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State of protein peroxidation in newborns with intrauterine growth restriction

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ABSTRACT
The main study group involved 56 newborns with intrauterine growth restriction (IUGR) The comparison group included 52 healthy newborns. It has been proved that in newborns with IUGR the levels of neutral-type aldehyde- and ketone derivatives with peak absorption at wavelengths of 356 and 370 nm were higher, as compared to healthy newborns ($p<0.05$), namely 1.74±0.08 and 1.58±0.13. The basic-type aldehyde-and ketone derivatives had a tendency to increase in healthy newborns as compared with IUGR newborns. The determination of protein oxidative modifications of basic and neutral-type aldehyde- and ketone derivatives in combination with clinical findings are recommended for establishing the prognosis of the severity of hypoxic CNS damage in newborns with IUGR.

Keywords: protein oxidative modifications, newborns with intrauterine growth restriction, healthy newborns.

1. Introduction

Experimental and clinical studies have established that pathological conditions in the human body in many cases are accompanied by activation of free radical processes in the patients' tissues and organs [1]. Free radicals (FR) include compounds which contain unpaired electrons and have greater reactivity as for their non-radical analogues. All functionally important free radicals which are formed in the human body contain oxygen. In modern scientific literature these compounds are defined as "reactive oxygen species" (ROS) [2]. Under the pathologic conditions the ROS synthesis is uncontrollable leading to the formation of oxidative stress [3], as a result causing damage to all biological structures. Antioxidant system provides maintenance of homeostasis and decreases the consequences of peroxidation syndrome. Until recently, while studying the modifying action of ROS the focus was given to lipids. Nowadays the researchers' interest upon the study of mechanisms of ROS interaction with proteins has greatly increased [4]. The significance of these studies is predetermined by the extreme importance of proteins as structural components of membranes, and also they play an important role in the regulation of processes, and ensuring the homeostasis of the human body.

Oxygen-dependent protein peroxidation is considered to be the early indicator of organ and tissue damage, and the processes of oxidative modification of proteins under all pathological conditions must be kept under continuous laboratory control [3].

It is known that the adverse factors of pregnancy (anemia, toxemia, fetoplacental insufficiency, threatened miscarriage, fetal intrauterine growth restriction (IUGR), mother's acute and chronic illnesses), newborn's congenital pneumonia leads to the damage of cell membranes, inactivation and transformation of enzyme systems, accumulation of inert products of polymerization, deranged biosynthesis of nucleic acids, reinforce the processes of lipid peroxidation in the organisms of both the pregnant and the newborn [5]. One of the components of pathogenesis of IUGR syndrome development and nosologic forms of diseases in newborns in early neonatal period is the activation of lipid and protein peroxidation systems with the damage to cell membranes and disfunctionality of different systems and organs [6].

Since the question concerning the damage of ROS of proteins or lipids is still under discussion [7], the study of protein oxidative modifications in newborns with IUGR is considered to be the topical issue.

Aim of the research work is to study the indices of protein oxidative modifications in blood plasma of newborns with intrauterine growth restriction and healthy newborns.

2. Material and Methods The main study group involved 56 newborns with IUGR. The comparison group included 52 healthy newborns. All newborns and their mothers were residents of Ivano-Frankivsk region. Products of oxidative modifications of proteins in blood serum were investigated by means of Dubinina O.Yu. method [7], which is based on the interaction of oxidated amino-acid residues of proteins with 2,4- dinitrophenylhydrazine. The approach of the method is based on the fact that the process of protein peroxidation leads to the formation of aldehyde and ketone groups in radicals of aliphatic amino acid residues. The latter interact with 2,4-dinitrophenylhydrazine resulting in the formation of 2,4-dinitrophenylhydrazones that have characteristic absorbtion spectrum. The samples were spectrophotometric at wavelengths equal to 356, 370, 430 and 530 nm. Neutral aldehyde- and ketone derivatives were registered at wavelengths of 356 and 370 nm, and those of basic type were recorded at wavelengths of 430 and 530 nm. Protein peroxidation level was evaluated taking into account the content of aldehyde- and ketone derivatives of both neutral and basic types. Statistical analysis of the research findings was conducted at personal computer using Student t-test. Mean-value distinction at $P<0.05$ was considered to be statistically valid. *Microsoft Excel* software was used for the statistical analysis of research findings.

3. Results of the investigation and their discussion.

Protein oxidative modification, which is observed in organs and tissues of the human body under normal conditions, rises sharply under the influence of oxidative stress. First of all free radicals modify the most reactive amino-acid residues. The latter are the part of local regions, the unique structure of which is associated with functional capacity of proteins. Therefore, inactivation of proteins occurs almost simultaneously with the modification. The attack of reactive oxygen intermediates on proteins leads to the formation of primary amino-acid radicals which undergo the secondary interactions with the adjacent amino-acid residues that generally creates a very complex picture of the damaging effect of oxidative stress on protein macromolecules [8]. This causes damage to cell membranes with subsequent pathological process development. Taking into account the above mentioned facts, we have analyzed the degree of POP in newborns with IUGR in comparison with healthy newborns.

Determination of neutral aldehyde- and ketone derivatives with peak absorption at wavelengths of 356 nm in newborns with IUGR made it possible to reveal the following levels of products: POM less than 1 was revealed in 28.51% of infants, from 1 to 3 – in 60.74% and more than 3 – in 10.75%. In contrast, the OMB_{356} fraction among healthy newborns didn't exceed the index of 3.0 (8.70%). A similar pattern was registered in neutral aldehyde- and ketone derivatives with peak absorption at wavelengths of 370 nm: among newborns with IUGR the number of examined patients with levels of OMB products from 1 to 3 and more was higher as compared to healthy newborns; 55.22 and 6.93 versus 52.64 and 5.14%, respectively. The study of basic-type OMB products' levels with peak absorption at wavelengths of 430 nm in newborns with IUGR revealed the same number of individuals with indices from 0.1 to 0.4 and from 0.4 to 1 (48.34%); among healthy newborns the number of individuals with indices from 0.4 to 1 was higher, and made up 54.42 %. The study of basic-type OMB products' levels with peak absorption at wavelengths of 530 nm revealed the preeminence of the investigated individuals with the index from 0.1 to 0.2 (61.52 %), at the same time the OMB levels in healthy newborns from 0.1 to 0.2 and from 0.2 to 0.3 hardly differed and made up 44.63 and 46.34%, respectively.

Taking into consideration the findings of OMB levels in blood serum of newborns with IUGR we have determined the increase of basic-type OMB products' levels with peak absorption at wavelengths of 356 and 370 nm (1.74±0.08) and (1.58±0.13), as compared to healthy newborns ($p<0.05$) (Chart 1).

As chart 1 shows the neutral-type OMB levels in newborns with IUGR prevailed the levels registered in individuals from the comparison group of study.

Taking into account the fact that newborns of both groups were under equal ecological conditions, lower levels of protein peroxidation intensification with accumulation of neutral aldehyde- and ketone derivatives in healthy newborns may point to more effective functioning of protective antiradical systems.

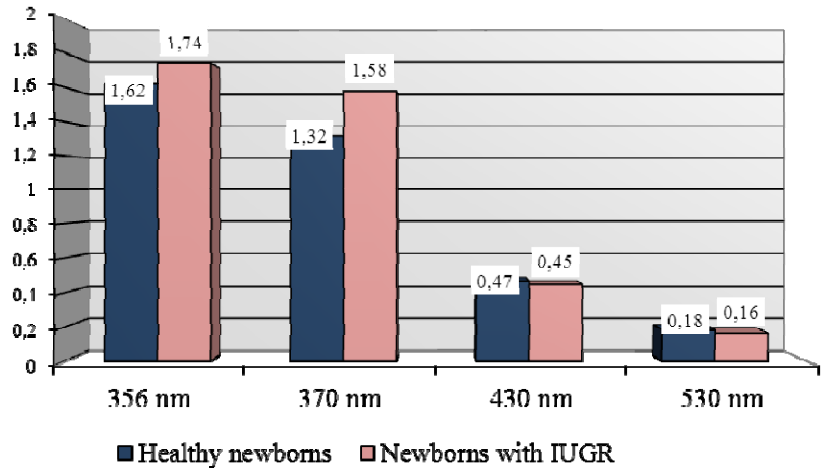

Chart 1: Indices of protein oxidative modifications in healthy newborns and newborns with IUGR
Note * - The probability of difference of newborns with IUGR as compared to healthy newborns ($p<0.05$)

The investigation of basic-type aldehyde-and ketone derivatives showed that in healthy newborns the level of these products in blood plasma was somewhat higher as compared with IUGR newborns ($p>0.05$).

Scientific investigations of other authors performed under different pathological conditions showed the ambiguity of dynamics of oxidative modifications of basic and neutral-type proteins depending on the pathology. The experimental study findings' on the influence of toxic compounds showed that changes of the level of basic-type aldehyde- and ketone derivatives were less evident than changes in the level of neutral-type aldehyde-and ketone derivatives [9]. Significant increase of both neutral-type aldehyde- and catalase derivatives and basic-type aldehyde- and ketone derivatives was noticed in blood serum of patients suffering from allergodermathosis [10].

The received data is important for identification of mechanism of hypoxic brain damage development in newborns with IUGR. Understanding of the pathogenic links of perinatal encephalopathy is based on the findings of investigations of the state of protein oxidative modifications in the hippocampus of rats under the conditions of ischemic and ischemic-reperfusion brain damage and administration of L-arginine. Thus the indices of protein oxidative modifications, which have high toxic effect on the neurons, may be the markers of cerebral ischemia. That's why it is recommended to use the study of processes of protein peroxidation with the aim to predict central nervous system (CNS) damage.

Hypoxic-ischemic impact on the newborns' CNS associated with placental insufficiency during the woman's pregnancy refers to negative pathological factors that influence further development of the infant's organism in general and its adaptive response [11 12]. It must also be taken into account that the above described damages are considered to be the leading causes of high lethality rate (from 20 to 50% in the structure of perinatal mortality) and subsequent children's disability. Babies with IUGR are very susceptible to the damaging effect of hypoxia on the brain because of their morphological and functional immaturity. CNS changes most often have diffuse character; however the newborn's reaction to different disease-producing factors is manifested in nonspecific neurological syndromes. Therefore, topical diagnosis of injury to the central nervous system, in most cases yields little information and only comprehensive study of behavioral and neurological symptoms together with indices of oxidative protein modifications allow predicting the recurrence of changes in the functioning of the central nervous system. The combination of findings on neuroendocrine state of children with ischemic CNS damage born in conditions of placental insufficiency makes it possible to define additional pathogenetic links of the development of remote effects of cerebral ischemia and serves the basis for the development of certain rehabilitation measures [13].

Consequently, integrated enhance study of dynamics of protein oxidative modifications with the analysis of clinical and neurological disorders in newborns will allow to conduct proper therapeutic correction of the latter and will contribute to the decrease of the levels of morbidity, disability and mortality.

4. Conclusions

1. It has been proved that in newborns with IUGR the levels of neutral-type aldehyde- and ketone derivatives with peak absorption at wavelengths of 356 and 370 nm were higher, as compared to healthy newborns ($p<0.05$), namely 1.74±0.08 and 1.58±0.13.
2. The basic-type aldehyde-and ketone derivatives had a tendency to increase in healthy newborns as compared with IUGR newborns.
3. The determination of protein oxidative modifications of basic and neutral-type aldehyde- and ketone derivatives in combination with clinical findings are recommended for establishing the prognosis of the severity of hypoxic CNS damage in newborns with IUGR.

The prospects for further research work in this field of investigation involve complex study of activity of protein peroxidation processes with the indices of glutathione system in newborns with IUGR and healthy newborns.

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