



BIOCHEMICAL CHARACTERISTICS, METABOLIC CHANGES IN POST-ASPHYXIA SYNDROME IN NEWBORNS IN THE EARLY NEONATAL PERIOD

X.B. Fayzullayeva

Assistant of the Department of Biological Chemistry

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ABSTRACT

The medical community is unswervingly joining forces to address issues of maternal and child health, which are acquiring political and social significance against the background of demographic problems of our time. At the heart of many conditions complicating the course of pregnancy and childbirth, there is a damaging factor that is universal for the fetus and newborn - hypoxia, which disrupts the course of basic energy-dependent processes, triggering a complex of pathological endogenous reactions that contribute to the development of multiple organ dysfunction.

One of the integral indicators of an adequately proceeding postnatal adaptation is the dynamics of loss and restoration of the initial body weight of a newborn child. The study of indicators reflecting the dynamics of body weight revealed significant differences in children who underwent intrauterine hypoxia from healthy children. The indices of newborns who underwent intrauterine hypoxia and were extracted by CS had significant differences from the children of the comparison group. They had a higher percentage of loss of the initial mass (7.7 ± 0.48 (%) versus 5.9 ± 0.36 (%), $p = 0.007$), a longer period of its loss (6.5 ± 0.35 days versus 5.1 ± 0.54 days, $p = 0.023$), as well as a protracted period of recovery of body weight (12.8 ± 0.48 days versus 11.2 ± 0.63 days, $p = 0.042$) with the maximum severity of changes in immature children, according to the severity of the condition,

were forced to be removed at a gestation period of 32 - 34 weeks.

The intensity of metabolic processes in the studied groups was studied according to the results of clinical, biochemical blood tests, acid-base state (CBS) and blood gas composition. The study of the acid-base state of the blood revealed in children who underwent hypoxia, regardless of the method of birth, significant differences from healthy children in terms of base deficiency ($p = 0.0002$ and $p = 0.001$), blood saturation ($p = 0.002$ and $p = 0.008$), and in group I, differences with healthy children were also obtained in terms of pH ($p = 0.016$) and blood bicarbonates ($p = 0.018$). The effect of intrauterine hypoxia in children extracted by CS contributed to a more significant decrease in pH compared with children of group II - 7.35 ± 0.01 versus 7.39 ± 0.02 ($p = 0.009$), bicarbonate levels 21.7 ± 0.31 mmol / L versus 22.9 ± 0.47 mmol / L ($p = 0.027$) and pronounced



base deficiency 3.9 ± 0.58 mmol / L versus 2.8 ± 0.36 mmol / l ($p = 0.032$), which reflected a more unfavorable intrauterine state of the fetus. The level of total protein in newborns who underwent hypoxia was comparable and significantly lower than in healthy children ($p = 0.0003$ and $p = 0.001$, respectively). At the same time, in children born by CS, a tendency towards lower values of total protein (53.2 ± 0.73 g / l) was shown against children in the comparison group (54.6 ± 0.87 g / l, $p > 0.05$), especially in the extracted CS at 32-34 weeks (46.5 ± 1.44 g / l). In children of group I, hypoproteinemia (total protein <45 g / l) was significantly more often recorded - 21.3% versus 12.4% in the comparison group ($\chi^2 = 6.15$, $p = 0.013$) with the highest frequency in those extracted at gestation 32-34 weeks (38%). A direct relationship was established between the incidence of hypoproteinemia and excessive loss of initial body weight ($r = 0.782$, $p = 0.001$).

The study of the enzyme activity of the blood showed that the average level of aminotransferases - alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the studied groups did not exceed the age values (up to 5 days of life ALT up to 50 U / L and AST - up to 140 U / L).

However, in children born by surgery, a significantly lower ALT level is shown (12.8 ± 0.65 U / L) versus the comparison group (18.3 ± 1.19 U / L, $p = 0.002$) and healthy children ($17, 3 \pm 1.75$ U / L, $p = 0.003$), as well as AST (63.3 ± 1.98 U / L) against children of the comparison group (70.8 ± 3.59 U / L, $p = 0.028$) and the control group (67.9 ± 1.09 U / L, $p = 0.034$), which indicated a decrease in the protein-synthetic function of the liver. Elevated

ALT and AST values were found in isolated cases.

The content of protein metabolism products in the comparison groups was comparable. However, in children extracted by CS, a tendency towards a higher level of blood urea (4.8 ± 0.19 mmol / L) versus the comparison group (4.4 ± 0.21 mmol / L, $p > 0.05$) was shown. Significant differences from healthy children (3.3 ± 0.17 mmol / L, $p = 0.034$) with the highest values in the extracted CS at 32-34 weeks (6.9 ± 1.07 mmol / L).

In the comparison groups, the frequency of azotemia (urea more than 8.5 mmol / l) was comparable (10% and 8.1%, $p > 0.05$), but the highest urea level was recorded in children extracted by CS - 13.5 ± 1.99 mmol / L versus 8.9 ± 0.48 mmol / L ($p = 0.036$) in naturally born children.

In newborns who underwent intrauterine hypoxia and extracted by CS, there was a tendency to higher creatinine values (90.9 ± 1.98 μ mol / L) versus the comparison group (85.8 ± 2.29 μ mol / L, $p > 0.05$) and especially against healthy children (57.6 ± 2.16 μ mol / l, $p = 0.001$). At the same time, hypercreatininemia was formed much more often in group I - 50.3% versus 32.9% of children in the comparison group ($\chi^2 = 13.86$, $p = 0.0002$) with significantly higher average creatinine values - 113 ± 2.46 μ mol / l against 104.1 ± 1.67 μ mol / l ($p = 0.042$).

In newborns who underwent hypoxia, regardless of the method of birth, in contrast to healthy children, a significantly higher level of tissue hypoxia - lactate was established ($p = 0.003$ and $p = 0.004$, respectively). At the same time, the lactate level in those extracted by CS was significantly higher than in the comparison group - 4.7 ± 0.58 mmol / L versus $4.1 \pm$



0.49 mmol / L ($p = 0.025$), especially in immature children extracted by CS at 32-34 weeks - 5.3 ± 0.66 mmol / L versus 4.0 ± 0.47 mmol / L when compared with children of similar maturity ($p = 0.049$).

Moreover, the frequency of lactic acidosis in children of group I significantly exceeded the same indicator in the comparison group - 34.1% (99 children) versus 22.7% (42%) ($\chi^2 = 7.08$, $p = 0.007$).

The activity of the enzymes lactate dehydrogenase (LDH), creatine phosphokinase (CPK), alkaline phosphatase (ALP) and a nonspecific indicator of C-reactive protein (CRP) inflammation in children undergoing hypoxia, regardless of the mode of birth, was increased and comparable, significantly differing from those of healthy children.

Evaluation of serum glucose showed comparable results in comparison groups. However, the incidence of hypoglycemia was higher in children born by CS - 36.8% versus 25.9% in the comparison group ($\chi^2 = 6.16$, $p = 0.013$) with significant differences among term infants - 22% versus 8% ($\chi^2 = 6.90$, $p = 0.008$).

It should be noted that regardless of the method of birth, the most significant decrease in glucose levels was found among premature infants with GA at 32-34 weeks, but of these, the lowest rates were recorded in 3 newborns born by CS ($0.9-1.1$ mmol / L). Hyperglycemia (an increase in glucose levels of more than 6.5 mmol / L on an empty stomach) was recorded with a comparable frequency in the comparison groups (5.2% and 5.4%, $p > 0.05$), with the highest frequency in children with GA at 32-34 weeks extracted by CS (14.3%).

Thus, against the background of impaired regulation of glucose metabolism, the most

unstable situation with pronounced fluctuations in glucose levels was observed in newborns extracted by the abdominal route, especially among premature infants.

The assessment of the hormonal status of newborns was carried out with an analysis of the indicators of the most significant adaptive hormones, which, as you know, have a wide range of metabolic and immunomodulatory activities. In the comparison groups, the level of thyroid-stimulating hormone (TSH), produced by the pituitary gland and regulating the thyroid gland, was comparable in mean values, but lower than in the control group, without going beyond the age values for newborns (up to 20 IU / ml). However, the level of the thyroid hormone thyroxine (T4) in children who underwent hypoxia, regardless of the mode of birth, did not reach the age values (22.0 - 49.0 pmol / ml) and significantly differed from the indicators of healthy children ($p = 0.024$ and $p = 0.038$ respectively). The lowest thyroxine values were found in children of group I - 15.9 ± 0.91 pmol / ml versus 18.8 ± 0.85 pmol / ml in the comparison group ($p = 0.042$) with significant differences in 3 subgroups - 15.2 ± 0.92 pmol / ml versus 19.9 ± 1.27 pmol / ml ($p = 0.003$), with a tendency to an increase in the incidence of hypothyroxinemia (decrease in the T4 level less than 22.0 pmol / ml) when compared with children of group II (74, 4% versus 65.9%, $p > 0.05$). Regardless of the mode of birth in newborns who underwent intrauterine hypoxia, the incidence of hypothyroxinemia increased with decreasing gestational maturity ($r = -0.934$, $p = 0.0001$) and was highest among immature children born at 32-34 weeks' gestation (90, 4% and 86.7%, $p > 0.05$). The level of cortisol (a hormone of the adrenal



cortex), which affects all types of metabolism (protein, fat, carbohydrate), regulates the processes of gluconeogenesis, catabolism, has an immunosuppressive, anti-inflammatory effect, in the children of the studied groups was comparable and did not go beyond the age range (55–304 nmol / L). In group I newborns, a tendency towards lower mean values of cortisol was shown against children in the comparison group (208.6 ± 35.63 nmol / L versus 211.5 ± 27.45 nmol / L, $p > 0.05$). However, the incidence of hypocortisolemia was significantly higher among those born by CS - 10.3% versus 3.2% in the comparison group ($\chi^2 = 8.13$, $p = 0.004$), especially in children extracted by CS at 32-34 weeks (42, 7% versus 13.3%, $p = 0.007$).

Gradually, towards the end of the neonatal period, the level of hormones was restored with a continuing tendency to lower values in children extracted by CS.

In newborns who underwent hypoxia, regardless of the mode of birth, higher but comparable mean values of the baseline bilirubin level were recorded compared with healthy children. However, among them, the formation of hyperbilirubinemia was registered already in the first day of life in more than half of the newborns (50.6% and 50.2%, $p > 0.05$), which had significant differences from healthy children ($p = 0.0001$). At the same time, by 5-6 days of life, the proportion of patients with hyperbilirubinemia was significantly higher in group I children - 68.2% versus 52.9% in the comparison group ($\chi^2 = 11.26$, $p = 0.0004$) with significant differences in 2 subgroups - 83.5% versus 62.5% ($\chi^2 = 11.84$, $p = 0.0003$). Children who underwent hypoxia, regardless of the method of birth, significantly differed from healthy children both in higher values of

the maximum bilirubin level and in the duration of hyperbilirubinemia with comparable indicators in the comparison groups ($p > 0.05$).

The average values of the hemoglobin level in the first day of life in children of the studied groups did not differ significantly, remaining within the admissible age range (134-198 g / l). In the early neonatal period in children who underwent hypoxia, a comparable frequency of polycythemia was revealed (with Hb 220 g / l and above) - 11% and 8% ($p > 0.05$). Further observation showed a decrease in the level of hemoglobin and by the end of the neonatal period more than a third of children in the comparison groups had anemia, in contrast to healthy patients ($p = 0.0003$ and $p = 0.0003$, respectively) with a tendency to a higher frequency of pathology among those born by CS (38.9% versus 32.4%, $p > 0.05$). The frequency of anemia increased with decreasing gestational maturity of children and was found most frequently in immature children extracted by CS at 32-34 weeks - 71.4% versus 46.6% ($\chi^2 = 4.52$, $p = 0.033$).

Thus, a comparison of the values of blood parameters in newborns who underwent intrauterine hypoxia revealed a more intense course of metabolic processes in the early neonatal period in children born by surgery, especially premature babies. Evaluation of the frequency of metabolic disorders, taking into account the urgency of the applied CS, showed more significant changes in blood parameters in children, the severity of the intrauterine state of which caused extraction by CS for emergency indications. In term infants extracted by emergency CS, lactic acidosis (33.3% (15/45), $p = 0.0001$), hypoproteinemia (20%, $p = 0.0001$) were



more often registered in the absence of these disorders. In term infants born with planned CS, as well as a significant increase in the incidence of hypoglycemia (53.3% versus 4% , $p = 0.0001$). In premature infants, with a higher and comparable frequency of metabolic disorders against the background of the severity of hypoxia, the deterioration of the condition, which entailed emergency extraction by CS, contributed to an increase in the incidence of lactic acidosis - 55.4% versus 30% ($\chi^2 = 7.60$, $p = 0.006$), hypoproteinemia - 35.9% versus 16.6% ($\chi^2 = 5.47$, $p = 0.019$) when compared with children of the same age, extracted by the planned CS. It should be noted that the high incidence of hypocortisolemia in premature infants, regardless of the urgency of the applied CS (14.2% and 16.4%, $p > 0.05$), correlated with delivery before the onset of labor ($r = 0.742$, $p = 0.004$). and hyperbilirubinemia with delayed onset of breastfeeding both in premature infants ($r = 0.858$, $p = 0.002$) and in term infants ($r = 0.768$, $p = 0.008$).

Taking into account the fact that the metabolic rate, as well as adaptation processes in newborns are closely related to the beginning of natural feeding, the analysis of the dynamics of natural feeding among children who underwent hypoxia was carried out. In children of group I, a lower frequency of the first attachment of newborns to the mother's breast in the delivery room was found - 64.4% versus 77.2% of the comparison group ($\chi^2 = 8.75$, $p = 0.003$), more often the joint stay of the child and the mother in the neonatal period - 68.2% versus 58.9% naturally born ($\chi^2 = 4.33$, $p = 0.037$). Reliably later dates of the onset of natural feeding were revealed in children extracted by CS (6.4 ± 4.84 days) compared with naturally born children (3.6

± 3.79 days, $p = 0.004$) with significant differences in 2- x subgroups (7.9 ± 3.71 days versus 5.3 ± 3.91 days, $p = 0.023$). In the remaining subgroups, a tendency towards a later onset of natural feeding was traced both among term infants (3.42 ± 2.99 days versus 2.5 ± 3.07 days, $p = 0.099$) and children with gestational age of 32-34 weeks ($12, 4 \pm 4.42$ days versus 9.8 ± 2.25 , $p = 0.125$). By the end of the first month of life of children, the proportion of mothers who retained lactation was lower among those delivered by CS compared with those who gave birth naturally - 33.7% versus 43.2% in the comparison group ($\chi^2 = 4.30$, $p = 0.038$) with significant differences among women who gave birth to full-term babies - 50% versus 66.6% in the comparison group ($\chi^2 = 5.21$, $p = 0.022$). Among premature babies, regardless of the method of birth, the frequency of breastfeeding was significantly lower and comparable, with a tendency to a lower frequency in children extracted by the abdominal route (22.6% and 27.2%, respectively, $p > 0.05$).

Thus, the indicators of metabolic adaptation in newborns who underwent intrauterine hypoxia significantly differed from healthy children with a more intense course in children born by CS. Changes in the acid-base state of the blood, the level of lactate in these children testified to the severity of hypoxic-mediated disorders. The catabolic orientation of metabolism in children of this group is confirmed by a higher frequency of hypoproteinemia, an increased content of protein metabolism products (urea, creatinine), and a decrease in the protein-synthetic function of the liver. A higher incidence of hypoglycemia, hyperbilirubinemia was found; revealed a hormonal imbalance with a violation of the



ratio between TTH and T4 with a significant decrease in the latter, a higher incidence of hypocortisolemia. It was shown that the frequency of metabolic

disorders is higher in children, the severity of the intrauterine state of which required emergency extraction by Cesarean section.

References:

1. Kh.B. Fayzullayeva, K.M. Xalikov, G.Sh. Nazarova The Intensity Of Metabolic Processes In Newborns With Intrauterin Hypoxia // J. Problems of biology and medicine 2022 № 2(135)
2. Абдуллаева М.Н., Файзуллаева Х.Б., Икрамова З.Х. Метаболические сдвиги как индикатор постгипоксических осложнений у новорождённых. //Journal of Cardiorespiratory Research -№1 (2022) DOI <http://dx.doi.org/10.26739/2181-0974-2022-1> p. 19-22
3. Fayzullayeva X.B., Abdullayeva M.N. Analysis of the specificity of antenatal and intrapartum risk factors in newborns with intrauterine hypoxia // J. Natural Volatiles & Essential Oils, 2021; 8(4) p 5949-5957
4. Akramova X.A. Characteristic features of placental growth factor in IUGR [Text] / X.A. Akramova., D.I. Axmedova // Pediatria 2014 № 3-4 P. 29-31
5. Zvizdić, Z. Significant patent ductus arteriosus as independent risk factor for necrotizing enterocolitis in preterm infants [Text] / Z. Zvizdić, S. Heljić, D. Zvizdić [et al.] // Folia Med. - 2015. - Vol. 50, № 2. - P. 92-95.
6. Thompson, L.P. Intrauterine hypoxia: clinical consequences and therapeutic perspectives [Text] / L.P. Thompson, S. Crimmins, B.P. Telugu [et al.] // Research and Reports in Neonatology. - 2015. - Vol. 5. - P. 79 - 89
7. Stokholm, J. Cesarean section changes neonatal gut colonization [Text] / J. Stokholm, J. Thorsen, B.L. Chawes [et al.] // . - Allergy Clin Immunol. - 2016. - Vol. 138, № 3. - P. 881-889.
8. Sallmon, H. Recent advances in the treatment of preterm newborn infants with patent ductus arteriosus [Text] / H. Sallmon, P. Koehne, G. Hansmann // Clin Perinatol. - 2016. - Vol. 43, № 1. - P. 113-129.
9. Palmer SR, Erickson LA, Ichetovkin I, Knauer DJ, Markovic SN. Circulating serologic and molecular biomarkers in malignant melanoma. Mayo Clin Proc. 2011 Oct;86(10):981-90. Review.
10. Chen H, Xu C, Jin Q, Liu Z. S100 protein family in human cancer. Am J Cancer Res. 2014 Mar 1;4(2):89-115. eCollection 2014. Review.
11. Sedaghat F, Notopoulos A. S100 protein family and its application in clinical practice. Hippokratia. 2008;12(4):198-204.
12. Fuchs, S.A. et al. Increased concentrations of both NMDA receptor co-agonists D-serine and glycine in global ischemia: a potential novel treatment target for perinatal asphyxia // Amino Acids. - 2012. - Vol. 43, № 1. - P. 355-363.