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PROCESSES OF LIPID PEROXIDATION, ANTIOXIDANT PROTECTION AND MEMBRANE DESTRUCTION OF RENAL EPITHELIUM IN THE PATHOGENESIS OF DYSMETABOLIC NEPHROPATHY IN CHILDREN

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Abstract. It should be noted that oxidative stress, as a universal mechanism of tissue hypoxia at the cellular level, accompanied by non-enzymatic free radical oxidation and accumulation of lipid peroxidation products (LPO) in the blood, has attracted particular interest among medical professionals in our time. Research in the last decade has shown that there are all reasons to consider the activation of free radical LPO as a nonspecific component of physiological and pathological reactions characterizing the stress of activation of homeostasis maintenance systems.

The aim of stady to establish the relationship between the impact of LPO processes, antioxidant defense, and membrane destruction of renal epithelium in children with dysmetabolic nephropathy.

Materials and methods. Two groups of examined children were formed from the examined group, including those with dysmetabolic nephropathy and secondary urinary tract infections: Group I - 52 individuals in whom dysmetabolic nephropathy was complicated by the superimposition of inflammatory processes in the kidneys and urinary tract - complicated DN (I-UDN), and Group II - 56 children with uncomplicated course of DN (II-DN), (a total of 108 children). The control group consisted of 65 healthy children. In children of all groups, the indicator of LPO process activity and the indicator of catalase activity in blood and urine were determined as a mechanism for regulating the antioxidant system of the body.

Results. Against the intensification of lipid peroxidation and membrane destruction processes in the bodies of children with DN, the possibilities of antioxidant protection are exhausted, which, in turn, leads to even greater intensity of the LPO process. The catalase activity indicator in urine is an informative, reliable, and sensitive marker not only for the result of the impact of epigenetic factors on a child's body but also a prognostic marker for a more severe course of dysmetabolic nephropathy in children.

Conclusions. The revealed facts allow us to assert that against the background of intensification of lipoperoxidation and membrane destruction processes in the body of children with DN, the possibilities of antioxidant protection are depleted, which in turn leads to an even greater intensity of the process of lipid peroxidation. And the index of catalase activity in urine is an informative, reliable and sensitive marker not only of the result of the impact of epigenetic factors on the child's body, but also a prognostic marker of a more severe course of dysmetabolic nephropathy in children.

Keywords: dysmetabolic nephropathy, lipid peroxidation (LPO), antioxidant defense, membrane destruction of renal epithelium.

Introduction. Nowadays, oxidative stress as a universal mechanism of tissue hypoxia at the cellular level, accompanied by activation of non-enzymatic free radical oxidation and accumulation of lipid peroxidation products (LPO) in the blood, attracts special interest of physicians [1]. A number of authors have established the pathogenetic role of damage to the lipid component of renal epithelial membranes in the presence of tissue hypoxia [2, 3]. Activation of lipid peroxidation is accompanied by changes in the conformation of lipids, which in turn leads to a violation of the structural and functional properties of biological membranes, increased lability and permeability, imbalance of membrane-localized enzyme systems, and disruption of mitochondrial electron transport chains [4]. The activation of LPO may also be associated with a decrease in the antioxidant defense of the cell [5, 6].

The final stage of LPO processes in the body is a violation of the morphofunctional state of membranes and metabolic processes in them, the release of acid hydrolases from lysosomes, a general increase in hydrolytic processes in tissues, the accumulation of toxic autolysis products, impaired DNA synthesis, membrane disintegration, destruction of their structure, and ultimately cell death [7, 8].

Studies of recent decades have shown that there is

Table 1. Indicator of lipid peroxidation and membrane destruction activity in children with dysmetabolic nephropathy (M ± m)

Indicators:	Groups of children:					
	I – UDN, *n* =52		II- DN, *n* = 56		III- Healthy-Control, *n* = 65	
	M ± *m*	%	*M* ± *m*	%	*M* ± *m*	%
Diene conjugates kmol/l	14,2±1,3*	96,15	13,83±0,97*	98,21	9,78±0,70	1,54
Plasma MDA, μmol/l	1,87±0,08*, #	94,23	1,28±0,17*, #	92,86	0,82±0,03	4,62
MDA erythrocyte, μmol/l	17,09±1,6*, #	98,08	13,85±1,53*, #	96,43	9,54±0,4	3,08
POL products in urine, units.	1,54±0,01*, #	100,0	1,27±0,02*, #	98,46	0,09±0,01	1,54
PL in urine, units.	1,02±0,02*, #	96,15	0,66±0,03*, #	92,86	0,22±0,15	2,6

* - significant difference between the data of children with dysmetabolic nephropathy and healthy controls; p<0.05
# - significant difference between two groups of children with dysmetabolic nephropathy; p1<0.01

every reason to consider the activation of free radical LPO as a nonspecific component of physiological and pathological reactions that characterize the stress of activation of homeostasis maintenance systems [9].

To determine the intensity of lipid peroxidation, antioxidant protection and the degree of membrane destruction of the renal epithelium in the pathogenesis of dysmetabolic nephropathy in children.

The aim of the study to determine the intensity of lipid peroxidation, antioxidant protection and the degree of membrane destruction of the renal epithelium in the pathogenesis of dysmetabolic nephropathy in children.

Methods and methods

From among the 108 children examined, two groups of subjects were formed: with dysmetabolic nephropathy and secondary urinary tract infection: Group I - 52 patients in whom dysmetabolic nephropathy was complicated by the layering of the inflammatory process of the kidneys and urinary tract - complicated DN (I-UDN), their examination was carried out in the period of stable (more than 3 years) clinical and laboratory remission of the inflammatory process, and group II - 56 children with uncomplicated DN (II-DN), in whom, in addition to clinical and ultrasound manifestations of dysmetabolic nephropathy, there was only persistent oxalate-phosphate crystalluria, which was detected in the laboratory. Children of both groups were exposed to tissue hypoxia in utero due to the influence of numerous epigenetic factors that acted on them during the entire pregnancy. The control group consisted of 65 healthy children whose data were collected during expeditionary visits to the districts of Ivano-Frankivsk region (III-Healthy-Control). In children of all groups, the index of the activity of the processes of lipid peroxidation and the index of catalase activity in the blood and urine were determined as a mechanism for regulating the antioxidant system of the body.

Indicators that characterize the activity of lipid peroxidation processes in the body and the resulting membrane destruction, in particular, in the renal parenchyma, include the content of diene conjugates in blood plasma, malondialdehyde in blood plasma and erythrocytes, the level of excretion of lipid peroxidation products and polar lipids (fragments of renal epithelial cytomembranes) in the urine [12, 14, 13]. The results of the study of these indicators are presented in Table 1

Analyzing the data presented in Table 1, it can be argued that tissue hypoxia, which was diagnosed earlier, led to the intensification of lipid peroxidation processes both in the whole body of children with DN and in the renal parenchyma. It was found that in the blood plasma of almost all children of both groups, the content of diene conjugates, intermediate products of the lipid peroxidation reaction, was significantly and significantly increased (14.2±1.3 μmol/l and 13.8±0.97 μmol/l, while its value in healthy children was 9.78±0.70 μmol/l). As for the content of malondialdehyde, the end product of the lipid peroxidation process, it was significantly higher than that of healthy children in blood plasma (1.87±0.08 μmol/l and 1.28±0, 17 μmol/l, while its value in healthy children was 0.82±0.03 μmol/l), and in erythrocytes (17.09±1.6 μmol/l and 13.85±1.53 μmol/l, while its value in healthy children was 9.54±0.4 μmol/l). Moreover, this indicator was significantly different not only from the data of children in the control group, but also between the groups of children examined: in the complicated course of dysmetabolic nephropathy, the content of MDA in both plasma and erythrocytes was significantly higher (Table 1).

Accordingly, the excretion of lipid peroxidation products in the daily urine was also significantly higher in children with DN of both groups with significantly higher rates in children of group I (1.54±0.01 u. and 1.27±0.02 u. U with the data of children of the control group 0.09±0.01 U), which indicates the intensification of lipid peroxidation and membrane destruction of cells directly in the kidney tissue (Table 1).

Similarly, the excretion of polar lipids, which indicates not only calciphylaxis in children but also is the

main indicator of renal epithelial membrane destruction, was significantly higher in almost all children of both groups with significantly higher numbers in children with complicated dysmetabolic nephropathy (Table 1).

Thus, under the influence of tissue hypoxia, which the child was exposed to in utero due to the influence of numerous epigenetic factors that acted on it during pregnancy, the child's body decreases the resistance of membranes to the action of other damaging factors due to the development of an energy-deficient state of cells. Regulated by the energy charge of cells, the process of membrane phosphorylation, which is the least resistant to hypoxia, is disrupted, leading to its destruction [13, 9]. Tissue hypoxia leads to an intensification of lipid peroxidation (LPO) processes. LPO products have a damaging effect on cell membranes, primarily renal epithelium, which leads to a violation of the vital functions of renal parenchyma cells.

Therefore, indicators of the intensity of the lipid peroxidation reaction in both blood and kidney tissue and the process of membrane destruction are specific, sensitive and highly informative markers of the impact of epigenetic factors on the child, which led to connective tissue dysplasia and manifestation of dysmetabolic nephropathy in utero. In addition, given the significant difference in data between the two groups of children, we can say that lipid peroxidation and nephrocyte membrane destruction are sensitive prognostic markers of more severe dysmetabolic nephropathy in children.

The rate of lipoperoxidation processes in the body is called upon to regulate the so-called antioxidant system of the body, one of the indicators of which is the activity of the catalase enzyme. The activity of catalase in blood and urine was studied, and the results are presented in Table. 2.

Results and Discussion

The results of the study of catalase activity indicate the depletion of antioxidant defense and a significant decrease in catalase activity both in the blood (0.57±0.14 u and 0.63±0.23 u) and in the urine (0.17±0.04 u and 0.45±0.09 u) in all examined children of both groups. At the same time, catalase deficiency in the urine was significantly different in children of the two groups, not only with the data of healthy children (0.87±0.04 units), but also with each other (Table 2).

Conclusion

Thus, under the influence of tissue hypoxia, which the child was exposed to in utero due to the influence of numerous epigenetic factors that acted on it during the entire pregnancy, the child's body decreases the resistance of membranes to the action of other damaging factors as a result of the development of an energy-deficient state of cells. Regulated by the energy charge of cells, the process of membrane phosphorylation, which is the least resistant to hypoxia, is disrupted, leading to its destruction. Tissue hypoxia leads to an intensification of lipid peroxidation (LPO) processes. LPO products have a damaging effect on cell membranes, primarily renal epithelium, which leads to impaired vital functions of renal parenchymal cells. Thus, indicators of the intensity of the LPO reaction in both blood and kidney tissue and the process of membrane destruction are specific, sensitive and highly informative markers of the impact of epigenetic factors on the child, which led to tissue hypoxia and manifestation of dysmetabolic nephropathy in utero. In addition, given the significant difference in data between the two groups of children, we can say that lipid peroxidation and nephrocyte membrane destruction are sensitive prognostic markers of more severe dysmetabolic nephropathy in children.

The revealed fact allows us to assert that against the background of intensification of lipoperoxidation and membrane destruction processes in the body of children with DN, the possibilities of antioxidant protection are depleted, which in turn leads to an even greater intensity of the process of lipid peroxidation. And the index of catalase activity in urine is an informative, reliable and sensitive marker not only of the result of the impact of epigenetic factors on the child's body, but also a prognostic marker of a more severe course of dysmetabolic nephropathy in children.

Ethical standards: The written informed consent was obtained from every patient.

Conflict of interests: The author declare that no conflict of interests exist.

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Table 2. Catalase activity in blood and urine of children with dysmetabolic nephropathy (M ± m)

Indicators:	Groups of children:					
	I – UDN, *n* =52		II- DN, *n* = 56		III- Healthy-Control, *n* = 65	
	M ± *m*	%	*M* ± *m*	%	*M* ± *m*	%
Blood catalase, f.u.	0,57±0,14*	100,0	0,63±0,23*	100,0	2,2±0,04	0,0
Urine catalase, etc.	0,17±0,04*, #	100,0	0,45±0,09*, #	98,21	0,87±0,04	1,54

* - significant difference between the data of children with dysmetabolic nephropathy and healthy controls; p<0.05
# - significant difference between two groups of children with dysmetabolic nephropathy; p1<0.01

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