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Copper Concentration in the Blood Serum of Low Birth Weight Newborns

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Until now in the information resources data on the reference values of the concentration of this essential trace element in biological fluids in low birth weight (LBW) newborns are absent. The purpose of our study was to study the copper content in serum in various categories of LBW children during the neonatal period. This prospective study included 173 newborns with LBW, including babies with intrauterine growth retardation (IUGR). The dynamic monitoring of copper concentration in the blood serum, as well as the analysis of these parameters depending on the birth weight has been performed. Quantitative determination of serum copper was carried out by the method of emission spectral analysis. When analyzing the level of copper in the blood serum on the 10th and 25th days of life, a lower content of this element was noted in extremely LBW children with (8.10±1.16 and 6.99±0.41, on the 10th and 25th days of life, respectively) and without IUGR (7.49±1.07 and 7.19±0.91, respectively). On the 25th day of life, serum copper levels were reduced in all groups of children (P<0.001). All LBW newborns and especially in children with IUGR has a deficiency of this micronutrient throughout the observation period. In newborns with ELBW or VLBW, there is a deficiency of serum copper throughout the neonatal period.

Keywords: copper, newborns, low birth weight.

The problems of nursing low birth weight (LBW) infants are becoming more urgent due to the consequences for mental and physical development in these children, their high disability, the economic costs associated with subsequent rehabilitation[1]. In utero, the fetus receives all the necessary nutrients through the placenta, that is, the placental supply of nutrients is a kind of parenteral nutrition through which the fetal organism receives food ingredients[2]. After birth, the supply of nutrients through the placenta ceases, while the high demand for nutrients persists. However, there may be difficulties in supplying low-birth babies due to their relative enzymatic suppression, multi-organ immaturity, in particular functional deficiency of the gastrointestinal tract[3].

The birth of a child is accompanied by profound metabolic changes of an adaptive nature. In this case, a special role in the adaptation of the child to extrauterine life belongs to essential microelements. They are of tremendous importance in maintaining adequate cell energy for carrying out oxidation-reduction processes, protecting cells from harmful metabolic products, participating in the synthesis of neuropeptides, biogenic amines and neurospecific proteins, so their deficiency can lead to irreparable metabolic disorders[4, 5].

A significant role in neonatal adaptation belongs to the essential microelement copper, which is part of many enzymes involved in erythropoiesis, forms elastin and myelin. As a component of cytochrome oxidase, copper stimulates phagocytosis in the mitochondrial chain, participates in the synthesis of connective tissue[6-8], protects against free radicals [9, 10]. The main places of accumulation of this microelement are the liver and brain of the fetus[4, 6, 11, 12]. In the liver, a synthesis of ceruloplasmin occurs, which carries the transport of copper to all organs and tissues[13, 14].

Cumulation of copper in the fetal tissues is carried out mainly in the second half of pregnancy[4, 5, 13]. Therefore, in children with a gestational age of 26-30 weeks and weighing less than 2,500 g, the content of copper in the blood serum is reduced in comparison with full-term newborns[15]. However, until now in the information resources data on the reference values of the concentration of this essential trace element in biological fluids in LBW newborns are absent.

The purpose of our study was to study the copper content in serum in various categories of LBW children during the neonatal period.

MATERIAL AND METHODS

Subjects

This prospective study included 173 LBW newborns with birth weight 500-2,499 grams and gestational age of 23-38 weeks, including babies with intrauterine growth retardation (IUGR). Exclusion criteria were newborns with surgical pathology and infectious diseases.

According with birth weight[16], all newborns were divided to six groups:
i) 42 extremely low birth weight (ELBW) neonates (500-999 grams) without IUGR,
ii) 17 ELBW neonates with IUGR,
iii) 30 very low birth weight newborns (VLBW) neonates (1,000-,499 grams) without IUGR,
iv) 38 VLBW neonates with IUGR,
v) 30 moderately low birth weight (MLBW) neonates (1,500-2,499 grams) without IUGR,
vi) 16 MLBW neonates with IUGR.

Main characteristics of newborns enrolled in this study are presented in Table 1.

Quantitative determination of serum copper was carried out by the method of emission spectral analysis. The state standard samples of the composition of a graphite collector of microimpurities (SSG-28) were used as standards.

Design of study

Clinical examination of patients included an objective examination, evaluation of the maturity of newborns according to gestational age and anthropometric parameters, mass dynamics, body length, head circumference, and the state of newborns and clinical syndromes during the neonatal period. Physical development was assessed by the method of Tanis R. Fenton[18].

The quantitative determination of copper in the blood serum was carried out by the method of emission spectral analysis (AU2700 Chemistry Analyzer by Beckman Coulter) on the 10th and 25th day of life of children.

Statistical analysis

All the data had a normal distribution, according to the Kolmogorov-Smirnov test results. For continuous variables, descriptive statistics are reported as the mean (M) with standard deviation (SD). Binary variables are presented as frequencies and percentages – n (%). The t-test was used to compare the means. The obtained estimations were considered statistically significant if $P<0.05$.

RESULTS

When analyzing the level of copper in the blood serum on both the 10th and 25th days of life, a lower content of this element was noted in ELBW children (Table 2).

On the 25th day of life, serum copper levels were reduced in all groups of children ($P<0.001$ for all groups, Table 2). The lowest level of this micronutrient was registered in ELBW newborns and children with ELBW and IUGR (Table 2).

All LBW newborns and especially in children with IUGR has a deficiency of this micronutrient throughout the observation period (copper reference ranges of newborns: 6–14 μmol/l)[19, 20].

DISCUSSION

The study showed that the content of serum copper in the observed low-birth-weight newborns was within the reference values. However, it should be noted its progressive decline in all groups of the examined newborns by the end of the observation period. The lowest indices of this microelement were observed in children with ELBW during the entire neonatal period. Significant differences in the content of serum copper were found depending on the weight categories. The most pronounced were the differences in the copper content between ELBW newborns and VLBW newborns with IUGR.

The results can be explained by the lack of the enzyme ceruloplasmin, which delivers copper to organs and tissues. Copper deficiency is particularly pronounced in children with IUGR, probably related to liver dysfunction, which plays a key role in the metabolism of these nutrients[21].

The data we obtained coincide with the results of the study by Sharda, Adhikari, and Ajmera (1999) who found a lower serum copper level in children with a gestational age of 26-30 weeks and weighing less than 2,500 g, compared with full-term newborns[15].

In the work of Odinayeva et al. (2002), on the contrary, it was shown that in LBW children higher levels of copper were found in comparison

Table 1. Main characteristics of studied LBW newborns

Variables	ELBW newborns without IUGR (n=42)	ELBW newborns with IUGR (n=17)	VLBW newborns without IUGR (n=30)	VLBW newborns with IUGR (n=38)	MLBW newborns without IUGR (n=30)	MLBW newborns with IUGR (n=16)
Gestational age, week	25.8±1.47	29.2±2.2	29.4±1.1	32.4±1.5	33.6±1.2	37.6±0.8
Postconceptual age, week	29.8±1.47	33.2±2.2	33.4±1.1	36.4±1.5	37.6±1.2	41.6±0.8
Apgar score	4.5±1.28	4.5±1.3	5.81±0.97	5.81±0.95	7.3±0.8	7.3±0.1
Formula feeding	42 (100)	17 (100)	15 (50.0)	23 (61.0)	15 (50.0)	9 (44.0)
Extragenital pathology	25 (59.5)	10 (58.8)	26 (86.6)	23 (60.5)	15 (50.0)	58 (50.0)
Preeclampsia & Eclampsia	32 (76.1)	11 (64.7)	18 (60)	28 (73.6)	2 (6.6)	1 (6.3)
Threatened miscarriage	38 (90.4)	10 (58.8)	26 (86.6)	22 (57.9)	5 (16.6)	1 (6.3)
Utero-placental insufficiency	40 (95.2)	42 (100)	27 (90.0)	38 (100)	17 (56.6)	15 (93.7)
Placental abruption	1 (2.3)	3 (17.6)	0	1 (2.6)	0	1 (6.3)
Smoking	5 (11.9)	2 (17.6)	11 (36.3)	9 (23.6)	1 (3.3)	5 (31.2)

Continuous variables presented as mean with standard deviation – M±SD. Binary variables presented as frequencies and percentages – n (%)

Table 2. Serum copper levels (μmol/l) in LBW newborns

Days	ELBW newborns without IUGR (n=42)	ELBW newborns with IUGR (n=17)	VLBW newborns without IUGR (n=30)	VLBW newborns with IUGR (n=38)	MLBW newborns without IUGR (n=30)	MLBW newborns with IUGR (n=16)
Cu at 10 day	7.49±1.07	8.10±1.16, P_1=0.578	8.62±0.69, P_2<0.001	8.68±0.81, P_1=0.743, P_2=0.037	9.04±0.78, P_2<0.001	8.95±0.90, P_1=0.726, P_2=0.026
Cu at 25 day	7.19±0.91	6.99±0.41, P_1=0.389	7.52±0.47, P_2=0.076	7.32±0.39, P_1=0.094, P_2=0.006	7.83±0.79, P_2=0.003	7.73±0.56, P_1=0.656, P_2<0.001

The data presented as mean with standard deviation – M±SD. Cu, copper. P_1, P-level of statistical differences (t-test) with newborns of similar weight (ELBW or VLBW or MLBW) without IUGR; P_2, P-level of statistical differences with ELBW newborns with or without IUGR.

with full-term children[22]. However, the content of copper in this study was determined in the hair of newborns, which is not a standard for determining the content of trace elements.

CONCLUSION

In the neonatal period, the content of serum copper in low birth weight infants is within the reference values. Among low-birth infants, there are significant differences in the content of serum copper. The lowest level of this microelement is observed in ELBW newborns. A decrease in the level of serum copper was observed in infants with IUGR in all weight categories.

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