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OPTIMIZATION OF MICROELEMENT BALANCE AT NEWBORNS WITH INTRAUTERINE GROWTH RETARDATION

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INTRODUCTION

Health status and quality of life of pregnant women considerably influences the course of perinatal period, especially in children with intrauterine growth retardation (IGR), the number of which in the general population of newborns has increased rapidly [1, 2]. Children with low birth weight are observed to have misbalance of microelements. Exchange of microelements in premature infants with IGR is characterized by a particular lability [3, 4]. Just intestinal way of all the elements' secretion of preterm infants gives us the reason to suggest that they have disorders in absorption of microelements in the gastrointestinal tract as well as increased excretion of microelements with urine [4].

The imbalance of microelements alongside with high level of metabolic processes and functional immaturity of organs and systems in this group of infants stipulates the actuality of searching the ways to correct the violations of the exchange of microelements in infants with IGR.

AIM OF RESEARCH

The aim of the following research is to study the effectiveness of correction of microelementosis of infants with IGR using the medicine called "Beresh Drops Plus".

MATERIALS AND METHODS

Peripheral venous blood of children with IGR taken in the morning on an empty stomach was used as the material for research. After centrifugation the content of microelements was investigated separately in serum and erythrocytes.

To determine the microelement supply of urine the collection of it was performed in a sterile bottle during urination after personal hygiene of external genitalia. To exclude the influence of daily rhythms on the excretion of microelements, the morning portion of urine that had been collected at 8-10 a.m. was investigated.

The content of microelements was defined by the method of atomic absorbed spectrophotometry on S-115M1 spectrophotometer produced by SPA "Selmi" (Ukraine) and equipped with a computer program for automatic identification of the content items in samples. The concentration of essential microelements - iron, zinc, and toxic element (lead) was also studied. The level of these microelements was controlled at the beginning and the end of treatment.

The research was carried out according to the international bioethical standards as for the parents' agreement for their child to be examined.

Analysis of the obtained results was performed by means of the program called "Statistics 6.0". Methods of varied statistics suitable for medical biological research [5] were used. An average (M) and arithmetic average error (m) were defined. Reliable index of R was estimated by means of Student criterion (t).

RESULTS AND DISCUSSION

We examined 100 children with intrauterine growth retardation, who underwent the course of treatment at the department of pathology of newborns and premature infants of Sumy Regional Children's Hospital. The children were divided into 2 groups: basic group numbered 70 newborns with IGR who were administered the "Beresh Drops Plus" medicine and routine treatment due to the protocol. Another group numbered 30 newborns with IGR that were breastfed only and received drug therapy due to the traditional schemes. Criteria of IGR of newborns were morphofunctional immaturity and gestational age gap of 2 weeks or so; moreover, the weight and growth parameters were below the 10th pertsintyle in comparison with the stage of pregnancy [2].

The newborns were divided in two groups before the course of treatment. Anthropometric indices of physical development of infants with IGR are introduced in Table 1.

Table 1

Anthropometric indices of physical development of infants with IGR

Index	Newborns with intrauterine growth retardation	
	Main group (n=70)	Comparison group (n=30)
Gestational age, weeks	38,6 ± 0,46	38,7 ± 0,43
Body weight, g	2438,5 ± 54,15***	2742 ± 37,44
Body length, cm	48,2 ± 0,34	48,6 ± 0,53
Head circumference, cm	32,55 ± 0,27*	33,6 ± 0,37
Chest circumference, cm	31,7 ± 0,39	32,6 ± 0,51

Note: p is credibility of indexes difference concerning the comparison group:
* - p<0,05, ** - p<0,01, *** - p<0,001

Clinical evaluation of the health of babies covered the assessment of neonatal adaptation, anthropometric parameters at birth, incidence analysis, and laboratory testing data.

Indices of morphofunctional immaturity (in descending order) appeared to be of the greatest diagnostic value: reduced suckling reflex, susceptibility to hypothermia, thinness and shortness of hair on the head, soft ear cartilages, and presence of light hair. Long and expressed transient conditions (primary pathological loss of body weight, disorders of thermoregulation) occurred in 51.4% (36) of infants of basic group, thus indicating the lack of adaptation at birth.

Almost all the children showed the signs of perinatal hypoxic violation of central nervous system of various severities. Among the syndromes of nervous system disturbances syndrome of excitation predominated. In 13 (18.6%) children of the basic group and 2 (6.7%) newborns of the compared group the syndrome of vegetovisceral disorders was identified in the early neonatal period that showed the disorders of microcirculation, thermoregulation and motility of the gastrointestinal tract.

Therefore, pathologic course of the perinatal period is a sign of metabolic disturbances and, particularly, ME that are considered to be predominative in the creation of adaptaional syndrome that requires correction.

According to the scheme developed and implemented, correction of microelementhosis was held individually. We selected aqueous solution (for oral use) of "Beresh Drops Plus" as it was a soluble concentrate which contained the optimum ratio of 14 vital trace elements including zinc and iron that were associated with organic substances (glycine, amber, ascorbic, tartaric and other acids).Organic substances possess antioxidant properties and improve the absorption of elements increasing their bioavailability. "Beresh Drops Plus" was prescribed in the rate of 1 drop per kg of the patient's body weight per day. The daily dose was divided into 2 intakes. The course of treatment lasted for three weeks (until discharge from the hospital). During the next anthropometric survey we got the data that showed a positive dynamics of anthropometric parameters (Table 2).

Table 2

Dynamics of anthropometric data during the period of observation of the compared groups (M ± m)

Index	Newborns with intrauterine growth retardation	
	Main group (n=70)	Comparison group (n=30)
Body weight, g	591,8 ± 59,4	528,7 ± 31,5
Body length, cm	3,0 ± 0,27	2,9 ± 0,49
Head circumference, cm	2,2 ± 0,74	2,1 ± 0,86
Chest circumference, cm	2,5 ± 0,46	2,3 ± 0,62

It should be noted that introduction of "Beresh Drops Plus" into the course of rehabilitation therapy for infants with IGR contributed to the positive dynamics of weight increase during the first months of life. The results of questioning of mothers showed that due to the use of the drug positive changes in behavioral reactions and more rapid restoration of sucking reflex appeared. The majority of

children were observed to have improved the general state; they demonstrated reduced syndrome of nervous and reflexive excitability, and sleep resetting. None of the complications and side effects was observed during the course of using “Beresh Drops Plus”.

Exchange of microelements in infants is rather intense, as it is evidenced by the high percentage of their retention in the body, and the prevalence of renal output over intestinal one. The content of iron and zinc in biological matrix of infants with IGR is low (Table 3, 4), as the release of these microelements from the depo is more intensive than the receipt with breast milk [3, 4]. In our opinion, misbalance of most microelements in newborns is stipulated by perinatal pathology, misbalanced artificial feeding and IGR as well.

We defined previously that the development of IGR was accompanied by serum iron deficiency. In all the groups of newborns its level was below 14 mmol/l- a critical level, which indicated deficiency of iron [6]. Erythrocyte pool of iron is more stable, to compare with serum one. It illustrates the level of microelements in the baby’s organism during the last weeks of pregnancy. Infants with IGR used to show deficient supply of red blood cells with iron as a result of insufficient revenues of the microelement from mother to child followed by the development of IGR. A three-week course of individual rate correction resulted in positive dynamics of serum and erythrocyte iron content ($p<0,001$) in infants with IGR (Table 3). It is known that one of the characteristic features of mineral metabolism of infants is iron deficiency and predeficiency, especially in premature, when the steady tolerance to therapy held by iron-containing medication [4] is observed. Results of evaluation of iron content in the clinical research allow us to conclude that "Beresh Drops Plus” is rather effective in stabilizing the level of microelements.

Thus, all the newborns with IGR were observed with the restoration of serum iron concentration and considerable increase of microelements in erythrocytes during the period of correction.

Table 3

Dynamics of iron content in infants with IGR by means of "Beresh Drops Plus" during the course of correction

IU content in the environment of newborns with intrauterine growth retardation		Groups of newborns with intrauterine growth retardation	
		Children who underwent treatment (n = 30)	Children who were breast fed (n = 30)
Serum, umol/l	At the beginning	11,6 ± 0,73	10,85 ± 0,686
	At the end	17,2 ± 0,45 p*** p_1**	14,43 ± 0,753 p***
Erythrocyte, mcg/mg of ashes	At the beginning	6,78 ± 0,56	6,72 ± 0,393
	At the end	11,65 ± 0,54 p*** p_1*	9,74 ± 0,717 p***
Urine, umol/l	At the beginning	2,72 ± 0,38	2,72 ± 0,225
	At the end	2,16 ± 0,44	2,83 ± 0,219

Note: p is credibility of indexes difference before and after treatment, p_1 – credibility of indexes difference concerning the comparison group: * - p<0,05, ** - p<0,01, *** - p<0,001

Iron excretion with urine was not affected by the method of correction. During the period of observation it only tended to decrease.

Each child's pathology has got its own portrait of microelements that reflects the individual components involved in the pathogenesis [3]. Our previous studies identified that zinc deficiency appeared to be one of the leading factors in the pathogenesis of IGR. It is considered that if concentration of zinc in serum is less than 8 mmol / l, it seems to become an unfavorable prognostic sign [7]. Since zinc is thought to be an important growth factor [7, 8], clinical signs of antenatal zinc deficiency result from morphological immaturity and prematurity, particularly in combination with IGR syndrome, and the evidence of IGR syndrome at full term pregnancy.

The deficiency of zinc was noted during the individual analysis of zinc content in blood serum and erythrocytes of infants with IGR (Table 4). It increased with the degree of prematurity, as the accumulation of microelements took place in the last 12 weeks of fetal growth.

Table 4

Dynamics of zinc content in infants with IGR by means of "Beresh Drops Plus" during the course of correction

IU content in the environment of newborns with intrauterine growth retardation		Groups of newborns with intrauterine growth retardation	
		Children who underwent treatment (n = 30)	Children who were breast fed (n = 30)
Serum, umol/l	At the beginning	6,5 ± 0,53	7,24 ± 0,554
	At the end	14,09 ± 0,94 p*** p_1***	9,57 ± 0,786 p*
Erythrocyte, mcg/mg of ashes	At the beginning	0,26 ± 0,018	0,26 ± 0,019
	At the end	0,6 ± 0,041 p*** p_1***	0,29 ± 0,023
Urine, umol/l	At the beginning	1,92 ± 0,19	1,58 ± 0,118
	At the end	1,1 ± 0,073 p** p_1***	1,67 ± 0,12

Note: p is credibility of indexes difference before and after treatment,
p_1 – credibility of indexes concerning the comparison group:
* - p<0,05, ** - p<0,01, *** - p<0,001

It is known that excretion of zinc with urine provides the correction of consumption of this element. Approximately 10% of zinc is removed from the body through the kidneys [7]; so, the investigation of its content in urine is important for the control of possible pathological loss. We identified that loss of zinc in the urine depended on gestational age and maturity of the newborn - the lower the indices were, the higher was the level of zinc in the urine which was likely to be related with functional immaturity of the urinary system. The proposed method of correction positively influenced the excretion of zinc – its (p<0,01)

decrease in particular (Table 4). The defined features seem to be a manifestation of zinc saving effect under the influence of the medication mentioned above.

So, usage of "Beresh Drops Plus" contributed to the increase of zinc level in serum and erythrocytes ($p<0,001$), and its decrease in urine on the contrary ($p<0,001$). Therefore, we consider this method of correction to be of great importance as it provides an optimal absorption of zinc by newborns with IGR.

Under the conditions of anthropogenic environmental pollution newborns are observed to obtain and accumulate toxic elements in the organism, including biochemical antagonist of zinc - lead that can compete with zinc and inhibit its assimilation. In newborns with IGR, especially premature, due to immaturity of their functional systems the phenomenon of using sibling elements in metabolic process with similar molecular weight but unable to fulfill physiological roles [3] is observed. Our research (Table5) confirmed this hypothesis.

Taking into account the ability of lead to penetrate through the placenta and cause the fetal growth retardation [9], high concentration of this element in blood serum of children with IGR seems to be quite natural. At the same time exceeding of the toxic level (0.48 mmol / L) was not observed in any case.

Table 5

Dynamics of lead content in infants with IGR by means of "Beresh Drops Plus" during the course of correction

IU content in the environment of newborns with intrauterine growth retardation		Groups of newborns with intrauterine growth retardation	
		Children who underwent treatment (n = 30)	Children who were breast fed (n = 30)
Serum, umol/l	At the beginning	0,44 ± 0,074 p_1***	0,28 ± 0,022
	At the end	0,25 ± 0,069	0,34 ± 0,023
Erythrocyte, mcg/mg of ashes	At the beginning	0,39 ± 0,049	0,45 ± 0,035
	At the end	0,111 ± 0,016 p*** p_1***	0,51 ± 0,04

Urine, umol/l	At the beginning	0,084 ± 0,0093	0,09 ± 0,0067
	At the end	0,21 ± 0,045 p* p_1***	0,097 ± 0,0075

Note: p is credibility of indexes difference before and after treatment, p_1 – credibility of indexes concerning the comparison group:

* - p<0,05, ** - p<0,01, *** - p<0,001

Biomarker of lead overbalance is considered to be its content in red blood cells which increases in proportion to the accumulation of heavy metals in soft tissues, and which reflects a prolonged contact with this microelement [4, 10].

Excretion of toxic elements in urine reflects the possibility of accumulation of heavy metal. Elimination of lead through the kidneys is the main way of its output, the part of which is about 75% [10].

Thus, low level of lead excretion is the common feature of lead content in the urine of newborns with IGR. Mild elimination of lead through the kidneys adds to its accumulation in the body that can unfavorably affect the organism of a newborn.

The results of the research showed that the correction of lead misbalances by usage of “Beresh Drops Plus” contributed to the optimal reduction of lead in blood serum and erythrocytes (p<0,001), and significantly increased elimination (p<0,05) of toxic metal with urine.

Therefore, the analysis of microelement supply in infants with IGR showed a pronounced imbalance of metabolism and essential microelements - iron and zinc, and accumulation of toxic lead that required definite correction.

Thus, on the basis of obtained results of our clinical data analysis, we can conclude that intake of "Beresh Drops Plus” has undoubtedly proved its effectiveness toward normalization of the content of vital elements in biological matrix of infants with IGR, and influenced positively the dynamics of basic anthropometric characteristics and clinical syndromes of this pathological case. “Beresh Drops Plus” is a new step in the complex of prevention, treatment and rehabilitation, which stimulates resistance and adaptive capacities of infants with IGR at prenosological stage.

CONCLUSIONS

1. Use of “Beresh Drops Plus” contributed greatly to the positive dynamics of the growth rate of body weight in infants with IGR during the course of rehabilitation therapy. The majority of children were observed with the improvement of their general state, decreased syndrome of nervous and reflexive excitability, and normalization of sleep.
2. Use of “Beresh Drops Plus” maintained renewal of serum concentrations of iron and zinc and a significant increase of their content in erythrocytes. Application of this medicine added to the reduction of toxic lead content in blood serum and red blood cells by its rapid elimination through urine.

The obtained results indicate the possibility of correction of microelements in newborns with IGR.

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