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The Role of Mother-Placenta-Fetus System's Protection Mechanisms Disturbance in Delayed Fetus Growth and Development

AhrarovaNigora Abdugapparovna[1],AshurovaDilfuza Tashpulatovna[2],UmarovMarguba Sayfutdinovna[3],TursunovaOliya Abduraufovna[4],MadrakhimovaDilafruz Mammatovna[5]

[1]MD, assistant professor of Propaedeutics childhood diseases, hematology Tashkent pediatric medical Institute

[2]DSc, Head of the Department of Propaedeutics childhood diseases hematology Tashkent pediatric medical Institute

[3]assistant Department propaedeutics childhood diseases, hematology

[4]assistant Department propaedeutics childhood diseases, hematology

[5]assistant Department propaedeutics childhood diseases, hematology

Email: [1]akhrarova.nigora@mail.ru, [3]Umarguba1963@gmail.ru,

Abstract.

The influence of the content of the balance of cobalt, nickel and lead on the mother-placenta-fetus system in children born with low birth weight was studied. Determination of trace elements was carried out in the blood serum and in the placenta of 30 pregnant women and their newborns. The comparison group consisted of 30 healthy women and their 30 healthy full-term newborns with normal weight. In the blood serum of low-birth-weight infants, the content of cobalt was significantly reduced, while the content of lead and nickel was, on average, 2 times higher in comparison with newborns with normal weight. It has been proven that an excess and imbalance of toxic microelements in a woman's body, dysfunction of the placenta lead to an imbalance of these microelements in the body of the fetus and the newborn, a violation of the conditions for fetal development, contributes to a delay in weight gain and the birth of children with low weight..

Key words: trace elements, placenta, fetus, newborn, low weight.

SUMMARY.

Current study presents the influence of the content of cobalt, nickel and lead on the mother-placenta-fetus system in children with low birth weight. Trace elements were measured in blood serum and in placenta of 30 pregnant women and their newborns. The comparison group consisted of 30 healthy women and their 30 healthy full-term newborns with normal weight. In the blood serum of low birth weight infants, the content of cobalt was significantly reduced, while the content of lead and nickel was on average 2 times higher in comparison with normal weight infants. This proves that an excess and imbalance of toxic microelements in a woman's body, dysfunctions of the placenta lead to an imbalance of these microelements in the body of the fetus and newborn, to disorders of fetal development, and contributes to the delay in weight gain and to the birth of low weight children.

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INTRODUCTION

Many studies have shown that the deficiency of bioelements and vitamins in mothers is a common cause of intrauterine fetal growth retardation, serious disorders of the functioning of organs and systems, anemia, which lead to the birth of low birth weight (CF) children and an increase in morbidity in the neonatal period [2]. The female body's need for these essential nutrients is especially great during pregnancy and lactation, deficiency damages the health of mother and child, increases the risk of developing perinatal pathology, increases infant mortality, is one of the causes of prematurity, congenital malformations, disorders of the physical and mental development of children [15, 16].
Vitamins and trace elements are important components for the growth and development of the fetus during the entire intrauterine development, as well as in newborns during the entire subsequent period of breastfeeding [5, 14]. Epidemiological studies have established a direct link between an insufficient supply of micronutrients and n-3 fatty acids and an increased risk of preterm birth and the development of postpartum depression, as well as behavioral disorders in children (attention deficit hyperactivity disorder) [17].
Deterioration of the ecological situation in modern conditions leads to an increase in the load on the body of toxic substances, in particular heavy metals, which lead to depletion of the adaptive reactions of the fetoplacental system and perinatal pathology [4]. In turn, newborns with perinatal pathology have a high risk of metabolic disorders of trace elements (ME) [11, 12]. The mechanism of perinatal pathology is complex and is caused by fetoplacental circulation disorders, endocrine, metabolic and immunological disorders in the mother-placenta-fetus system, the characteristics of the course of labor and the degree of maturity of the fetus and newborn [6].

The toxic effect of heavy metals in the prenatal period is determined by their penetration through the placental barrier with subsequent teratogenic, embryotoxic, carcinogenic effects, impaired immunity and reproduction [10]. With an imbalance of trace elements, conditions arise for damage to the structure of genes, violations of mitosis processes, differentiation of cell death, which is important for organogenesis, the development of hereditary and congenital diseases. The growth and development of a child are the main indicators of his health. The intensity of growth and development processes is the main feature of childhood [3]. Recent data indicate the unsatisfactory provision of children and women of reproductive age with macro- and microelements (calcium, cobalt, fluorine, iodine, etc.). Initial nutritional deficiencies in women (in 40-77% of pregnant women) entail inadequacy of food supply and storage during pregnancy [7].

The negative impact of ME deficiency and imbalance on the fetus in later life is manifested by delayed physical and mental development, impaired adaptation of functions and chronic diseases, and in most infants and young children dictates the need to develop comprehensive measures for its prevention [8]. In these children, at an older age, ME deficiency is accompanied by rapid fatigue, decreased emotional tone, weakened concentration, impairment of other cognitive functions, limited social contacts, quarrels with peers, and

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inability to study science [13]. The role of microelement homeostasis disorders in the pathogenesis of hypoxia has not been sufficiently studied.

Purpose of the study.Determine the role of violation of the protection mechanisms of the mother-placenta-fetus system in case of microelement imbalance in mothers in delayed growth and development of the fetus.

MATERIALS AND METHODS

The determination of trace elements - cobalt, nickel and lead (Co, Ni, Pb) in the blood serum and erythrocytes of 30 pregnant women and their 30 newborns born with CF was carried out. The comparison group consisted of 30 healthy women and their 30 healthy full-term newborns born with normal weight (HB). To group newborns by low or normal birth weight, the WHO table for assessing the physical development of a child was used, indicating the body mass index (BMI) by the ratio of weight to length (height). This table can be used for all children under 5 years old [1]. With BMI values above 12.0, it corresponds to children born with HB in relation to height at birth and their gestational age, and children with indicators below this indicator correspond to those born with CF. The gestational age of the surveyed was 38 weeks or more.

To determine the ME content in biosubstrates, the method of atomic absorption mass spectrometry (Japan) was used, which was equipped with a computer attachment for automatic calculation of the ME content.

Statistical processing of research results was carried out using the programs "Statistica" and "Excel". Methods of variation statistics were used, suitable for biomedical research [9].

Results and its discussion. When examining the ME content in the mother-placenta-fetus-newborn system, we found that the serum content of cobalt in mothers who gave birth to children in hypoxia and with CF was significantly lower than in women with physiological pregnancy. Conversely, the content of lead and nickel was 2.6 and 1.2 times higher, respectively, than in women with physiological pregnancy (Table 1).

Table 1.

The content of trace elements in the blood serum of women with the physiological course of pregnancy and women who gave birth to children with CF and their newborns

ME (µmol / l)	Serum of mothers who gave birth to children with HB	Serum from mothers who gave birth to children with CF	Blood serum of newborns with HB	Blood serum of newborns with CF
Co	**6,24 ± 0,6**	**4,71 ± 0,46 p, p1**	**5,0 ± 0,7**	**3,27 ± 0,21 p2**
Ni	**0,60 ± 0,04**	**0,73 ± 0,04 p**	**0,50 ± 0,09**	**0,81 ± 0,04 p2**
Pb	**0,08 ± 0,004**	**0,21 ± 0,02 p**	**0,10 ± 0,01**	**0,26 ± 0,02 p2**
	n=30	**n=30**	**n=30**	**n=30**

Note:p - reliability of the difference in serum parameters of mothers with physiological course of pregnancy and serum of mothers who gave birth to children with CF ($p < 0.05$); p1 - reliability of the difference in serum indices of mothers and children with PGP of the central nervous system ($p < 0.01$); p2 - the reliability of the difference in serum with HB and infants with CF ($p < 0.01$).

In newborns with HB, the serum levels of cobalt, nickel and lead were the same as in their mothers. In newborns with hypoxia and CF - cobalt in the blood serum was 1.4 times less, and nickel in 1.1 times less than in their mothers, while the average lead content slightly increased.

When comparing the content of ME in the blood serum of newborns, it was found that the concentration of cobalt in newborns with hypoxia and CF was 34.6% less, and nickel - 38.2% more, in contrast to children with HB, the lead content was 2.6 times more in contrast to children with HB (Table 1).

Thus, in the blood serum of pregnant women who gave birth to children with CF in hypoxia, cobalt deficiency was observed, and the content of lead and nickel was significantly increased. In the blood serum of newborns with CF, the content of cobalt was also significantly lower, while the content of lead and nickel was, on average, 2 times higher than in HB.

In the erythrocytes of the blood of mothers who gave birth to children with CF in hypoxia, the nickel content was 42.6%, and the lead content was 7.9% higher than in healthy women, and the saturation with cobalt was almost the same as in those who gave birth with HB. The content of ME in erythrocytes of infants with CF differed significantly from those of infants with NV. Thus, the average level of cobalt, nickel and lead was significantly higher (by 40%) than in children with HB (Table 2).

Taking into account such features, the content of ME in blood serum and erythrocytes in mothers who have given birth to children with CF and their newborns, there naturally arises a need to study the role of the placenta in ensuring the trace element balance of the mother-placenta-fetus system.

Table 2.

The content of trace elements in the erythrocytes of mothers and their newborns

ME (µmol / l)	**Serum of mothers who gave birth to children with HB**	**Serum from mothers who gave birth to children with CF**	**Blood serum of newborns with HB**	**Blood serum of newborns with CF**
Co	0,059 ± 0,005	0,062 ± 0,004 p	0,033± 0,003 p2	0,056 ± 0,005 p1
Ni	0,086 ± 0,003	0,15 ± 0,009 p	0,029 ± 0,002 p2	0,044 ± 0,004 p1
Pb	0,58 ± 0,006	0,63 ± 0,027 p	0,25 ± 0,024 p2	0,41 ± 0,040 p1
	n=30	n=30	n=30	n=30

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Note:p - reliability of the difference in erythrocyte counts of mothers with physiological pregnancy and erythrocytes of mothers who gave birth to children with CF (p <0.001); p1-reliability of the difference in erythrocyte counts in children with HB and newborns with CF (p <0.01); p2-reliability of the difference in erythrocyte indices of mothers with physiological pregnancy and their children with HB (p <0.001); p3-reliability of the difference in erythrocyte counts of mothers who gave birth to children with CF and their newborns (p <0.001).

Quantitative determination of the content of cobalt in the placenta showed that under hypoxia the concentration of this ME was almost three times less than in the case of the physiological course of the gestational process. Conversely, the concentration of nickel and lead is significantly higher (Fig. 1).

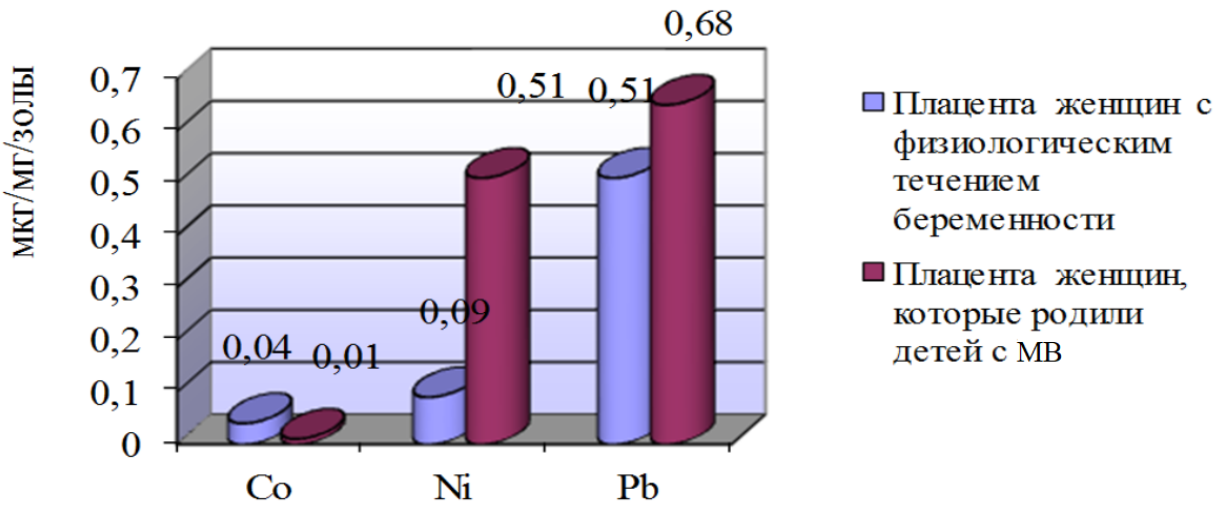

Fig. 1. The content of trace elements in the placenta of mothers (µg / mg)

According to our data, the penetration index for cobalt during hypoxia was higher than in the control group and amounted to 96.2% versus 80.1%. However, the accumulation index was 1.5 times less. These indicators indicate that in the case of a cobalt deficiency in the placenta, conditions are created for its faster penetration to the fetus, and the accumulation function is suppressed.

That is, the function of preserving ME, which are actively involved in the development of the fetus, is impaired. The penetration index for nickel was 34.9% lower than in the control group, while the accumulation index, on the contrary, was 15.3% higher (Table 3).

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Table 3.
Indicators of transplacental migration of ME

ME	Penetration index (%)		Accumulation index (%)	
	newborns with CF	newborns with HB	newborns with CF	newborns with HB
Co	96,2	80,1	79,3	121,2
Ni	54,2	83,3	325,5	275,8
Pb	145,2	125,0	246,1	204,0

The concentration of lead in the placentas of women who gave birth to children with CF tended to increase compared with the placentas of those who gave birth to newborns with HB. So, for this ME, the index of penetration through the placenta during hypoxia was higher than in the case of physiological pregnancy and amounted to 145.2% versus 125.0%, the accumulation index was also slightly higher and amounted to 246.1% versus 204%.
The data obtained indicate a violation of the protection mechanisms existing in the placenta under normal conditions of fetal development.
The ratio of the ME content plays a significant role in the exchange of trace elements and ensuring their physiological role, since it is known that there is synergy or antagonism between them in their action. Therefore, it was important to study the indicators of the ME ratio in the biological environment of women and their newborns with CF.
Analysis of the ME ratio in the blood serum of mothers who gave birth to children with CF indicates a clear imbalance in Co / Ni, Co / Pb vapors, which occurs due to cobalt deficiency and serum supersaturation with lead and nickel. The ratios of individual MEs in the biological media of women and their newborns with CF and hypoxia, as well as in the placenta, are shown in Table 4.

Table 4.
ME ratios in the mother-placenta-fetus system

ME ratios	Co/Ni	Co/Pb	Ni/Pb
Serum of mothers with physiological course of pregnancy	10,4	0,08	0,007
Serum from mothers who have given birth to children with CF	6,2	0,02	0,003
Blood serum of newborns with HB	10,0	0,05	0,05
Blood serum of newborns with CF	4,5	0,01	0,03
Placenta of women with physiological pregnancy	0,43	0,07	0,18
Placenta of women who have given birth to children with CF	0,02	0,03	0,75

Significant ME imbalance also took place in blood serum and erythrocytes of both mothers and children with CF. It manifests especially brightly in Co / Pb, Co / Ni pairs. The factor of these changes, to a certain extent, is a violation of the depot function and the transport

function of the placenta. Thus, during hypoxia in the placenta, a clear imbalance was observed in all pairs of MEs that were studied. This indicates that impaired placental function is a factor in the emergence of ME imbalance in the fetus and newborns.

Mothers who gave birth to children with CF were deficient in serum cobalt and, conversely, increased levels of lead and nickel. An increased level of lead in the blood of pregnant women is associated with a shorter gestation period, a decrease in fetal weight at birth and the occurrence of malformations in newborns. Even very low levels of lead in the blood of the fetus can lead to a significant decrease in the mental capacity of the child [12, 13].

Under the influence of this metal, women develop asthenia, hypotension, myocardial dystrophy, thrombocytopenia. In response to contact of the body with lead, angiopathies occur, although the metal content in the blood may not exceed the permissible limits [4].

Immaturity of enzymatic and excretory systems contribute to the deposition of heavy metals in the newborn's body, especially lead and nickel, and their negative impact in the neonatal and subsequent stages of development of children who were born with CF.

Thus, the ME imbalance in infants with CF is caused by impaired transport and depot function of the placenta. In the placenta of pregnant women who gave birth to children with CF, there was an imbalance in ME, largely due to cobalt deficiency. The effectiveness of the placental barrier with respect to toxic lead and nickel is low, which leads to the penetration of these metals into the fetus and enhances the negative effect of hypoxia. In turn, the damage to the membrane structures of the cell, which occurs against the background of a microelement imbalance, is accompanied by hemocoagulation disorders, a decrease in the ability of the placenta to absorb oxygen, which is one of the reasons for hypoxia and disruption of compensatory-adaptive mechanisms in the fetoplacental complex, and contributes to the occurrence of chronic intrauterine hypoxia of the fetus.

CONCLUSIONS

1. As a result of studies, a significantly low content of cobalt in blood serum and erythrocytes in newborns with CF and in the placenta of their mothers was revealed, which leads to its deficiency in their bodies. Whereas the content of lead and nickel was on average 2 times higher than in newborns with HB. The mean levels of cobalt, nickel and lead in erythrocytes of infants with CF were 40% higher than in the comparison group.
2. The revealed imbalance reduces the effectiveness of the placental barrier in relation to lead and nickel, and also leads to the accumulation of these toxic ME in the fetus.
3. The data obtained indicate a violation of the protection mechanisms existing in the placenta under normal conditions of fetal development, which leads to an intrauterine delay in weight gain and the birth of low-weight newborns.

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