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Some Aspects of Hemostasis Disorders in Newborns with Perinatal Encephalopathy

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Abstract: According to WHO, 10% of newborns worldwide have neurological disorders in the form of encephalopathy and brain dysfunctions, caused by hypoxic-ischemic damage to the brain of the fetus and newborn. It is known that cerebral circulation disorders in newborns are accompanied by the development of hemorrhagic and thrombohemorrhagic complications largely due to the peculiarities of the hemostasis system in the early postnatal period. The causes of these changes in the hemostasis system, as well as their role in the development of the disease, have not been fully studied. Purpose of the study: To study the state of the coagulation system in newborns with perinatal encephalopathy and to develop criteria for the severity of encephalopathy based on coagulogram data. Study materials and methods: the results of the study of 110 newborns with perinatal encephalus are presented. Study materials and methods: the results of a study of 110 newborns with moderate to severe perinatal encephalopathy are presented. Methods of laboratory analysis of hematology parameters, blood coagulation system parameters were applied: bleeding time, fibrin, fibrinogen, thrombotest, prothrombin time, prothrombin index, activated partial thromboplastin time. Results and discussion: In children with moderate perinatal encephalopathy in the early and late neonatal period, changes in the hemostasis system consist of prolonged bleeding time (4,0-5,1/min at a rate of 3,3-3,4/min) and increased fibrinogen levels (3,190-4,43 at a rate of 1,25-3,0 g/L) above the age limit. In children with severe perinatal encephalopathy, there is increased clotting according to APTT (3,35-37,1 s.), Above the age norm; bleeding time is prolonged (4,1-3,6 with a norm of 3,3-3,4 minutes); increased values of prothrombin time indicators and fibrinogen: 20,4-26,7 s at a rate of 15-18 s.; 3,88-4,79 g/l at a rate of 1,25-3,0 g/l.

Key words: newborns, perinatal encephalopathy, hemostasis, coagulability

The rising birth rate of infants with perinatal central nervous system lesions has become one of the major issues in pediatrics in recent years, both domestically and outside of the post-Soviet region. Perinatal ischemic-hypoxic CNS lesions are attributed a significant etiological role in the structure of childhood morbidity, primarily because there are few reliable ways to predict the likelihood of their development and few opportunities for newborns from high-risk groups to receive adequate monitoring and care [1]. Changes in the hemostasis system, of which disseminated intravascular coagulation syndrome (DIC), which is accompanied by mixed-genesis thrombo-hemorrhagic manifestations, is the most dangerous, play a significant role in the complex of pathogenetic mechanisms of perinatal hypoxic-ischemic lesions of the CNS. The rationale for the criteria for predicting the health status of the specified contingent of children is that studies in this direction can

identify some clinical and pathogenetic aspects of the features of vascular adaptation, the formation of endothelial dysfunction, and hemodynamic disorders depending on the state of the hemostasis system in children from high perinatal risk groups. [2].

The purpose of the study: to identify the type of blood coagulation system problems present in neonates with perinatal encephalopathy.

Methodology: The neonatal pathology and neonatal resuscitation departments of the Samarkand Regional Children's Multidisciplinary Medical Center in Samarkand hospitalized 80 newborns between the years of 2019 and 2022 who had moderate to severe perinatal encephalopathy. The results of this study were examined using laboratory data. There were 40 babies in Group I who had moderate perinatal encephalopathy. There were 40 babies in Group II who had severe perinatal encephalopathy. Thirty unharmed infants made up the control group.

The clinical diagnosis of the patients under observation was made based on the examination of the anamnesis's features, the severity of the disease's course and dynamics, the results of general laboratory tests, the coagulogram, the results of neurosonography, and, if required, the results of brain computed tomography.

In the lab, we conducted general and biochemical blood tests, investigated the condition of blood coagulation, and measured the levels of fibrinogen and fibrin: bleeding time, thrombin time, prothrombin index, thrombotest, prothrombin time, and APTT.

Result and discussion. *Hemostasis parameters in healthy newborns.* When analyzing the indicators of the hemostasis system in 30 healthy newborns, the data shown in Table 1 were obtained.

Table 1. Comparative indicators of hemostasis in healthy children of the early and late neonatal period

Index	Meaning		P
	Early neonatal period (n=15)	Late neonatal period (n=15)	
Bleeding time (min)	3,4±0,3	3,3±0,1	>0,05
Thrombin time (s)	78,0±1,1	80,7±1,3	>0,05
Prothrombin time (s)	16,2±0,2	16,7±0,3	>0,05
Prothrombin index	87,8±0,6	88,1±2,1	>0,05
Thrombotest (st)	4,1±0,1	4,2±0,1	>0,05
Activated partial thromboplastin time (s)	30,3±0,5	31,7±0,6	>0,05
Fibrin (g/l)	17,3±0,2	17,5±0,2	>0,05
Fibrinogen (g/l)	2,44±0,08	2,99±0,06	>0,05

The majority of the indicators in the coagulation system of healthy newborns born in the early and late neonatal periods do not significantly change from one another, i.e., they are identical, according to our investigations (table 1). Our research therefore supported the hypothesis that the blood coagulation system in healthy infants is a stable system that is independent of the child's body's environmental adaption during its early or late development.

Neonates with hypoxic-ischemic encephalopathy and hemostasis markers. The information in Table 2 was gathered after indications of the hemostasis system in 50 babies with moderately severe HIE were examined.

Table 2. Comparative indicators of hemostasis in newborns of the early and late neonatal period with HIE of moderate severity (I group)

Index	Meaning		P
	Early neonatal period (n=23)	Late neonatal period (n=27)	
Bleeding time (min)	4,0±0,3	5,1±0,1	<0,05
Thrombin time (s)	76,4±1,2	78,3±1,3	>0,05
Prothrombin time (s)	16,4±0,2	17,1±0,3	>0,05
Prothrombin index	86,4±0,5	87,1±2,0	>0,05
Thrombotest (st)	4,0±0,1	4,2±0,1	>0,05
Activated partial thromboplastin time (s)	31,3±0,5	31,9±0,6	>0,05
Fibrin (g/l)	17,5±0,2	17,7±0,2	>0,05
Fibrinogen (g/l)	3,19±0,07	4,43±0,06	<0,05

Note: p - statistical significance of differences in indicators between the early and late neonatal periods (according to the Wilcoxon T-test).

In children with HIE II degree in the early and late neonatal period, analysis of the data obtained revealed changes in the hemostasis system that included an increase in bleeding time (4.0-5.1/min at a rate of 3.3-3.4/min) and an increase in the level of fibrinogen (3.19-4.43 at a rate of 1.25-3.0 g/l) above the age norm. Most likely, these outliers are connected to the child's lengthy anhydrous period, persistent intrauterine hypoxia, and umbilical cord entanglement with asphyxia at birthing.

The information reported in Table 3 was gathered after indications of the hemostasis system in 30 neonates with severe HIE were examined.

Table 3. Comparative indicators of hemostasis in newborns of the early and late neonatal period with severe HIE (group II)

Index	Meaning		P
	Early neonatal period (n=18)	Late neonatal period (n=12)	
Bleeding time (min)	4,1±0,3	3,6±0,1	<0,05
Thrombin time (s)	78,3±1,1	80,5±1,3	>0,05
Prothrombin time (s)	20,4±0,2	26,7±0,3	<0,05
Prothrombin index	85,9±0,6	87,9±2,1	>0,05
Thrombotest (st)	4,2±0,1	4,2±0,1	>0,05
Activated partial thromboplastin time (s)	35,3±0,5	37,1±0,6	<0,05
Fibrin (g/l)	17,4±0,2	17,6±0,2	>0,05
Fibrinogen (g/l)	3,88±0,08	4,79±0,06	<0,05

Note: p - statistical significance of differences in indicators between the early and late neonatal periods (according to the Wilcoxon T-test).

According to APTT (3.35-37.1 s.), above the age standard, we discovered enhanced clotting in the II group of neonates while examining laboratory data. Additionally, the bleeding duration was extended (from 4.1 to 3.6 at a pace of 3.3 to 3.4 minutes). Prothrombin time and fibrinogen indicators both showed elevated values: 20.4-26.7 s at a rate of 15–18 s and 3.88–4.79 g/l at a rate of 1.25–3.0 g/l, respectively. These findings support our theory that neonates with HIE III-degree have

a violation in the body's coagulation system throughout the early and late neonatal periods, resulting in DIC in the stage of compensation.

Thus, our data show that in early and late neonatal periods in children with II and III-degree hypoxic-ischemic encephalopathy, the blood coagulation system is in an imbalance, which can serve as an initiating moment to the first phase of the syndrome of disseminated intravascular coagulation, which progresses without severe clinical symptoms.

The early and late neonatal periods of 30 healthy babies and 80 neonates with hypoxic-ischemic encephalopathy were used for the research of the correlation between blood hemostasis system markers. The results are shown in table 4 of the report.

Table 4. Comparative indicators of hemostasis in healthy newborns of the early and late neonatal period and in children with HIE (groups I and II)

Index	Meaning							
	Early neonatal period				late neonatal period			
	Healthy (n=15)	I gr. (n=23)	II gr. (n=18)	p	Healthy (n=15)	I gr. (n=27)	II gr. (n=12)	p
Bleeding time (min)	3,4±0,3	4,0±0,3 p_1<0,05	4,1±0,3 p_1<0,05 p_2>0,05	<0,05	3,3±0,1	5,1±0,1 p_1<0,05	3,6±0,1 p_1>0,05 p_2<0,05	<0,05
Thrombin time (s)	78±1,1	76,4±1,2 p_1>0,05	78,3±1,1 p_1>0,05 p_2>0,05	>0,05	80,7±1,3	78,3±1,3 p_1>0,05	80,5±1,3 p_1>0,05 p_2>0,05	>0,05
Prothrombin time (s)	16,2±0,2	16,4±0,2 p_1>0,05	20,4±0,2 p_1<0,05 p_2<0,05	<0,05	16,7±0,3	17,1±0,3 p_1>0,05	26,7±0,3 p_1<0,05 p_2<0,05	<0,05
Prothrombin index	87,8±0,6	86,4±0,5 p_1>0,05	85,9±0,6 p_1>0,05 p_2>0,05	>0,05	88,1±2,1	87,1±2,0 p_1>0,05	87,9±2,1 p_1>0,05 p_2>0,05	>0,05
Thrombotest (st)	4,1±0,1	4,0±0,1 p_1>0,05	4,2±0,1 p_1>0,05 p_2>0,05	>0,05	4,2±0,1	4,2±0,1 p_1>0,05	4,2±0,1 p_1>0,05 p_2>0,05	>0,05
APTT (s)	30,3±0,5	31,3±0,5 p_1>0,05	35,3±0,5 p_1<0,05 p_2<0,05	<0,05	31,7±0,6	31,9±0,6 p_1>0,05	37,1±0,6 p_1<0,05 p_2<0,05	<0,05
Fibrin (g/l)	17,3±0,2	17,5±0,2 p_1>0,05	17,4±0,2 p_1>0,05 p_2>0,05	>0,05	17,5±0,2	17,7±0,2 p_1>0,05	17,6±0,2 p_1>0,05 p_2>0,05	>0,05
Fibrinogen (g/l)	2,44±0,08	3,19±0,07 p_1<0,05	3,88±0,08 p_1<0,05 p_2>0,05	<0,05	2,99±0,06	4,43±0,06 p_1<0,05	4,79±0,06 p_1<0,05 p_2>0,05	<0,05

Note: p - statistical significance of differences in indicators between groups according to Kruskal-Wallis ANOVA; p1 - statistical significance of differences in indicators compared with healthy newborns; p2 - statistical significance of differences in indicators compared with the data of children in group I (according to the Mann-Whitney U-test).

The bleeding time in the early neonatal period was examined, and groups I and II showed a significant lengthening when compared to healthy newborns. Group II's bleeding time was slightly higher than group I's, but this difference was not statistically significant (3.4, 4.0, and 4.1 min). The bleeding time is substantially longer in group I neonates in the late neonatal period (3.3 0.1 and 5.1 0.1 min) compared to healthy newborns; in group II, it is similarly longer but not statistically significant (3.3 0.1 and 3.6 0.1 min) compared to healthy newborns. The difference between groups I and II (5.10.1 and 3.60.1 min) is likewise statistically significant.

It should be highlighted that physiological hypercoagulability is seen in healthy, normal babies, and that this is an indication of the mother's hemostasis throughout pregnancy.

In children with moderate HIE, the bleeding time is prolonged in the early neonatal period and maintains this trend in the late neonatal period, when it has a hypocoagulable orientation. In contrast, in children with severe HIE, the bleeding time is prolonged in the early neonatal period and returns to the normal range in the late neonatal period, which corresponds to the state of hypercoagulability.

In group I, the prothrombin time indicator conforms to the age standard for healthy babies (16.2 and 16.4 seconds), however in group II, the indicator is statistically substantially longer than that of healthy children and children in group I (20.4 seconds). Prothrombin time dynamics are comparable in the late neonatal period (16.70.3 s, 17.10.3 s, and 26.70.3 s). As a result, one of the criteria for the severe course of hypoxic-ischemic encephalopathy (grade III) is the existence of a longer prothyrombin time.

The indicator of activated partial thromboplastin time in HIE of moderate severity during the early neonatal period did not statistically differ from the indicators of healthy newborns (30.30.5 s and 31.30.5 s), but in group II, APTT was significantly higher than with healthy newborns and kids from group I (35.30.5 s). The dynamics of AVHT in the late neonatal period are the same as those in the early neonatal period (31.70.6 s, 31.90.6 s, and 37.10.6 s). Another indicator of grade III hypoxic-ischemic encephalopathy is a lengthening of the activated partial thromboplastin time.

Although there is no statistically significant difference between the fibrinogen levels in children with HIE of moderate and severe severity, the indicator of the amount of fibrinogen in the early neonatal period was statistically significantly longer compared to healthy newborns in both groups I and II (2.44±0.08 g/l, 3.19±0.07 g/l, 3.88 ±0.08 g/l). Although there were statistically significant differences between groups I and II, differences between healthy newborns and children with HIE of moderate severity (2.99±0.06 g/l and 4.43±0.006 g/l) were not found (4.43±0.006 g/l and 4.79±0.06 g/l). Given that a healthy newborn is born in a state of physiological hypercoagulability, it is reasonable to conclude that an increase in fibrinogen levels during the early and late stages of HIE with severity II and III represents a state of pathological hypercoagulability that may not be clinically relevant. compensated DIC appeared.

There were no statistically significant differences from age norms in the comparison groups for markers such thrombin time, prothrombin index, thrombotest, and fibrin.

Conclusion. As a result, there are differences between neonates with HIE who are healthy and those who are ill, according to several hemostasis system indications. Given that physiological hypercoagulability, which replicates the coagulation system's condition during the mother's last trimester of pregnancy, is the age standard for healthy newborns and is required to prevent potentially fatal blood loss during childbirth and in the postpartum period. When HIE is moderately severe in infants, the blood coagulation system is in the "borderline" type and is more prone to hypocoagulation. A pronounced tendency to hemostasis hypercoagulation is once more observed in newborns with severe grade III HIE in the late neonatal period, without the pronounced clinical manifestations that were present in the early neonatal period, in various clinical manifestation combinations, such as intracranial hemorrhages. The development of severe cerebral disorders, more

frequently of the hypoxic-ischemic type than the hemorrhagic type, is caused by the presence of several high-risk factors for perinatal pathology, the immaturity of brain structures, and a physiological or pathological tendency to hypercoagulation at birth.

Our study demonstrated that newborns with moderate to severe (II and III degree) hypoxic-ischemic perinatal encephalopathy have blood coagulation system disorders in the form of compensated blood hypercoagulation in the early and late neonatal period, which in the future may be the cause of activating the initial, clinically unexpressed phase of the syndrome of disseminated intravascular coagulation.

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