life (3, 15). However, in the domestic and foreign literature, studies devoted to the analysis of the state of clinical, neurological and neuropsychological conditions of premature infants, early diagnosis, rehabilitation and therapy using complex modern technologies are insufficient and difficult to interconnect with each other (8, 20). In the light of the above, the study of the health status of premature infants, the prognosis for complications from the central nervous system, in the neonatal period and in the first year of life, is timely. The neurological service dealing with newborn children has more than a century of history. For the first time, Kennedy (1836) mentions birth injuries of the nervous system (1, 23). Despite this, the issues of pathogenesis, structure and frequency of neurological changes (complications) in newborns are quite controversial and debatable. This is primarily due to the age feature, the difficulty of examining and diagnosing patients, the lack of a unified approach to the interpretation of clinical symptoms and diagnosis. A large number of studies by specialists: neonatologists, pediatricians, neurologists conducted among newborns does not make it possible to fully present the frequency and variants of cerebral pathology (2, 14). In addition, many contradictory ideas about the causal-factor pathomechanism of CNS disorders in premature infants are interpreted. Thus, there is an opinion about the predominant influence of antenatal factors (7, 19), distinguishing among them socio-biological ones. The opinion of other authors, preference is given to natal injuries (10, 18), most of them focus on the method of delivery. The very formation of the nervous system in a premature baby differs significantly from a full-term newborn, due to premature birth, is most likely due to the pathology of pregnancy, where not only the normal formation of the fetus slows down, but also is disrupted. It follows from this that children born prematurely, in the absence of gross disorders of the nervous system at birth, have a high risk of subsequent clinical, neurological and intellectual insufficiency (11, 17). Thus, the state of neuropsychiatric development of children from this risk group, at the stage of early childhood, needs timely corrected treatment, on which the child's usefulness in social society depends. Another factor in the complexity of determining and evaluating the condition of patients is the result of a frequent combination of perinatal pathology of the central nervous system and pathology of the visual and auditory analyzers, the lack of evaluation criteria for premature infants in such cases (4, 22). It is also necessary to take into account the high percentage of compensatory capabilities of the central nervous system in the first year, directly related to the phenomenon of neuroplasticity, which takes into account the mechanism of the so-called "delayed damaging effect" of hypoxia (13, 21). It is the diagnosis of such disorders that is further correlated with the dynamic improvement of neuroimaging and neurophysiology methods that allow images of a functioning brain to be obtained directly at the time of the study, with the possibility of determining a topical deficiency [6, 22]. All the above-mentioned features and functions of premature babies for today, and determined the purpose of the study.

The aim of the study was to identify and establish the significance of factors of clinical and neurological changes in the assessment of predisposing adverse outcomes in premature infants.

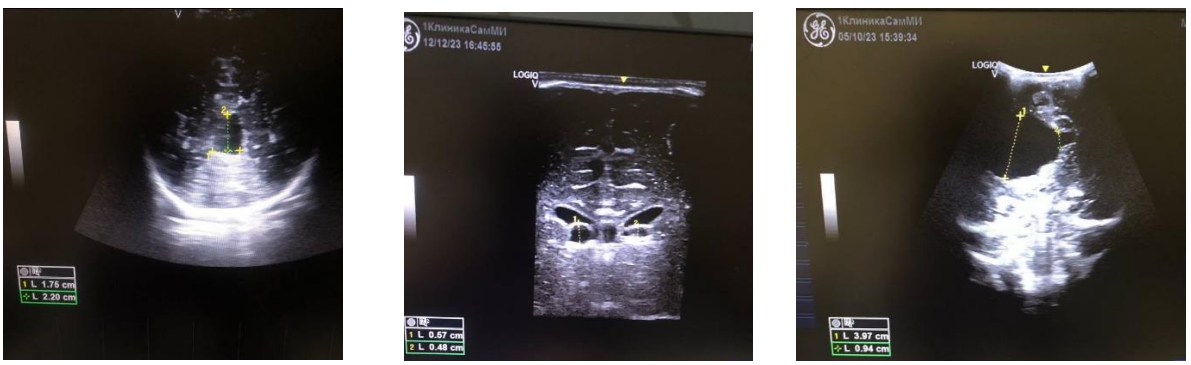
RESEARCH MATERIALS AND METHODS

The research was conducted over the period 2022-2024, on the basis of the Department of Obstetrics and Gynecology of the SamSMU, the Department of Neonatal Pathology of the Regional Children's Multidisciplinary Hospital, the Department of Pediatric Neurology of the MC SamSMU. 66

premature infants were subject to examination, 36 of them were born weighing 1500-2500 g and made up group 1; 30 children born weighing 1000-1500 g., made up group 2. The control group consists of 20 healthy newborn children. The parents of all children included in the survey signed a voluntary information consent to participate in the study. At the initial stage of the study, important issues were the study of the anamnesis of the somatic state of mothers before pregnancy, during pregnancy and childbirth; the nature and result of delivery. These indicators were determined by a survey and anamnesis collection method. The next stage was the assessment of the neurological status at the time of the child's age, where the GMFCS scale was used to determine the level of motor changes, psycho-speech disorders were studied using the Griffiths scale and the calendar calculation method. Additional research methods included a standard examination by a neonatologist, an ophthalmologist, a laboratory blood test, and an ultrasound examination of the heart. Additional instrumental methods include neurosonography for children (without exception), in the dynamics of observation; partial use of neuroimaging on an MRI machine: SIEMENS (children from 9 months. up to a year old, born prematurely in the dynamics of observation), a total of 21 patients out of 66 children were carried out, in addition, by random sampling, MRI was studied in healthy children with parental consent, five children out of 20, a healthy group of identical age. The statistical analysis was performed on an individual computer using standard Student's t-test software packages. It should be noted that all the percentages received were presented in the work in rounded and average percentages, for a better analysis of the results obtained.

RESULT OF INVESTIGATION

As the result of the survey of mothers whose children were born prematurely and underweight shows, the main and unfavorable factors were reliably: pregnancy - multiple pregnancy (twins), where out of two children, one fetus (child) initially had pathologically defective development (ultrasound indicators during pregnancy), which amounted to 10% of the main groups of premature babies. The frequency of intrauterine development delay in comparison with the main group had the following indicators: 1GR- 24%, 2GR- 21%. The percentage of threat of termination of pregnancy was the highest, which was 96% in 1 GY, 71% in 2 GY, $P<0.05$. Infectious diseases suffered during pregnancy were the third most important in terms of occurrence: TORC infections, SARS-COV-2, ARVI, which accounted for 26% in the main group in terms of occurrence; uteroplacental insufficiency in 1 GY was detected in 18%, 2 GY - in 11% of cases.



A **B** **C**

Fig. 1., 2, 3. NSG of premature infants. A - persistence of the transparent septum cavity 16 days from birth, B - subependimal pseudocyst 18 days from birth, C - Asymmetric internal hydrocephalus 10 days from birth

Subsequently, an analysis of the results of childbirth was performed with an assessment of

the status at birth of newborn children. The standard indicator of the level of usefulness of the birth of a child is the APGAR scale, which is calculated in the first minutes at birth. In 1 GY, this indicator varied from 2.5 to 5 points, when in 2 GY, it was in the range of 4.5 -7 points, where, in comparison with healthy children, the level of P <0.005. At the same time, the rate of asphyxia in children at birth in 1 GY was 30%, in 2 GY -22%. Delivery by caesarean section according to the indication was revealed in a large percentage, 1GR-83%, 2GR-80%, almost identical (which coincides with the literary data of Pavlyukova E.V. 2018, Asimova N.M. 2019), where a frequent indication for surgery is considered: previously, the outflow of amniotic fluid, in our cases it is 60%; placental abruption of 5% of the total sample; in other cases, the threat of termination of pregnancy.

The most common complication in children born prematurely and underweight is considered to be signs of infection, which are characterized by intrauterine infection. Thus, in children of the main group (66 children), congenital pneumonia was detected after birth in 44% of cases, subsequently, a sign of enterocolitis was fixed in the department of neonatal pathology in 28% of cases from the entire sample of premature infants. Along with these disorders, the accompanying sign of respiratory failure is 100% in children with pneumonia and 65% in children with signs of respiratory impairment. In parallel with these indicators, signs of insufficiency of cardiovascular insufficiency are noted in premature infants, in 33% of cases out of the total number of the main group, where P<0.001, compared with healthy children. In addition, congenital heart disease occurs in 23% of cases in the study (which is also confirmed by literary sources, Bobyleva E.S. 2020, Burov A.A. 2021).

It should be noted that all children born prematurely and underweight (premature) needed support, especially in the first hours of birth, in activating breathing in newborns, to maintain breathing and prevent the development of severe respiratory pathologies. One of these devices is considered to be CPAP - with variable flow for non-invasive respiratory support of newborn premature infants, where a combination of modes in one device with diagnosis and correction of apnea, synchronized pressure supply in the generator is provided.

Against the background of all somatic indicators, signs of neurological insufficiency have been identified in premature infants, in the form of separate syndromes. Signs of depression syndrome come to the fore: the main symptoms of which are lethargy, inactivity, weak or sluggish sucking (in some cases, the child was completely unable to "take the breast"), the absence or decrease in the swallowing reflex, signs of hyporeflexia, depression or lack of normative reflexes of newborns. In the general sample of the main group, this syndrome was noted in 72%, where separately, for 1GR patients - in 59% of cases. In addition, the depression syndrome was accompanied in combination by signs such as arousal up to the development of convulsive readiness (in 53% of cases, where a larger percentage accounted for 1 GY); horizontal nystagmus; in one case, asymmetry of facial muscles was found (the mother of this child had high cytomegalovirus titer); in several cases (3 patients) developed bulbar syndrome, in 5 cases pseudobulbar syndrome with the appearance of violent crying. Often, CNS depression syndrome in premature infants, especially those born with less than 2000 grams of weight, there was a decrease in pain response. In the structure of the motor disorder syndrome, there was a difference or asymmetry of tendon reflexes, in 20% of 1G, when in 2G - 16%. The most difficult complication in premature infants was the manifestation of CNS ischemia; the degree of impairment in a larger percentage had an average level (grade 2), in 1 GY it was detected in 34% of cases, in 2 GY, respectively, in 18%, where P<0.05.

Fig. 5, 6, 7. MRI of children 12 months from birth. Those born prematurely and underweight

To date, the gold standard for the diagnosis of neurological dysfunction is considered to be a neurosonography examination. The study of patients used the nature of dynamic control, that is, the first result was analyzed at birth, then a month later and then every three months once, respectively, the following changes were determined on the first day: intraventricular hemorrhage, as the most common condition in children born prematurely and underweight (1500 g.), which include 1 GY (29%, grade 2 VZHK) of the examined children (the data coincide with literary sources, Imambetova A.S. et al., 2020, Kirtbaya A.R., 2022). Signs of hemorrhage in the heart were noted in the same group in 17% of cases. In addition, signs of periventricular leukomalacia were relatively frequent in 33% of cases in the sample of the main group of patients (out of 66 cases examined). Thus, according to the NSG data, children born prematurely and underweight have signs of ventricular dilation, while a greater percentage of children have 1 g, whose weight is 1000-1500 g.

During the period of dynamic observation of children born prematurely, the parameters of clinical neurological, somatic, laboratory, instrumental research methods were studied, with an assessment of indicators of motor and psycho-speech development, to fulfill the purpose of the work, where the initial context is to determine and evaluate the prognosis (adverse outcome) of this category of children. The assessment of the indicators of children born prematurely and underweight was carried out on the GRIFFITHS scale and by the method of Calendar analysis, which are designed for ages up to 24 months (in our case, the calculation was carried out for 12 months), where, by means of the characteristics of the compiled items (subscales), motor, psycho-speech, locomotor parameters are characterized, with the calculation these indicators, in the future, determine the potential of the examined patients (children). At the same time, at 6 months, 1GR children had 66 points (on average), 2GR children - 82 points, $P<0.05$. By 12 months, 1GR children scored 130 points, 2GR - 155 points. The delay in psycho-speech development (at 6 months), in 1 year - was noted in mild form in 25%, in moderate form 22%; then (at 12 months), in mild form 20%, in moderate form 7%. 2 GY by 6 months had indicators of mild delay in psycho-speech development of 18%, medium-severe 3%; By 12 months in the same group, mild psycho-speech disorders were noted in 13%, medium-severe form 5%, where $P<0.05$. The neurological status of disorders was significantly more often diagnosed in children of 1 GY (by 6 months), signs of inconsistency were noted in 68%, in 2 GY - 39%, in cases where $P<0.05$.

The main syndrome in children, the general sample of patients, turned out to be muscular dystonia; motor disorders. By 6 months, in 1GR, muscular dystonia was noted in 53%, in 2GR - 36%; motor (motor) disorders in 1GR - 31%, in 2GR - 11%, respectively. Using the GMFCS scale (distribution of motor disorders by severity), 14% of the most frequent and more severe motor disorders were found in 1 GY (at 6 months), 3% in 2 GY, where $P<0.05$. By 12 months, the indicator of motor

disorders was more pronounced, so in 1 GY the percentage varied to 17%, in 2G- 4%, where P<0.001. At the same time, muscular dystonia by 12 months in 1GR was detected in 30%, 2GR - 17%, p<0.05. Points on the CMFCS scale, in group 1 in 16% corresponded to 2-3, in 2GR - 2% corresponded to 1-2 points. Thus, as children born prematurely develop, the definition of motor and psycho-speech shifts is better diagnosed, due to more pronounced symptoms that at birth had a blurred or masking picture of neurological dysfunctions against the background of somatic unstable indicators.

As noted above, several children underwent brain neuroimaging by MRI for a period of 12 months. The images mainly revealed the following structural indicators: ventriculomegaly, expansion of external cerebrospinal spaces, periventricular leukomalacia, cerebellar worm hypoplasia, subatrophic changes in the parenchyma of the brain (these changes coincide with the literary sources Meleshkina A.V. 2015, Teberdieva S.O. 2019, Himaldinova N.E. 2021). Thus, in 1GR - ventriculomegaly was detected in 13% (from among those examined), in 2GR this variant of the disorder was not detected; expansion of external cerebrospinal fluid spaces in 1G- 3% of cases; detection of periventricular leukomalacia in 1G - 4%, in 2G -2%.

Based on the results obtained, the examined children born prematurely and underweight, for the period of birth and in dynamics up to 12 months, using the main diagnostic methods: clinical neurological, somatic, paraclinical, instrumental, neuroimaging, neuropsychological scales, predictors of neurological disorders were obtained, which for the period of birth of children with these indicators, it is possible a preliminary assessment of the threat of the formation of diseases with neurological deficits, where children born weighing up to 1,500 grams turned out to be the most vulnerable, at a gestation period of less than 33 weeks.

CONCLUSIONS

Thus, it should be noted that the factors of further neurological disorders of the central nervous system in premature infants are the following signs: unstable somatic status in the mother (SARS infection first of all), Pregnancy with the threat of termination; severe asphyxia at birth; low gestation period, low score on the Apgar Scale within 5 points; cerebral ischemia; congenital respiratory failure; enterocolitis; convulsive readiness. The use of Griffiths and GMFCS scales reliably reveal signs of motor and psycho-speech disorders in the early stages. Evaluation of the results of neurosonography in dynamics and neuroimaging make it possible to identify congenital malformations of the brain at an early level, which is also an indicator of the risk of neurological disease in children.

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