

## THE SMALL – FOR – DATE NEWBORNS' ENERGY METABOLISM ENZYMES ACTIVITY

Nasirova U.F.

*The Tashkent pediatric medical institute, Tashkent, e-mail: Asichev@nsi.ru*

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The cellular energy exchange research results at the newborns with SFDN have been presented. A total of 158 infants, of whom in 83% (e.g. 131) of the cases, having diagnosed, as the asymmetric one, and in 17,0% (e.g. 27) of the cases of the SFDN symmetric form have been examined. It was revealed, that the newborns had had the quite varying degree of the hypoxic – ischemic lesions of the central nervous system (CNS), having manifested by the following syndromes: the neuro – reflex hyper-excitability, the depression, the vegetative – visceral disorders, and the muscular dystonia. So, the cellular energy exchange parameters study has been shown their activity decrease, in comparison with the control group. The enzymes activity reduction at the infants with the symmetric SFDN form has considerably been higher, than those ones with the asymmetric form. The perinatal hypoxemia has been influenced in the way of the energy exchange.

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The intrauterine growth retardation (IUGR) is considered one of the most common causes of the newborns' high sickness rate and the babies' high incidence in the neonatal period, the nervous and the mental disorders of the children's development. In the later life's years, the abnormalities' high percentage, as physical, well as the psychomotor development has been revealed at this patients' group. [1, 2].

At present, the intrauterine growth retardation (IUGR) is considered by the experts and the specialists, as the disease, having accompanied by the rather serious and the severe metabolic ones, including the dis-energy violations [3, 4, 5, 6, 7, 8].

One of the most significant mechanisms, having led to the different and the various metabolic shifts at the intrauterine growth retardation (IUGR), is the hypoxic – ischemic lesions of the central nervous system (CNS). In the basis of the further formation, which are laid the cerebro-vascular disorders and the brain blood circulation strokes. [1, 2, 3].

So, the latent energy deficit presence has the negative impact upon the post – adaptation period course at the newborns with SFDN.

That is why, the cellular metabolism enzymes identification in the human blood is the major one in the energy deficient state diagnostics.

In connection with the above – stated material, the main purpose of the study has been – the cellular energy change enzymes' activity study at the newborns with the SFDN, on the basis of the comparative analysis with the healthy children.

### Materials and methods of research

Thus, a total of the 316 infants and the newborns have been examined, on the basis of the 1-st Municipal Perinatal Center of the Tashkent city and the Republic Specialized Scientific and the Practical Medical Center of the Obstetrics and Gynecology.

So, the children's state and their condition at the birth have been determined by the «Apgar» scale on the

1-st and the 5-th minutes of the infants' life. Then, the born infant's status has been assessed, on the basis of these general clinical and the neurological examinations. After that, the biological maturity has been assessed by the «Ballard» scale. The newborns' physical development evaluation and the intrauterine growth retardation (IUGR) classification have been carried out, in accordance with the WHO recommendations. The nervous system pathology assessment has been carried out, according to the nervous system perinatal lesions classification at the small infants and the young children, having suggested by the Russian Association of Perinatal Medicine Specialists and Experts (e.g. 2000).

The main study group has been made up 158 newborns with the intrauterine growth retardation (IUGR) and the control group – 158 born infants and the babies, who had no any clinical manifestations of the SFDN ones. In the main study group, having consisted in 158 small children has been diagnosed with the asymmetric one – in 83,0%, and in 17,0% cases, the symmetric form of the intrauterine growth retardation (IUGR).

So, the examined infants and the newborns have been matched by the gestational age. Thus, the infants and the newborns with the symmetric form have been consistent with the gestational age period 35–36 weeks (e.g. 245–252 days), the ones with the asymmetric form have been consistent with the gestational age period 36–37 weeks (e.g. 252–259 days), the control group small children have been corresponded to the gestational age period 38–40 weeks (e.g. 266–280 days).

So, the infants' and the newborns' average body weight (BW) with the intrauterine growth retardation (IUGR) has been made up 2,417 g, the average body length – 46,05 cm, the head circumference – 32,4 cm, the chest circumference – 30,9 cm.

So, the infants' and the newborns' average body weight (BW) from the control group has been made up 3,912,0 g, the average body length – 53,2 cm, the head circumference – 33,9 cm, the chest circumference – 32,7 cm, the small children's morphological and the functional maturity has been consistent with their gestational age.

At the children with the asymmetric form of the intrauterine growth retardation (IUGR), the average body weight (BW) has been made up 2,390,6 g, the average length – 47,2 cm, the head circumference – 32,4 cm, the chest circumference – 30,8 cm. The newborns' and infants' anthropometric indicators with the symmetric form of the development delay have been made up, respective-

ly, 2,445,7 g, 44,9 cm, 32,4 cm, and 31,0 cm. The significantly lower rates of the body's weight and length have been revealed at these small children, in comparable with the newborns and the infants with the asymmetric form of the intrauterine growth retardation (IUGR).

The cytochemical analysis of the mitochondrial enzymes activity has been carried out by the reagents sets of the «Himtechmash» MRPC LLC company, the «IREA» State Research Institute: the succinate dehydrogenase – CDG, the alpha-glycerophosphate dehydrogenase – GPHDG, the glutamate dehydrogenase – GDG, the lactate dehydrogenase – LDG of the peripheral blood leukocytes (e.g. the method of Pierce (1957) in the Nartsisov R.P. modification (1986)) with the subsequent visual morphometry (e.g. the «VIDEOTEST» programs package, the Sukhorukov V.S., Tozliyan E.V. technique).

The enzymatic activity at the visual morphometry is expressed in the standard units, corresponding to the average number of the formazane granules, having had the cytochemical reaction product. So, the basic information on the enzymes activity in the peripheral blood lymphocytes are obtained at the mean value, which is equal to the granules number ratio in each cell to the cells number.

In addition to the mean value determination of the enzymes activity (e.g. in the standard units), the specific factors K1 (e.g. GPHDG/CDG), K2 (e.g. GDG/CDG), K3 (e.g. GPHDG/GDG) have been determined. So, these factors identification is allowed to be determined the relationship between the mitochondrial enzymes, which is increased the method sensitivity. The enzymes are reflected the activity of the different pathways of the cellular energy transfer that is why, their relationship definition is improved the cytochemical method diagnostic value [3].

The cytochemical reaction statement has been performed in the genetic laboratory of the «Mother and Child Screening» National Center.

The results statistical processing and the analysis is included the reliability assessment of the different mean values measurements by the Student's test with the given level of the reliability (e.g.  $p < 0,05$ ).

### Results of research and their discussion

In retrospect, it has been revealed during the examination, that the average gestational period at the delivery in the newborns and the infants with the symmetric form has been made up 36,1 weeks (e.g. 252,1 days), and with the asymmetric form, respectively, 37,3 weeks (e.g. 259,3 days). The Cesarean section operation has been performed at 58 she-patients. So, the newborns and the infants with the asymmetric intrauterine growth retardation (IUGR) form have been born with the estimate by the «Apgar» scale less 6,9 points, the newborns and the infants with the symmetric form, respectively, – 6,7 points, 53 she-patients (33,5%) have been needed in the intensive care unit transfer, 66,5% (e.g. 105 ones) have been transferred at the second phase of the patients' management with due respect to both medical treatment and the general care. The degree of the perinatal CNS lesions in the 22,2% cases has been regarded, as the mild one, in 53,2% – as the medium – heavy one, and at 24,6 – as the severe one, respectively.

So, the studies have been shown, that the newborns and the infants with the SFDN have often been born in the asphyxia of the varying extent, than in the control group, though in the main group in 2 times more often it has been observed in the children born asphyxiated in the moderate and the severe degrees. In the control group, mainly, the children have been born with the estimate by the «Apgar» scale 8–10 points.

Every 3-rd infant with the intrauterine growth retardation (IUGR) at their birth the resuscitation measures have been carried out, in the form of the mucus suction from the upper respiratory tract, the humidified oxygen supply, and the artificial pulmonary ventilation. Then, the both newborns have been needed in the closed chest cardiac massage, the epinephrine administration, and also the circulating blood volume substitutes.

The indicators have been improved on the 5-th minute of all the examined infants' life with the SFDN, however the resuscitation measures have been continued to be done for the newborns and the infants from the main group, in the form of the artificial pulmonary ventilation and the humidified oxygen supply. It should be noted, that to the 5-th minute of their life in half of the newborns and the infants the asphyxia state of the moderate severity had been maintained, whereas such newborns and the infants were not at all in the control group.

The dysembryogenesis stigmata have been detected at the newborns children and the infants with the intrauterine growth retardation (IUGR). The range from 3 to 5 stigmata has been observed at the newborns and the infants with the asymmetric form, and at the children with the symmetric form – the range from 4 to 7 ones. The low – lying, and the different – sized, the deformed floors of the auricles, the short hair stature on the head, the turned – up nose, the «Gothic» palate, the overhanging occipital bone, the eyes and the nipples hypertelorism, the progenia (or the prognathism), the narrow palpebral fissures, the sandal – formed fissure have been the most frequently met.

The trophic disasters of the skin have been found at 34 from 158 newborn children and the infants with the developmental delay of 27 infants with no signs of the SFDN, with no any significant differences in the groups have not been found.

So, it has been revealed, in analyzing the body weight (e.g. BW) dynamics at the examined newborns and the infants that the indicator, such as the maximum body mass decrease in 8% cases has been made up 5–8%, and it has been the same in all the examined groups. The maximum loss indicator of the body weight (e.g. BW) (e.g. in 24 hours) has

been higher at the newborns and the infants of the main group, than in the control one. So, it should be noted, that the recovery period duration of the initial body weight (e.g. BW) has been significantly greater, than at the newborns and the infants with the intrauterine growth retardation (IUGR) up to 5 days (e.g. 120 hours), which is significantly greater, than in the control group. The body weight (BW) dynamics at the newborns and the infants with the quite different clinical forms of the intrauterine growth retardation (IUGR) has not been significantly different.

So, almost all the newborns and the infants with SFDN after their birth, have been placed into the couveuses or the infant incubators.

The appearance days of the suckling reflex at the newborns and the infants have been quite different. In the main group, due to the severity condition, no one infant has been attached to the chest. All the children with the intrauterine growth retardation (IUGR) have been on the tube feeding, and there had not such small children among the newborns and the infants of the control group. Moreover, the sucking reflex recovery has been dependent upon the SFDN form. Additionally, it was revealed, that the sucking reflex recovery had been faster at the newborns and the infants with the asymmetric form of the intrauterine growth retardation (IUGR) (e.g.  $19 \pm 1,3$  days and nights or  $456 \pm 24,3$  hours), than at the newborns and the infants with the symmetric form (e.g.  $28 \pm 2,6$  days and nights or  $672 \pm 48,6$  hours;  $p < 0,001$ ).

So, the hepatitis has had the conjugation character at all the newborn children and the infants. The newborn babies and the infants with the intrauterine growth retardation (IUGR) have had a longer period of jaundice, than the newborn children and the infants without any developmental delays. Besides, the general and the indirect bilirubin levels have been significantly higher at the newborns and the infants from the main group. So, no the significant differences in the hepatitis syndrome characteristics at the newborns and the infants with the various forms of the intrauterine growth retardation (IUGR) have been received.

Practically, all the examined small children have had the hypoxic – ischemic CNS lesions signs with the severity different degrees. So, the CNS mid degree of the lesion has been observed in two times more often at the newborns and the infants with the SFDN, in comparison with the control group. The CNS lesion average degree involvement has been more common at the newborns and the infants from the main group. So, it should be noted, that the hypoxic – ischemic CNS damage of the se-

vere degree has been showed at 8 newborns and the infants of the main group, whereas such lesions have not been observed at all in the control group. Besides, 6 newborns and the infants with the symmetric form of the intrauterine growth retardation (IUGR) have had the hypoxic – hemorrhagic CNS lesions involvement with the intracranial hemorrhage signs. The depression syndrome, having associated with the hypoxic factors exposure, has mainly been dominated among the CNS lesions involvement syndromes at the newborns and the infants.

The motor activity has been reduced at 42,4% (e.g. 67) newborn children and the infants with the intrauterine growth retardation (IUGR). The muscular tension has been changed for all the small children of the main group, and the muscular hypotonia has been occurred at 67% (e.g. 106) small children, and the muscular hypertension – only at 32,9% (e.g. 52). So, it should to be emphasized, that the muscular hypotension, as the result of more severe CNS lesions, has been observed at all the newborns and the infants with the symmetric form of the intrauterine growth retardation (IUGR). And the hyporeflexia and the rapid exhaustion of the unconditioned reflexes have been observed at all the newborns and the infants, as the main group, well as the comparison group.

So, the CNS depression syndrome at the newborns and the infants in the control group has been met almost in 4 times less, likely, than at the newborns and the infants of the main group. The motor activity has been defined also in 2 times less. The unconditioned reflexes have significantly more caused at the newborns and the infants of the control group, than at the newborns and the infants of the main group. (see the Table 1).

As it can be seen from the presented data, the vegetative – visceral disorders syndrome has been diagnosed at the 39,8% (e.g. 63) newborns and the infants with the intrauterine growth retardation (IUGR). It has been manifested by the microcirculation, the thermoregulation, and the gastrointestinal tract motor activity disorders. The microcirculatory disorders (e.g. the «mottled» skins, the pallor, the acrocyanosis) and the thermoregulation disturbances equally likely have often been distributed, which required the need for their presence in the couveuses or in the infant incubators. The gastrointestinal tract dysmotility, in the form of the regurgitations and the constipations in 2 times more likely have been registered at the newborns and the infants of the main group, than at the small children from the control group.

**Table 1**

The CNS Post – Hypoxic Lesion Syndromes at the Newborns with SFDN

Syndromes	The Main group, (n = 158)		The Control group, (n = 158)		P
	Abs.	%	Abs.	%	
Increased neuro – reflex excitability	40	25,3 ± 3,5	19	12,0 ± 2,6	< 0,01
Depressions	88	55,7 ± 3,9	22	13,9 ± 2,7	< 0,01
Vegetative – visceral disorders	63	39,9 ± 3,8	28	17,7 ± 3,0	< 0,01
The muscular dystonia:					
– hypotonia	106	67,1 ± 3,7	38	24,1 ± 3,4	< 0,01
– hypertonia	52	32,9 ± 3,7	24	15,2 ± 2,8	< 0,01

More common mild degree has significantly been met at the small children with the asymmetric form of the intrauterine growth retardation (IUGR), and fairly rare – the moderate and the severe CNS lesions involvement, in comparison with newborns and the infants, having had the symmetric form. The depression syndrome with more severe developmental delay has been met at the newborns and the infants almost in 2 times more likely, than the increased neuron – reflex excitability. The mo-

tor activity violation has been observed almost at all the small newborns and the infants. (see, the Table 2).

The indicators study of the cellular energy has been revealed the enzymes activity reduction at the 80 newborns and the infants, in comparison with the control group. So, the enzymes activity at the newborns and the infants with the symmetric form of the SFDN has been lower, in comparison to those with the asymmetric form. (see, the Table 2).

**Table 2**

The Energy Exchange Enzymes Activity Indicators at the Newborns with SFDN

The Enzymes Activity	The SFDN Forms		The Control group, (n = 23)
	Asymmetric (n = 67)	Symmetric (n = 13)	
CDG	18,67 ± 0,46*	18,26 ± 0,54**	22,29 ± 0,14
GDG	14,2 ± 0,47*	13,7 ± 0,8**	14,9 ± 0,27
GDPHG	13,1 ± 0,93**	14,1 ± 0,36*	15,1 ± 0,25
LDG	18,9 ± 0,44*	17,59 ± 0,91**	21,27 ± 0,64
GPHDG/CDG (K1)	0,77 ± 0,03*	0,78 ± 0,02**	0,68 ± 0,01
GDG/CDG (K2)	0,79 ± 0,03*	0,70 ± 0,03**	0,67 ± 0,01
GPHDG/GDG (K3)	1,0 ± 0,04	0,98 ± 0,07	1,0 ± 0,02

Note. \* – the data accuracy, compared to the control (\* – P < 0,05; \*\* – P < 0,01).

It should to be noted, that the GPHDG content at the small children with the symmetric form has been higher, in comparison with the asymmetric form of the SFDN, which is consistent with the researches' several data [5].

Thus, the obtained results showed that the more significant cellular metabolism disturbances had been detected at the newborns and the infants with the SFDN. It was also revealed, that the enzymes activity indicators with the symmetric form had significantly been lower, in comparison with the small children, having had the asymmetric form of the SFDN.

The activity changes of the succinate dehydrogenase – CDG at the symmetric form is characterized by the progressive depression of

the aerobic metabolic pathway. In parallel, the lactate dehydrogenase – LDG level is also reduced. As a whole, this is reflected the inhibition, as the aerobic, well as the anaerobic cellular energy change of the pathway, that is the energy «catastrophe» for the cell [5].

Thus, the identified changes of the bioenergetic exchange rates are shown on the cytochemical activity indicators decrease of the lymphocytes mitochondria of the newborns and the infants with the SFDN. So, the most significant changes have been detected at the newborns and the infants with the symmetric form. Then, the perinatal hypoxemia is usually exacerbated by the metabolic disorders, which are accompanied by the changes in the energy and the electrolyte balance of the cells.

### References

1. Barashnev Yu.E., The Nervous System Lesions at Asphyxia // *The Perinatal Neurology*. M.: Triadah, 2001. – P. 249–289.
2. Dementjeva G.M. The Low Body Weight at Birth. The Fetus' and Newborn' Hypoxemia // *The Russian Journal of Perinatology and Pediatrics*. – 2003. – №2. – P. 89–98.
3. Sukhorukov V.S. The Challenges of Cellular Energy Disorders in the Modern Medicine. In the book: *The Violation of Cellular Energy Exchange at the Children* / Edited V.S. Sukhorukov, E.A. Nikolaeva. – M.: Atec Medica Soft, 2004. – P. 3–17.
4. Nikolaeva E.A. The Pathogenetic Therapy Effectiveness of the Mitochondrial Diseases, Caused by Defects in Respiratory Chain and Oxidative Phosphorylation at Children. – M.: Atec Medica Soft, 2004. – P. 18–27.
5. Chugunova O.L., Sukhorukov V.S., Kazantzeva E.A., Simonova L.V., Bokeriya E.L., Kleimenova N.V. The Metabolic Correction of Cellular Energy Exchange Violation at Children with the Intrauterine Growth Retardation in the Neonatal Period // *The Russian Journal of Perinatology and Pediatrics*. – 2008. – №2: 53. – P. 13–15.
6. Helton E., Darragh R., Francis P. Metabolic Aspects of Myocardial Disease and a Role for L-carnitine in the Treatment of Childhood Cardiomyopathy // *Pediatrics*. – 2000. – 105: 6. – P. 1260–1270.
7. Roe C.R., Coates P.M. Mitochondrial Fatty acid Oxidation Disorders / C.R. Scriver, A.L. Beaudet, W.S. Sly, D. Valle eds. // *The Metabolic and Molecular Bases of Inherited Disease*. – New York: McGraw Hill 1995. – P. 1501–1533.
8. Campos Y., Huertas R., Lorenzo G. Plasma Carnitine Insufficiency and Effectiveness of L – Carnitine Therapy in Patients with Mitochondrial Myopathy // *Muscle Nerve*. – 1993. – 16. – P. 150–153.