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## **INFLUENCE OF THYROID HORMONES AND DRAG FOR ANESTHESIA ON HOMEOSTASIS OF THE HUMORAL PART OF THE IMMUNE SYSTEM AND RED-OX SYSTEM IN THE RAT'S BODY**

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### **Abstract**

*Introduction.* The increase in the prevalence of hyperthyroidism justifies the feasibility of experimental studies to study the mechanisms of thyroid hormones on a number of metabolic processes and homeostasis in euthyroidism and hyperthyroidism in the experiment and increases against the background of preoperative stress.

*The aim of the study:* to find out the peculiarities of the reaction of the immune system and free radical processes of experimental animals under conditions of simulated hyperthyroidism to the action of various drugs for anesthesia.

*Research methods.* To simulate the state of hyperthyroidism, rats received L-thyroxine for 21 days. The effect of euthyroidism and hyperthyroidism on the level of homeostasis of the humoral part of the immune system and free radicals on the introduction of sodium thiopental and dexmedetomidine in the experiment compared.

*Results and discussion.* In the blood plasma of animals with experimental hyperthyroidism, changes in the level of the humoral part of the immune system and free radicals were observed under the influence of sodium thiopental and dexmedetomidine hydrochloride under conditions of hyper- and euthyroidism.

*Conclusions.* Activation of metabolic processes of the thyroid gland affects the universal defense systems of the body, which is especially evident in conditions of operational and perioperative stress by disruption of homeostasis of the immune system and the activity of free radicals.

**Key words: free radicals; humoral immunity; hyperthyroidism; sodium thiopental; dexmedetomidine.**

The increase in the prevalence of hyperthyroidism justifies the feasibility of experimental studies to study the mechanisms of influence of thyroid hormones on a number of metabolic processes and homeostasis in euthyroidism and hyperthyroidism in the experiment [1, 2]. High risks of intra- and postoperative complications are associated with the direct toxic effects of excess thyroid hormones on the cardiovascular, nervous, endocrine and other body systems [1, 2, 3]. The high degree of variability of these effects on the body, justifies the urgency of the problem of optimization of anesthesia in emergency surgery for various nosologies on the background of pathology of the thyroid gland, which had exacerbated by preoperative stress [4]. Most pathological processes in the body are universal. One of such mechanisms is their effect on the pro- and antioxidant defense system [2]. Peculiarity of the influence of thyroid hyperfunction on the processes of free radical oxidation, formation of reactive oxygen species, on the processes that perform numerous regulatory functions [2, 5, 6]. Hyperthyroidism leads to an imbalance of factors of the humoral part of the immune system of experimental animals.

**Purpose:** to find out the peculiarities of the reaction of the immune system and free radical processes in the body of experimental animals to the action of various drugs for anesthesia in simulated hyperthyroidism.

#### **Research methods and materials**

The study was performed on 60 adult outbred white male rats weighing  $(160 \pm 5)$  g, which were kept in standard vivarium conditions. All manipulations with experimental animals were carried out in compliance with the rules of the "European Convention for the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes", as well as in accordance with "Scientific and Practical Guidelines for Keeping and Working with Laboratory Animals" [7].

Experimental animals were divided into 10 groups: group I - intact (10 rats); II group of animals simulated experimental hyperthyroidism (10 rats) was in; sodium thiopental on the background of euthyrosis were administered group III animals (10 rats); group IV animals

had received thiopental sodium on the background of experimental hyperthyroidism (10 rats); group V animals were administered dexmedetomidine on the background of euthyroidism (10 rats), group VI was administered dexmedetomidine on the background of experimental hyperthyroidism (10 rats) (Table 1).

Hyperthyroidism simulated by intragastric administration of L-thyroxine in 1% starch solution at 200 mg / day per 1 kg of body weight daily for 21 days [2]. Sodium thiopental administered intraperitoneally at a rate of 20 mg / kg body weight of rats [8, 9]. Dexmedetomidine hydrochloride administered intraperitoneally at a rate of 1 mg / kg body weight of experimental animals [10].

Table 1 - Division of animals into groups

animals groups	Number of animals	Type of anesthesia
I group	10	euthyroidism
II group	10	hyperthyroidism
III group	10	sodium thiopental + Euthyroidism
IV group	10	sodium thiopental + hyperthyroidism
V group	10	dexmedetomidine + euthyroidism
VI group	10	dexmedetomidine + hyperthyroidism

Immunological studies performed by immunochemiluminescent and enzyme-linked immunosorbent assays using commercial test systems "Hema" (Czech Republic), "Human GmbH" (Wiefbaden, Germany) according to the attached instructions on the boom enzyme-linked immunosorbent assay "Stat Fax 303 Plus" (USA).

The level of oxidative stress in rats was studied by the content in the blood plasma of diene conjugates (DC) by the method described by V.B. Gavrilo [11] and malon dialdehyd (MDA) active product [12, 13]. The digital material obtained as the result of the experiment systematized and processed using the methods of variation statistics using the program "Microsoft Exel 9.0".

### **Results and discussion**

The study of the effect of various drugs for anesthesia on the immunological reactivity of animals under experimental hyperthyroidism evaluated by the state of humoral immunity

(concentrations of immunoglobulins A, M, G).

Thus, the concentration of immunoglobulin A in the second group of animals increased 1.4 times compared with the control group ( $1.63 \pm 0.03$ ) g / l ( $p < 0.05$ ), while against the background of euthyroidism (and the control group of animals) this figure was ( $2.26 \pm 0.14$ ) g / l.

The introduction of sodium thiopental on the background of hyperthyroidism showed an increase in Ig A level by 1.5 times ( $2.41 \pm 0.08$ ) g / l, ( $p < 0.05$ ), compared with the control group and no significant changes in the group of animals with sodium thiopental on the background of euthyroidism ( $p < 0.05$ ). The level of Ig A with dexmedetomidine in V group of animals on the background of euthyroidism does not change ( $1.65 \pm 0.09$ ) g / l, respectively, approached the control group ( $1.63 \pm 0.03$ ), ( $p > 0.05$ ). This figure was ( $2.31 \pm 0.10$ ) g/l in VI group animals, which did not differ from the II group animals ( $2.26 \pm 0.14$ ) g / l, ( $p > 0.05$ ) (Table 2).

Table 2 - Changes in the humoral immunity in the experiment under conditions of euthyroidism and experimental hyperthyroidism and the action of various drugs for anesthesia (M  $\pm$  m)

group	I	II	III	IV	V	VI
Ig A, g/l	$1,63 \pm 0,03$	$2,26 \pm 0,14^*$	$1,67 \pm 0,06$	$2,41 \pm 0,08^*$	$1,65 \pm 0,09$	$2,31 \pm 0,10^*$
Ig M, g/l	$0,55 \pm 0,03$	$0,84 \pm 0,03^*$	$0,58 \pm 0,02$	$0,79 \pm 0,03^*$	$0,59 \pm 0,03$	$0,88 \pm 0,02^*$
Ig G, g/l	$2,57 \pm 0,06$	$3,43 \pm 0,10^*$	$2,49 \pm 0,09$	$3,45 \pm 0,08^*$	$2,51 \pm 0,07$	$3,23 \pm 0,14^*$
MDA, mkmol/l	$3,67 \pm 0,6$	$7,05 \pm 0,14^*$	$4,83 \pm 0,13^*$	$7,84 \pm 0,1^*$	$4,31 \pm 0,07^*$	$6,79 \pm 0,16^*$
DC, unit	$1,18 \pm 0,07$	$2,21 \pm 0,05^*$	$1,34 \pm 0,08^*$	$2,56 \pm 0,13^*$	$1,29 \pm 0,09^*$	$2,32 \pm 0,09$
Note: *-	values that are statistically significant from similar indicators in the control group of animals ( $p < 0,05$ )					

Analysis of the results showed that experimental hyperthyroidism significantly changes the serum of animals. Ig G and Ig M increased 1.3 and 1.5 times, respectively, in II

group animals compared with the control group (group I). Thus, the level of Ig G in euthyroidism (group I) reached  $(2.57 \pm 0.06)$  g / l and  $(3.43 \pm 0.10)$  g / l in hyperthyroidism (group II) in experimental animals, ( $p < 0.05$ ), which significantly exceeded the indicators of the control group. Ig M values were  $(0.55 \pm 0.03)$  g / l in euthyroidism and  $(0.84 \pm 0.03)$  g / l in experimental hyperthyroidism, which was 1.5 times higher than the control, ( $p < 0, 05$ ).

The level of Ig G and Ig M in the serum of animals on the background of euthyroidism with the introduction of sodium thiopental (group III) and dexmedetomidine (group V) does not increase. The level of Ig G in group III was  $(2.49 \pm 0.09)$  g / l against the background of the introduction of sodium thiopental and  $(2.51 \pm 0.07)$  g / l in group V of animals using dexmedetomidine, compared with those in the group of intact animals, respectively, ( $p > 0.05$ ). Hyperthyroidism leads to metabolic disorders. The level of Ig G and Ig M in the groups with simulated hyperthyroidism with the introduction of sodium thiopental (group IV) significant increase in 1.34 times  $(3.45 \pm 0.08)$  g / l, ( $p < 0.05$ ) and only 1.26 times  $(1.26 \pm 0.14)$  g / l, ( $p > 0.05$ ) in the group with dexmedetomidine (group VI).

Imbalance in the immune system accompanied by a sharp activation of the pool of free radicals initiated by experimental hyperthyroidism.

The results of the study of the membrane toxicity of various drugs for anesthesia in experimental hyperthyroidism evaluated by the activity of the antioxidant enzyme system and lipoperoxidation.

Analysis of the results showed that experimental hyperthyroidism significantly activates the redox system. Compared with euthyroidism, hyperthyroidism caused an increase in the initial products of lipid peroxidation. The concentration of DC in the serum of experimental animals increased and was, respectively, in the first group of animals  $(1.18 \pm 0.07)$  units and  $(2.21 \pm 0.05)$  d. from - in the second ( $p < 0.05$ ). The use of thiopental in euthyroidism (third group) leads to an increase in DC 1.1 times, respectively  $(1.34 \pm 0.08)$  units ( $p < 0.05$ ). In the fourth group of animals with experimental hyperthyroidism and the use of sodium thiopental, these indicators reach a value of  $(2.56 \pm 0.13)$  units, which is 1.6 times higher than intact animals ( $p < 0.05$ ). Under the use of dexmedetomidine in euthyroidism (group V), the level of DC was  $(1.29 \pm 0.09)$  units and  $(2.32 \pm 0.09)$  d. from ( $p < 0.05$ ), respectively, in hyperthyroidism (group VI) (Table 2).

Indicators of MDA increased in 1.8–1.9 times in comparison with the group of intact animals. Thus, the initial products of lipid peroxidation (diene conjugates) reached the level  $(1.18 \pm 0.07)$  units with euthyroidism and  $(2.21 \pm 0.05)$  units from - in hyperthyroidism in experimental animals ( $p < 0.05$ ) in comparison with the group of intact animals. The

concentration of the intermediate indicator of lipid peroxidation - malonic dialdehyde (MDA) in euthyroidism was  $(3.67 \pm 0.6) \mu\text{mol} / \text{l}$ , and in experimental hyperthyroidism increased to  $(7.05 \pm 0.14) \mu\text{mol} / \text{l}$  ( $p < 0, 05$ ).

With the introduction of thiopental sodium (group III) and dexmedetomidine (group V) in euthyroid animals, the concentration of MDA in the serum of animals increased. In particular, the concentration of MDA in animals of the third group was  $(4.83 \pm 0.13) \mu\text{mol} / \text{l}$ , which is 1.3 times ( $p < 0.05$ ) higher than normal, and in the fifth group of animals used dexmedetomidine -  $(4.31 \pm 0.07) \mu\text{mol} / \text{l}$ , which is 1.2 times higher compared with indicators in the group of intact animals ( $p < 0,05$ ).

Hyperthyroidism accompanied by increased processes of free radical oxidation. There was a significant increase in MDA activity in groups with simulated hyperthyroidism with the introduction of sodium thiopental (group IV) by 2.1 times  $(7.84 \pm 0.10) \mu\text{mol} / \text{l}$  ( $p < 0.05$ ) and 1.8 times  $(6.79 \pm 0.16) \mu\text{mol} / \text{l}$  ( $p < 0.05$ ) in the group with dexmedetomidine (group VI) (Table 2).

### **Conclusions**

Therefore, our research results showed that in the experiment, the toxic effect of anesthetics manifested in conditions of hyperthyroidism more pronounced than in euthyroidism.

Activation of free radical processes leads to an increase in the level of initial and final products of lipid peroxidation and changes in immunological reactivity and disruption of physiological compensatory processes, which is the basis for recommendations for additional therapy in complex preoperative preparation on the background of hyperthyroidism.

Activation of metabolic processes of the thyroid gland affects the universal defense systems of the body, which is especially evident in conditions of operative and perioperative stress disorders in immunological reactivity, which leads to the search for drugs to correct disturbed homeostasis.

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