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CHARACTERISTICS OF PERINATAL DAMAGE TO THE NERVOUS SYSTEM IN BABIES BORN ON THE BACKGROUND OF CHRONIC INTRAUTERINE HYPOXIA

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Key words: hypoxia, hemostasis, endothelin-1, fibrinogen, cerebral blood flow velocity, resistance index.
Tayanch so‘zlar: gipoksiya, gemostaz, endotelin-1, fibrinogen, bosh miya qon oqimining tezligi, qarshilik indeksi.
Ключевые слова: гипоксия, гемостаз, эндотелин -1, фибриноген, скорость мозгового кровотока, индекс резистентности.

The aim of this study is to investigate the impact of chronic intrauterine hypoxia on cerebrovascular pathology in newborns. This is an important topic because hypoxia (a lack of oxygen) in the womb can have a significant effect on the development of the brain and the central nervous system of the child. The authors conducted research on the levels of endothelin-1 in the blood of newborns. Endothelin-1 is a biologically active substance produced by vascular endothelial cells. Elevated level of this marker may indicate vascular endothelial damage or dysfunction.

SURUNKALI HOMILA ICHI GIPOKSIYA FONIDA TUG‘ILGAN CHAQALOQLARDA ASAB TIZIMINING PERINATAL ZARARLANISH XUSUSIYATLARI

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Ushbu tadqiqotning maqsadi surunkali intrauterin gipoksiyaning yangi tug'ilgan chaqaloqlarda serebrovaskulyar patologiyaga ta'sirini o'rganishdir. Bu muhim mavzu, chunki bachadondagi gipoksiya (kislorod etishmasligi) bolaning miyasi va Markaziy asab tizimining rivojlanishiga sezilarli ta'sir ko'rsatishi mumkin. Mualliflar yangi tug'ilgan chaqaloqlarning qonida endotelin-1 darajasini o'rganishdi. Endotelin-1 qon tomir endotelial hujayralari tomonidan ishlab chiqariladigan biologik faol moddadir. Ushbu markerning yuqori darajasi qon tomir endotelial shikastlanishi yoki disfunktsiyasini ko'rsatishi mumkin.

ОСОБЕННОСТИ ПЕРИНАТАЛЬНЫХ ПОРАЖЕНИЙ НЕРВНОЙ СИСТЕМЫ У НОВОРОЖДЕННЫХ, РОДИВШИХСЯ НА ФОНЕ ХРОНИЧЕСКОЙ ВНУТРИУТРОБНОЙ ГИПОКСИИ

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Целью данного исследования является изучение влияния хронической внутриутробной гипоксии на цереброваскулярную патологию у новорожденных. Это важная тема, поскольку гипоксия (недостаток кислорода) в утробе матери может оказать значительное влияние на развитие головного мозга и центральной нервной системы ребенка. Авторы провели исследование уровня эндотелина-1 в крови новорожденных. Эндотелин -1 - биологически активное вещество, вырабатываемое эндотелиальными клетками сосудов. Повышенный уровень этого маркера может указывать на повреждение или дисфункцию эндотелия сосудов.

Introduction. Frequency of perinatal hypoxia is not decreasing. 60-80% of all central nervous system (CNS) diseases in children are associated with perinatal hypoxia [1,2].

In the development of chronic intrauterine fetal hypoxia, transitioning to neonatal hypoxia, three main groups of causes are identified:

1. Maternal extragenital diseases - thyroid diseases, bronchial asthma, anemia, heart rhythm disorders, smoking, neurocirculatory dystonia, obesity, diabetes.
2. Disorders of uteroplacental circulation (maternal hypertension or arterial hypotension).
3. Disturbances of fetal-placental circulation (tight coiling of the umbilical cord around the neck, body, true knots of the umbilical cord, placental abruption) [2].

The main causes of hemorrhagic and ischemic brain damage in newborns are disorders of cerebral hemodynamics [3]. Hypoxia is recognized as a leading etiological factor in particular cerebrovascular disorders, leading to the development of hemorrhagic and ischemic damage to the central nervous system (CNS) in newborns [4].

One of the most important factors leading to structural brain damage is a disturbance in cerebral blood flow against the background of hypoxia. Hemodynamic changes that occur during an unfavorable perinatal period and are related to the impairment of cerebral blood flow autoregulation contribute to the development of hemorrhagic complications and subsequent destructive changes in brain tissue. Effective hemodynamic support depends on the tone of cerebral vessels. According to recent studies, a healthy full-term newborn is born with a high resistance index (RI), which quickly decreases by the end of the first day of life and stabilizes by the end of the early neonatal period (RI - 0.69-0.73) [5].

A thrombogenic tendency in hemostasis characterizes newborns in the first day (especially the first hours) of life, which changes to a tendency for hypocoagulation and hypoaggregation on the 3rd to 4th day of life. In children with asphyxia, this tendency is more pronounced. However, in cases of severe asphyxia, there is a significant increase in the blood's coagulation potential [6].

Elevated endothelin-1 (ET-1) has been observed in umbilical cord blood in newborns with hypoxic brain damage [2,7]. The primary mechanism of action of ET involves the activation of calcium release, leading to:

1. Stimulation of platelet adhesion and aggregation and secondary hemostasis.
2. Contraction and growth of vascular smooth muscle, leading to vessel wall thickening and vasoconstriction [2,8].

A significant increase in the levels of ET-1 in the blood, along with a significant decrease in endothelial nitric oxide production, indicates a predominance of vasoconstriction over vasodilation in patients who have experienced acute cerebral blood flow disturbances. This results in vasospasm slow blood flow [2]. The degree of brain tissue damage directly correlates with the severity of endothelial dysfunction [7,8].

ET-1 influences cerebral autoregulation processes by narrowing cerebral blood vessels and reducing cerebral blood flow below the ischemic threshold encourage cerebral infarction [8]. It has been found that ET-1 initiates cerebral artery spasm as a result of its direct action on the vascular wall and through the depolarization of neurons, which is caused by the activation of endothelin receptors type A and phospholipase C [2,8].

The aim of this study is to investigate the state of certain hemostasis parameters, vascular endothelium, and cerebral hemodynamics in newborns who experienced chronic intrauterine hypoxia.

Methods and materials. 59 newborn infants of various gestational ages with perinatal nervous system damage were under the observation. The newborns were divided into 2 groups: Group I consisted of healthy newborns. Group II comprised 37 newborns who experienced chronic intrauterine hypoxia. Children in this group were diagnosed with CNS damage of severity levels II and III, determined by the duration of the depression syndrome, the presence of neonatal seizures, and the dynamics of structural changes in the brain based on ultrasound examination. In terms of gender distribution, 37% were boys and 63% were girls.

The causes of chronic intrauterine fetal hypoxia were as follows: severe anemia (8%), exacerbation of chronic pyelonephritis (10%), severe preeclampsia (16%), threatened preterm labor (20%), late toxemia (10%), fever (3%), transverse fetal position (5%), ascites and anasarca (17%), in vitro fertilization with multiple pregnancies (3%), oligohydramnios (5%), low placental location (3%)

The distribution of children in this group by body weight was as follows: ≤ 1000 g - 9%, 1000 - 1499 g - 13%, 1500 - 2499 g - 43%, 2500 - 3999 g - 32%, more than 4000 g - 3%.

The assessment on the Apgar scale at birth for newborns who experienced chronic intrauterine hypoxia was as follows: 0-3 points in 19%, 4-5 points in 52%, 6-7 points in 19%, and 8-10 points in 10%.

The diagnosis of "perinatal encephalopathy" was established according to the classification of perinatal nervous system damage in newborns by Sarnat and Sarnat (1976).

Methods of the research. Laboratory coagulation studies included prothrombin time (PT), prothrombin index by Quick (PI), international normalized ratio (INR), activated partial thromboplastin time (APTT), fibrinogen, and thrombin time (TT) and were determined using the Human clot junior (2000) apparatus. The specific marker of endothelial dysfunction, endothelin-1 in the blood, was determined by an enzyme-linked immunosorbent assay (ELISA) using the Mindray BS-380 apparatus.

Instrumental studies consisted of ultrasound examination of the brain's structure in B-mode (neurosonography), Doppler ultrasound of the brain's blood vessels using color scanning and spectral Doppler ultrasound, performed on the GE Logic F 8 apparatus (USA) using multi-frequency convex transducers of 5.5 MHz, a linear transducer with a scanning frequency ranging from 7 to 10 MHz. Scanning was performed in standard planes. Spectral Doppler was performed in the anterior cerebral artery (ACA), middle cerebral artery (MCA) on the right and left, and the Galen vein. The resistance index (RI) was assessed in the anterior cerebral artery (ACA), middle cerebral ar-

tery (MCA) on the right and left, and blood flow velocities in the Galen vein.

Statistical data analysis was conducted using specialized software, including Statistica 10.0, Microsoft Excel 2017, and SPSS (version 29, IDV Co. Armonk, NY, USA).

Results and discussion. In the analysis of the obtained coagulation parameters, such as PT, INR, APTT, and TT, there were changes observed in both healthy and newborns with chronic hypoxia, but these changes did not exhibit statistically significant differences. For instance, in healthy newborns, PT averaged 14.14 ± 1.02 seconds, while in newborns with chronic hypoxia, it averaged 12.75 ± 0.82 seconds. Similarly, PI was 93.43 ± 6.91% in healthy newborns and 110.15 ± 6.03% in newborns with chronic hypoxia.

However, among the coagulation parameters studied in umbilical cord blood, only the fibrinogen level in newborns with chronic conditions showed a statistically significant difference ($p < 0.01$), increasing to an average of 3.96 ± 0.58 g/L (1 table).

1 table.

Indicators of the blood coagulation system and vascular endothelium in the examined newborns (M±m).

№	Indicators	Group 1 (n=22)	Group 2 (n=37)
1	PT (sec)	14,14±1,02	12,75±0,82; P>0,2
2	PI (%)	93,43±6,91	110,15±6,03; P>0,1
3	INR	1,35±0,16	1,06±0,08; P >0,1
4	APTT (sec)	39,01±4,80	33,34±1,38; P >0,2
5	TT (sec)	46,43±8,52	48,15±6,59; P >0,5
6	Fibrinogen (g/l)	2,11±0,42	3,96±0,58; P <0,01
7	Endotelin (pg/ml)	0,04±0,001	1,06±0,24; P <0,001

Note: p –chaqaloq guruhlari orasidagi ko'rsatkichlar farqlarining ishonchliligi.

At the same time, in newborns who experienced chronic hypoxia, there was an increase in the level of endothelin-1 to 1.06 ± 0.24 pg/ml, which was statistically significant ($P < 0.001$) compared to the values of the group of healthy newborns.

2 table.

Comparative characteristics of cerebral hemodynamics in examined newborns (M±m).

№	Indicators	Group 1 (n=22)	Group 2 (n=37)	P
1	RI (PMA)	0,680±0,006	0,913±0,04	<0,001
2	RI (CMA) right	0,680±0,006	0,904±0,05	<0,001
3	RI (CMA) left	0,674±0,011	0,89±0,05	<0,001
4	V скорость кровотока (см/сек)	7,128±0,075	3,3±0,12	<0,001

Note: P - indicates the significance of differences between the parameters of healthy newborns and newborns who experienced chronic intrauterine hypoxia.

When studying cerebral hemodynamics using Doppler ultrasound in healthy newborns and those who experienced chronic hypoxia, changes were observed. For instance, in healthy newborns, the RI (Resistance Index) of the anterior cerebral artery (PCA) was 0.680±0.006, whereas in those with chronic hypoxia, it was 0.913±0.04, with a statistically significant difference ($P<0.001$). The RI of the middle cerebral artery (MCA) on the right in healthy newborns was 0.680±0.006, while in those with chronic hypoxia, it was 0.904± 0.05 ($P\leq0.001$), and the RI of the left MCA was 0.674±0.011 and 0.89±0.05 in healthy and affected individuals, respectively ($P\leq0.001$). The blood flow velocity in the vein of Galen averaged 7.128±0.075 cm/s in healthy individuals and 3.3±0.12 cm/s in affected individuals, with a statistically significant difference ($P\leq0.001$). (Table 2).

Conclusions. Thus, the conducted research reveals that in cases of chronic intrauterine fetal hypoxia, there is an increase in Endothelin-1 (ET-1) and fibrinogen levels. These changes are accompanied by a decrease in cerebral hemodynamics, characterized by vasospasm, which leads to the development of severe neurological complications in children.

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