THE STATE OF PRO- AND ANTIOXIDANT SYSTEMS OF KIDNEYS IN CASE OF EXPERIMENTAL HYPOTHYROIDISM

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Key words: experimental hypothyroidism, lipid peroxidation, protein oxidative modification, renal tissue.

Summary. *The experiments, carried out on 18 rats with hypothyroidism, demonstrated that due to the exhaustion and failure of compensatory intrarenal antioxidant system, the intensity of accumulation of nephrotoxic lipid and protein peroxidation end-products in the renal tissue of hypothyroid rats tends to become excessive, causing renal dysfunction, leading to the ischemic, toxic or immunologic damage of renal tissue.*

Резюме. *Эксперименты, выполненные на 18 крысах с гипотиреозом, показали, что, вследствие истощения и срыва компенсаторных возможностей внутрипочечных антиоксидантных систем, интенсивность накопления нефротоксичных продуктов липо- и протеинопероксидации в ткани почек гипотиреоидных крыс оказывается чрезмерной, что может стать причиной развития ренальных дисфункций, привести к ишемическому, токсическому, иммунологическому поражению почечной ткани.*

Introduction. Nowadays a great attention is paid to the study of free radical oxidation processes, which can be considered both as adaptational body reaction and as universal mechanism of alteration of biostructures in case of pathology, including thyropathies [1]. Pluripotent influence and universality of biologic effects of thyroid hormones determines the close connection between their level and the intensity of free radical oxidation, lipid and protein peroxidation processes – non-specific markers of the dysfunction of inner organs, including kidneys [4, 5]. Functional condition of the latest is known to influence all metabolic processes in the body. The fact of mutual influence of thyroid status of the body, lipid and protein peroxidation processes and renal function status is undisputed [3]. The investigation of peroxidation processes and antioxidant system state (AOS) in renal tissue in case of thyropathy will widen the possibilities of targeted pathogenic corrective influence on the initial stages of renal dysfunction in order to prevent its chronization [2].

The objective. of this study was to establish the character of influence of thyroid hormone deficiency on the processes of lipid and protein peroxidation in the renal tissue.

Material and methods. The experiments were carried out on 28 matured nonlinear male rats under the standard conditions of vivarium. For the experimental modeling of hypothyroidism 18 animals were administered mercazolil (Mercazolilum, LLC «Pharmaceutical company «Zdorovye», Ukraine) intraperitoneally in a dose of 10 mg/kg. 14 days after the beginning of pathology formation 18 hypothyroid rats and 10 animals of control group were euthanized by decapitation under the slight diethyl ether anesthesia. The object of the research was renal tissue, removed, washed out of blood and homogenized for the further investigations right after animals' decapitation [2].

The state of lipid peroxidation (LPO) was assessed by quantification of malondialdehyde (MDA) and diene conjugates (DC), antioxidant protection – by the contents of enzymatic (superoxide dismutase (SOD), catalase (CT), glutathione peroxidase (GPO)) and non-enzymatic systems (glutathione S-transferase (GST), sulfhydryl groups (SH-groups). Dinitrophenylhydrazones (DPH) concentration was determined to assess the intensity of protein oxidative modification (POM) [2].

Statistical processing of the obtained data was performed with the establishment of Student's coefficient (t).

Results.

As the results of investigation showed (table), MDA level in renal tissue of hypothyroidal rats was twice higher as compared with control parameters ($p<0,001$), DC contents was found to be increased by 38,1% ($p<0,001$) despite the reliable increase (by 28,6%) of SOD activity ($p<0,01$). Such biochemical changes were possible under the excessive intensity of reactive oxygen species generation, confirmed by the increase of CT activity by 58,5% ($p<0,001$) and two-fold reduction of the basic intrarenal antiradical enzyme – GPO ($p<0,001$). The elevation of GST activity by 21,0% ($p<0,001$), probably, hasn't compensated these changes, since the level of free SH-groups in renal tissue was reliably decreased ($p<0,001$).

On this background the intensive peroxidation has involved protein molecules of renal structures – the contents of neutral and basic DPH in renal tissue was found to be elevated by 82,5 и 81,4% ($p<0,001$) respectively.

Table 1. Characteristics of changes of pro- and antioxidant systems in renal tissue of rats with experimental hypothyroidism (X±Sx)

Indices	Group, number of animals	
	Control, n=10	Hypothyroidism, n=18
Malondialdehyde, μmol/1 mg of tissue	83,71±0,76	168,23±2,78 p<0,001
Diene conjugates, nmol/1 mg of protein	1,18±0,03	1,63±0,06 p<0,001
Superoxide dismutase activity, un./1 min./1 mg of protein	0,28±0,01	0,36±0,02 p<0,01

Catalase activity, µmol/1 min./1 mg of tissue	94,80±0,89	150,31±4,52 p<0,001
Glutathione S-transferase activity, µmol/1 min./1 mg of tissue	14,30±0,53	17,30±0,45 p<0,001
Glutathione peroxidase activity, µmol/1 min./1 mg of protein	87,31±1,08	42,02±1,31 p<0,001
Level of SH-groups, mmol/1 mg of tissue	0,029±0,001	0,021±0,001 p<0,001
Neutral dinitrophenylhydrazones, mmol/1 g of protein, 370 nm	1,03±0,06	1,88±0,01 p<0,001
Basic dinitrophenylhydrazones, un.o.d./1 g of protein, 430 nm	9,14±0,49	16,58±0,56 p<0,001

Note: P – statistically significant difference in comparison with control group;
n – number of experimental animals.

Conclusion. Mentioned above findings evidence, that due to the exhaustion and failure of compensatory intrarenal antioxidant system, the intensity of accumulation of nephrotoxic lipid and protein peroxidation end-products in the renal tissue of hypothyroid rats tends to become excessive, causing renal dysfunction, leading to the ischemic, toxic or immunologic damage of renal tissue.

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