

# NEUROSONOGRAPHIC STUDY OF CHILDREN WITH HYPOXIC-ISCHEMIC BRAIN INJURY

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## ABSTRACT

The study is aimed at neurosonographic characteristics of brain injury in newborn patients with perinatal hypoxic-ischemic injury of central nervous system, complicated with inflectional process (meningitis, ventriculitis). It is settled that brain immaturity, hydrocephalic syndrome, ischemia of the brain tissue and intraventricular hemorrhages are found 2 times more often in infants with perinatal hypoxic-ischemic injury of central nervous system, complicated with inflectional process. This fact generally characterizes disorders of the hemato-encephalic barrier and the development of destructive processes in the tissue of the brain.

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**Introduction.** Currently, according to Ministry of health of Ukraine statistics, one can see a growing rate of child disability [6], including those due to diseases of the nervous system 9% [4]. Diseases of the nervous system occupy the second place among the causes of childhood disability [4]. Most diseases of the nervous system resulted in disability and maladjustment in childhood in 70-80% of cases are caused by the influence of perinatal factors [1, 8]. Perinatal lesions of the nervous system constitute up to 65-75% of all diseases of the nervous system in children [5] and lead to disability 15-30% of full-term newborns, 40-60% of prematurely born, including a significant number of children born with extremely low birth body weight [5, 7]. Hypoxic-ischemic injury of CNS in infants – is one of the main risk factors for the development of various serious neurological diseases. The gestational age of the newborn is a very important indicator, as it is one of the main variables in determining neuropathology pattern of hypoxic-ischemic injury of the brain. According to N. Vasilieva & V. E. Potapova (2017) and J. C. Wellons (2009) approximately 50% of cases of hypoxic-ischemic lesion of the nervous system is complicated by intraventricular hemorrhage (IVH) [3, 14], which remain one of the most serious problems [3, 15], and is one of the main causes of neonatal mortality [2, 14]. According to the data of Ministry of health of Ukraine, IVH and subarachnoid hemorrhage take second place (12.5%) among the causes of newborn deaths [4]. IVH occur in 3.5-cases out of 1,000 newborns and is a major neurological disorder in newborns [11]. Almost all hemorrhagic lesions of the brain manifest at the end of the early neonatal period and only 10% later [9]. In preterm infants, IVH occurs in 20-25% of cases, in infants with extremely low body weight — in 45% [13], usually at birth or during the first 96 hours [10]. Hemorrhagic lesions in 3-15% of cases are complicated by periventricular hemorrhagic infarction, with the possible formation of porencephalic cysts [9]. In patients with hypoxic-ischemic injury of CNS, infectious disease, including bacterial meningitis, can complicate the prognosis of the disease. In the structure of diseases of children with hypoxic-ischemic lesion of CNS, which is complicated by the infectious process (secondary meningitis, ventriculitis) there is a high fatality rate [2, 12]. The question of early diagnosis of various forms of brain injury in

neonates and infants remains one of the urgent problem of neonatology and Pediatrics. Difficulties of topical diagnostics are explained by anatomical and functional immaturity of the CNS and nonspecific polymorphic brain response to various pathological processes. Diagnosis of inflammatory diseases of the nervous system is one of the complex problem in neonatology and pediatric neurology. The benefits of ultrasound methods in the examination of a newborn brain and infant are not in doubt.

**Purpose:** to carry out instrumental examination (neurosonography, examination of eyeground) of neonates with hypoxic-ischemic CNS injury.

**Materials and methods.** During the 2017-2019 on the base of the neonatal intensive care unit and neonatal pathology Department of Regional Clinical Children's Hospital (Zaporizhzhya) it was undergone a comprehensive clinical investigation of newborn children. It was examined 100 newborn children. All children were divided into 3 groups of observations. The first (main) group included 31 patients with hypoxic-ischemic CNS injuries, which is complicated by the infectious process (meningitis, ventriculitis), the second group (comparison) – 35 patients with hypoxic-ischemic injuries of the CNS without the presence of an infectious process, the third (control) group – 34 conditionally healthy children born without signs of hypoxic-ischemic injuries of the nervous system and inflammatory diseases (Table 1). The condition of the child was evaluated on admission at intensive care unit. The presence of infectious complication of hypoxic-ischemic CNS injury was proved by biochemical investigation of cerebro-spinal fluid.

Table 1. Distribution of patients according to gestational age and group of investigation

	Control group	Comparison group	Main group
Prematurely born	5	16	24
Full-term newborns	29	19	7
In general	34	35	31

Criteria for inclusion in the major groups of the study:

- children from period of birth up to 11 months 29 days;
- diagnosis "hypoxic-ischemic injury of CNS", "interventricular hemorrhage", "purulent meningitis, ventriculitis";
- parental consent to conduct the study.

Exclusion criteria from the study:

- children older than 1 year;
- the presence of organic pathology of the cardiovascular and respiratory systems;
- anomalies of development of CNS;
- the presence of other malformations in the stage of compensation;
- not obtained parental consent to conduct the study.

In the course of the work it was used instrumental methods (neurosonography, examination of eye ground), methods of mathematical statistics.

In accordance to the objectives of the study the documentation was framed, it was used for collecting and recording data concerning the health status of the mother: obstetric history (pregnancy, childbirth and the postpartum period), and physical status; and child's health status: clinical status (assessment of gestational and physical development of child according to gestational age).

The neurosonography (NSG) was conducted in the first two days of hospital admittance, with a help of equipment "Medison SA 8000 Live" with convexed linear transducer of 5 MHz through the large Fontanelle in the three standard planes (coronary, sagittal and parasagittal). NSG was conducted at admission to the neonatal intensive care department for newborns of the main group and the comparison group. In the work we complied with the principles of bioethics: key provisions of the Convention of the Council Of Europe on human rights and Biomedicine (04.04.1997), GCP (1996), Helsinki Declaration of the World Medical Association on ethical principles for the conduct of medical research involving human subjects (1964-2000) and the order of MOH of Ukraine № 281 (01.11.2000).

Statistical processing of obtained results was performed on a personal computer using the licensed software package Statistika 13.0 (StatSoftInc, serial number JPZ8041382130ARCN10-J) by calculating the average arithmetic ( $M$ ), standard deviation ( $\sigma$ ) and average errors ( $m$ ). The relationship between individual parameters were evaluated using the methods of Pearson's correlation. To assess differences in the indices in the groups that were compared, we used Student's criterion,  $t$ . The reliability of differences of compared values was considered significant in case  $p < 0.05$ .

**Research results.** The clinical picture of hypoxic-ischemic CNS injury is polymorphic and is not always specific. It reflects not only the brain lesions but also multiple organic failure, hemodynamic and metabolic disorders. Topical diagnosis of the brain lesions in patients with hypoxic-ischemic CNS injury is in most cases uninformative; only a comprehensive assessment of neurological status, using clinical, neuroimaging methods, can diagnose either brain injury or transient abnormalities of CNS functioning.

One of the most accessible imaging techniques of the brain is neurosonography, with a help of which it is possible to evaluate the structure and echogenicity of the brain, the size and shape of the ventricles and other cerebrospinal fluid spaces. High information content, non-invasiveness, painlessness, absence of radiation exposure, the possibility of multiple studies in the dynamics put the neurosonography among the primary diagnostic tool in perinatal neurology. Neurosonography is currently an integral and important part of the traditional examination in neonatology and Pediatrics. The technique allows to assess brain structure and condition of the cerebrospinal fluid pathways (ventricular system, subarachnoid space), to identify the various pathological changes (hemorrhage and ischemic injury, congenital malformations, changes in the brain infections, etc.). The method allows estimating the dynamics of morphological changes of the brain in neonates and infants, in the early stages to identify the periventricular leukomalacia, cystic degeneration, the presence of peri- or intraventricular hemorrhage and to determine the degree of their severity.

Patients with hypoxic-ischemic CNS injury at the time of admission to the intensive care department were conducted a study of the cerebrospinal fluid (CSF). The presence of neutrophils, lymphocytes, the level of total cell count and protein content in cerebro-spinal fluid were evaluated, the reaction Pandy, evaluated in the "+" was carried out. The presence of infectious complications in patients with hypoxic-ischemic CNS injury was determined by positive bacterial culture of CSF. All patients of the main group (31 patients) had a positive bacteriological culture, which revealed infectious agents. Found that six patients of the main group (24%) (including two prematurely born, four were born in time), CSF was almost transparent, "+", the level of protein was 0,396 g/L. In all patients among the cells segmented leukocytes, namely neutrophils, dominated, in four cases, the cell count was less than 100 cells/mm<sup>3</sup> or within the normal range, in two cases it was significantly exceeded, reaching 768 cells/mm<sup>3</sup>. In nine patients of the main group (36%), the reaction Pandy was evaluated as "++", CSF was turbid. Among these children, only one child was born in term, the last eight were born prematurely. Protein levels of CSF were 0,419 g/l, in five patients (55.6%) the level of the cell count was within normal limits and did not exceed 100 cells/mm<sup>3</sup>, in four patients there were much higher index and ranged from 149 cells/mm<sup>3</sup> to 596 cells/mm<sup>3</sup>. Among cells neutrophils dominated. In eight patients of the main group (32%) (1 child born at term, 7 – prematurely born) CSF was turbid "+++". The protein level was significantly higher than in children with a transparent CSF and was 0,896 g/l. Only in three cases (37.5%) cytositis was within the normal range or less than 100 cells / mm<sup>3</sup>, in five patients (62.5%) the cytositis was significantly higher and reached 1600 cells/mm<sup>3</sup>. Neutrophils also prevailed among cells. Pandey's ++++ response was found only in one patient of the main group (4%). A high level of protein (5.61 g/l), expressed cytositis of 152 cells/mm<sup>3</sup>, which was mainly represented by neutrophils, characterized his CSF. The result of bacteriological sowing was positive.

Neurosonography in patients with hypoxic-ischemic CNS injury without an infectious process was revealed a homogeneous increased echogenicity in periventricular region, due to the immaturity of brain structures, it decreases during the follow-up period. In this group of patients intraventricular hemorrhage was revealed in 10 cases (29,4%) (among them 6 cases (19,4%) of premature born), in 8 cases (23,5%) – ischemia of the brain, among them 6 cases (19,4%) of premature born, in 7 cases – the incidence of hydrocephalic syndrome (20,6%), among them three (9,7%) were premature born, 12 cases (35,3%) of immaturity of the tissues of the brain, among which 11 cases (32,4%) were observed in prematurely born children. In 8 cases (23,5%) of newborns of this group it was observed an increased echogenicity of the brain parenchyma and basal ganglia, unclear visualization of the sulci

and gyrus of the brain, the absence of pulsation vessels. On that background, due to edema, it was determined a constriction and blurred imaging of the lateral ventricles.

Often, purulent meningitis in infants are of secondary nature, occurring on the background of intracranial hemorrhage, sepsis, immunodeficiency. In children of the main group, as a whole, intraventricular hemorrhages were revealed in 13 cases (52%) including 12 cases (48%) in preterm patients, ischemia was detected in 15 cases (60%), overall, 12 cases (48%) also premature born children; hydrocephalus – in 10 cases (40%), of which nine (36%) were found in preterm, immaturity of brain tissue was revealed in 14 cases (56%) and it was presented exclusively in preterm infants. In 12 cases (48%) in preterm patients with meningitis was also noted the increase in echogenicity of gyrus and extension of sulci, their "roughness" in combination with accumulation of fluid in on convexital surfaces of the hemispheres. These changes are due to the accumulation of inflammatory exudate in sulci and fissures around blood vessels pia and arachnoid membranes of the brain, which leads to compression of the walls. It was noted the expansion of the longitudinal cerebral fissure, especially in anterior regions, enlargement of subarachnoid spaces due to accumulation of exudate and pus. Almost in all patients of the main group it was observed an enlargement of the ventricular system of different severity. Ventricular dilatation appeared due to the overproduction of CSF on the background of chorioamnionitis, and obstruction of cerebrospinal fluid pathways with pus or adhesive process.

Thickening and increased echogenicity of the walls of the lateral ventricles with the presence of additional inclusions caused by pus or other decomposition products were defined in the cavity of ventricles. The increase of echogenicity of the cerebrospinal fluid, blurring or deformation of the contours of the vascular plexus and extension of the ventricular system in general show the development of the inflammatory process in the ventricular system (ventriculitis) on the background of meningitis. Neurosonographic signs of ventriculitis were identified in 15 patients (48.39%), of whom three were born in time and 12 were premature born. The changed ultrasonic characteristics of the cerebrospinal fluid were observed. Normally, the cerebrospinal fluid is anechoic, that is not giving the reflected echo signal on the screen. Biochemical changes in the contents of cerebrospinal fluid under the influence of the inflammatory process and its hyperproduction facilitate its visualization. The accumulation of pus or other degradation products in ventricles leads to increased echogenicity and heterogeneity of the liquor in the form of multiple additional signals (symptoms of "starry sky"), representing pavestone level of protein revealed by biochemical study of cerebrospinal fluid. In three cases (9.67%) among children of the main group, it was revealed the presence of septal structures within the lateral ventricles, which look like a linear echogenic pulsating formations in the coronary and parasagittal planes. In addition, in these patients it was observed an increased echogenicity of chorioideal plexus, with blurring and deformation of their contours and an enlargement of the ventricular system, which coincided with the presence of hydrocephalic syndrome.

According to the analysis of the eyeground of patients, it was found that in children of the comparison group with intraventricular hemorrhages without infectious process any changes were not revealed. On the contrary, in children of the main group, in whom IVH was complicated by an inflammatory process in 7 cases (28%) dilatation of the eyeground veins was observed, among them three were born in time and four – prematurely born. In five patients (20%) it was revealed a hemorrhage in the eyeground, in two cases – on the background of varicose veins of the retina (one born in time, one prematurely born), and in three patients – separate hemorrhages in the retina (one of them was born in time, two – prematurely born).

**Conclusions.** Thus, the ultrasonic method of research clearly assesses the structure of the brain, allows giving a more thorough characteristic of the pathological process, to assess prognosis and to follow the dynamics of development of pathological process. In the work on the base of data of the neuroimaging method, it is established that immaturity of brain tissue, hydrocephalic syndrome, ischemia of the brain tissue and intracerebral hemorrhage are found 2 times more often in patients with hypoxic-ischemic CNS injury, complicated by infectious-inflammatory process. All these illustrate the development of destructive processes in the brain tissue, which may occur as aseptic necrosis, or with the adherence of infectious agents. Subsequently, neurosonographic studies at different stages of the pathological process make it possible to evaluate the results of therapy and to determine the tactics of further treatment, as well as it may be used for dispensary monitoring of children with CNS lesions within the first year of life.

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