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# CHANGES OF THE THYROID HORMONES CONCENTRATION AND THE BIOCHEMICAL PARAMETERSFEAUTURES OF LYMPH AND BLOOD OF RAT WITH HYPOTHYROIDISM

**Abstract.** The article considers the influence of the mercazolilum management on the hormonal state in the lymph and blood of rates. The study shows that after mercazolilum management and the hypothyroidism signs appearance in rats, there was a decrement of lymph flow from the thoracic lymphatic duct. Changes in the hormonal and biochemical composition of the lymph were observed. There were disturbances not only of the metabolism in the lymph, but also of the functional state of the body. There were disturbances of rheologic and physicochemical parameters of lymph and blood at the experimentative hypothyroidism of rats: viscosity has been increased, coagulability and number of erythrocytes have been decreased, thrombocytes and leucocytes in blood have been increased. It has been led to a decrease of rats of the 2$^{nd}$ experienced group in $T_3$, $T_4$ content and increase of thyrotropic hormone in lymph and blood which reflected the occurrence of their hypothyroidism. Experiments showed that $T_3$content in rats with hypothyroidism has decreased by 45.7% and $T_4$by 35.6% in lymph, and in blood $T_3$by 43,5% and $T_4$by 41,6% have decreased compared with the control group of animals.

**Key words:** hormones, blood, rats, lymph, lymph flow, thyroxin, triiodothyronine.

The most relevant topic among the current medical and social issues is thyroid bodypathology. This is due to the fact that thyroid body diseases depend on many factors and conditions: geochemical, demographic, social and ecological and climatic, etc. [1, 2]. Hypothyroidism is one of the most prevalent pathologies of endocrine system due to persistent and long lasting deficit of thyroid hormones in the body or a decrease of their action on target organs [3-5].

Hypothyroidism in popularity is among the highest in all endocrine diseases, and its prevalence increases with age. Primary hypothyroidism is associated with thyroid body pathology leading to a decrease in glandular tissue mass of thyroid body and inhibition of the synthesis of thyroid hormones. This may be due to aplasia or agenesis of the thyroid body, autoimmune processes, deficit iodine, Selena deficit [6]. Secondary hypothyroidism ("central") is associated with loss of the hypophysary tropic function (decrease in thyreotrophin production). Insufficient intake of thyroid body hormones leads to disturbance of protein and carbohydratemetabolism, flattening of the sugar curve after glucose loading, to disturbance of lipid and water-salt metabolism [7]. The variety of clinical symptomatology inherent in underactive thyroid body is largely due to metabolism processes disturbance associated with thyroid hormone deficit.Thyroid body pathology reflects on the provision of endocrine, immunological, energy homeostasis of the body [8, 9]. Hypothyroidism occurs at approximately 19 per 1,000 in women and 1 per 1,000 in men. Despite its prevalence, hypothyroidism is very often detected late [10].

Taking into account the important role of lymphatic system in homeostasis maintaining in the body [11, 12], the study of its role at thyroid insufficiency is of current importance. The literature has no data of the functional state of the lymphatic system at hypothyroidism. The purpose of this research is the study

of experimental hypothyroidism on lymphatic flow, hormonal and biochemical parameters in the lymph and blood in rats.

**Materials and methods.** The work has been done on 55 white sexually mature non-pedigree rat-males weighing 230-250 g. Rats feeding has been carried out according to standard diet of the vivarium. Rats of the 1st group (15 rats) were control. They were in the same conditions of feeding and keeping with animals of experienced rats. The 2nd group (20 rats) and the 3rd group (20 rats) were experienced. Experimental hypothyroidism of trial rats has been modeled according to Orlov method, 2002 [13, 14]. The rats of the experienced groups have been administered mercazolilum in a dose of 20 mg per 100 g of body mass with drinking water daily within 15 and 30 days for the state development of experimental hypothyroidism. All groups of animals were in the same conditions of feeding and keeping.

The speed of lymph flow and its rheological properties of control and experimental groups of animals have been studied. In lymph of all groups of animals physical and chemical parameters, coagulation time, lymph according to Sukharev, viscosity using a viscometer CT-4, biochemical parameters in lymph, blood plasma of control group of animals have been determined. The alanine aminotransferase (ALT) and aspartate aminotransferase (AST) level, total protein, cholesterin, triglycerides, bilirubin, urea, creatinine have been determined in samples of lymph and blood using automatic biochemical analyzer COBOS INTEGRA 400 [15].

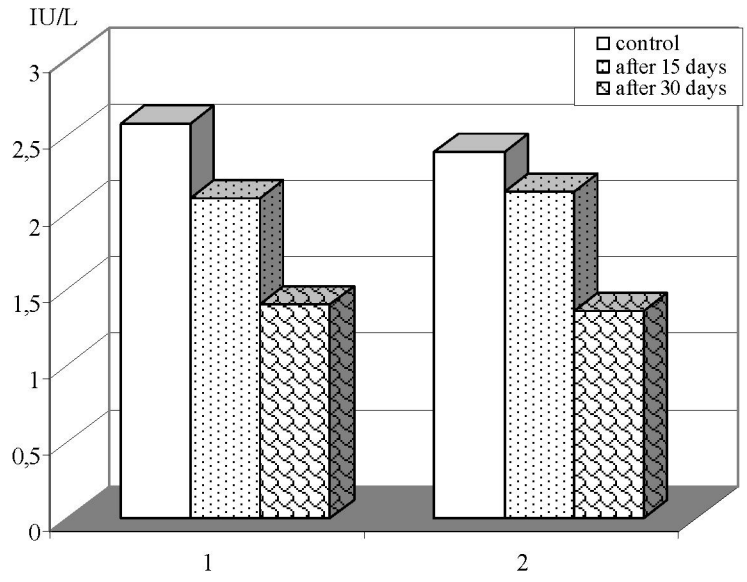
The development of hypothyroidism has been controlled by the level of thyroid-stimulating hormone, triiodothyronine, thyroxin in blood and lymph. The concentration of thyroid-stimulating hormone (TSH), triiodothyronine and thyroxin in lymph and blood of intact animals on 15th and also on 30th days of experimental hypothyroidism have been determined by electro-chemiluminescent method using standard test-system in accordance with enclosed production instructions IMMUNOTECH (Czechia), with further processing of the results obtained on the analyzer COBOS INTEGRA 400 (USA). Experience results have been processed by variation statistics method on ECM using Student's t-test. The results have been considered accurate at $p<0,01$, $p<0,05$.

**Results and its discussion.** The results show that hypothyroidism in rats has been formed after mercazole management, it was characterized by a decrease in body mass and change in their behavior – hyperactivity has been watched. The research showed that a decrease of thyroid hormone in lymph and blood has been occurred at hypothyroidism. There was a decrease of concentration in lymph $T_3$ 1,2 times, $T_4$ 1,14 times in the second week, that is, after 15 days of the research, and hormonal state of the parameters under the research have been decreased 1,8 and 1,7 times accordingly on the 30th day of the research.

Similarly, the picture of the hormonal state showed that $T_3$и$T_4$ level in blood had reduced 1,12 times after 15 days, and accordingly 1,8 and 1,6 times after 30 days (table 1, figure 1, 2).

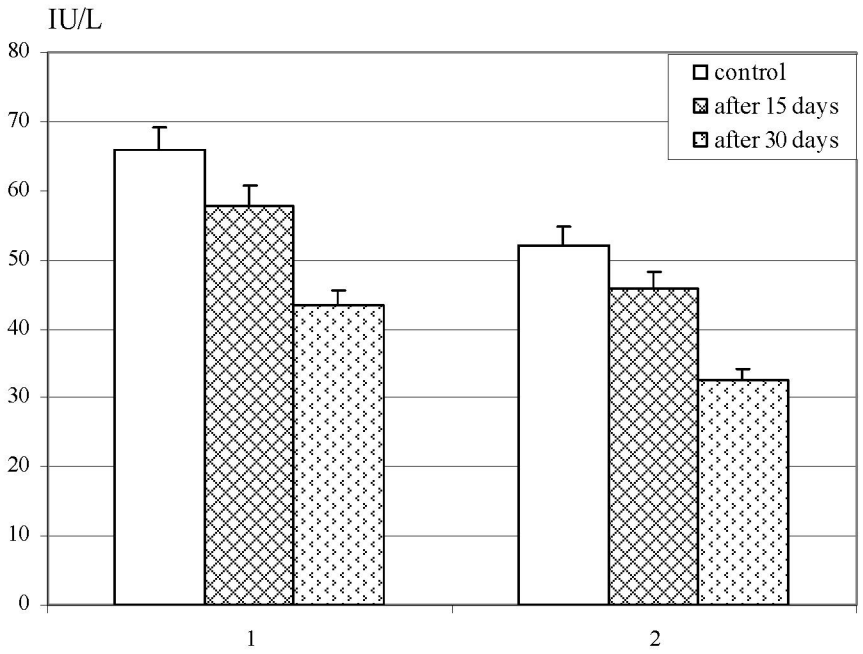
Table 1 – Change of thyroid hormones in lymph and blood of rats of control group and at experimental hypothyroidism

| Parameters | Control | Experimental | |
|---|---|---|---|
| | | 15 days | 30th day |
| Lymph | | | |
| TSH – thyroid-stimulating hormone, IU/L | 0,14±0,002 | 0,26±0,001** | 0,27±0,003** |
| $T_3$ – triiodothyronine, IU/L | 2,58±0,01 | 2,09±0,01* | 1,40±0,01** |
| $T_4$ – thyroxin, IU/L | 65,8±3,3 | 57,8±2,5* | 42,4±1,7** |
| Blood | | | |
| TSH – thyroid-stimulating hormone, IU/L | 0,03±0,001 | 0,05±0,001** | 0,07±0,002** |
| $T_3$ – triiodothyronine, IU/L | 2,39±0,03 | 2,13±0,01* | 1,35±0,07** |
| $T_4$ – thyroxin, IU/L | 52,2±2,4 | 45,8±2,1* | 32,5±1,3** |
| Note - * accurate compared to control $p<0,05$,* -$p<0,01$**. | | | |




Notations: By Y-axis: triiodothyroninelevel ($T_3$) in IU/L. By X-axis: 1-lymph, 2 – blood plasma.

Figure 1 – Triiodothyronine content ($T_3$) in lymph and blood in control and at experimental hypothyroidism

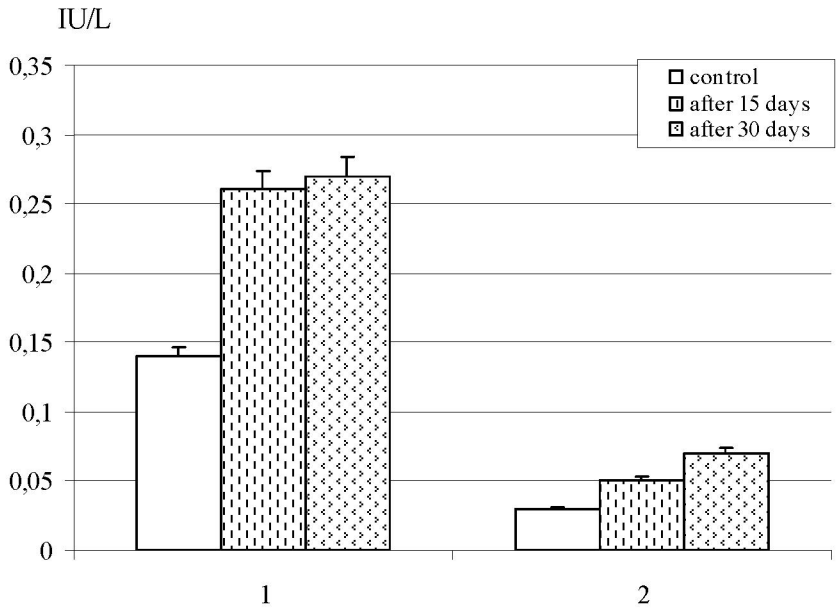



Notations: By Y-axis: thyroxin level ($T_4$) in IU/L. By X-axis: 1-lymph, 2 – blood plasma,

Figure 2 – Thyroxin content ($T_4$) in lymph and blood in control and at experimental hypothyroidism

There was a decrease in $T_3$, $T_4$content and increase of thyrotropic hormone in lymph and blood in rats of the 2nd experienced group with hypothyroidism, which reflect the occurrence of their hypothyroidism. Experiments have shown that in rats with hypothyroidism $T_3$ content decreased by 45.7% and $T_4$ by 35.6% in lymph, and inblood $T_3$ decreased by 43.5% and $T_4$ by 41.6% compared with the control group of animals.

The level of thyroid-stimulating hormone (TSH) in the lymph and blood showed an increase of 92.9 and 133.3%, accordingly, compared to intact animals (table 1, figure 3).




Notations: By Y-axis: Thyroid-stimulating (TSH) level, in IU/L. By X-axis: 1-lymph, 2 – blood plasma.

Figure 3 – Thyroid-stimulating hormone level (TSH) in lymph and blood in control and at experimental hypothyroidism

Lymph flowspeed from thoracic duct of rats showed that lymph flow decrease at experimental hypothyroidism was from 0,34±0,02 to 0,25±0,02 ml/hour, it is 26% higher compared to parameters of control group.

The results of the research showed that hemoglobin contents in blood of rats of the 1st group did not have significant changes during experiment, it was within 152.3 to 156.6 g / l. Hemoglobin content has decreased compared to control group by 1,24-1,25 times (by 122.6-124.8 g / l) after mercazolilum management in 15 days at experimental hypothyroidism. Its value has been decreased compared to the control group by 1.41 times (70%, by 112.2 g / l) / by the 30th day from the beginning of the experiment.

The erythrocyte parameters in the blood of the control groups of animals ranged from 7.59 to 7.84 ± 0.9 × 1012 / l. Its value in the blood in the experimental groups showed a decrease of 31% from the initial level. Experiment has observed a decrease of hematocrit by 10.7% compared to control group after mercazolilum administering. The background value of thrombocyte in the blood of rats was detected in the range from 225 to 243.3 ± 11.3 h109 / l.

The thrombocytes content of animals of the 2nd group, which received mercazolilum within a month, increased by 1.6 times (experimental groups 395.7 ± 10x109 / l) compared to the control group. Leukocyte parameters in experimental hypothyroidism have increased by 87.9% compared to rats of the control group. The leukocytes level of intact animals showed from 12.87 to 14.38 ± 1.7x109 / l. According to the biochemical research data there was a decrease in the concentration of total protein and alkaline phosphatase in the lymph by 26-29 and 50.6%, in the blood plasma by 20-25 and 50.2%, accordingly, as well as an increase in the enzymatic activity of alanine aminotransferase and aspartate aminotransferase compared with intact rats in lymph by 63-61%, and blood by 187-131% (table 2) at experimental hypothyroidism.

Data obtained shows that leukocytosis and thrombocytosis, a slight decrease in the number of erythrocytes compared with the control are in evidence at hypothyroidism. Analysis of the research results showed a decrease in the volumetric flow rate of the lymph flow and changes in the biochemical and rheological properties of lymph. We found that a decrease in the viscosity of the lymph had contributed to a decrease in the speed of lymph movement. Changes in the physicochemical parameters and rheological properties of lymph contribute to changes in lymph viscosity in our experiments.

The research results showed that the thyrostatic administering of thyrostatics, i.e. mercazolilum causes experimental hypothyroidism state in animals. According to scientific literature data mercazo-

Table 2 – Biochemical parameters of blood of control rats and at hypothyroidism

| Parameters | Control | Hypothyroidism |
|---|---|---|
| Lymph | | |
| Total protein, g /l | 42,8±1,4 | 30,3±1,7 |
| Alanine aminotransferase, mmol/l | 84,4±2,9 | 138,2±10,1 |
| Aspartate aminotransferase, mmol/l | 159,7±10,8 | 257,5±10,9 |
| Alkaline phosphatase, mmol/l | 584,3±10,6 | 295,7±10,5 |
| Blood | | |
| Total protein, g/l | 65,2±2,3 | 52,8±1,5 |
| Alanine aminotransferase, mmol/l | 78,4±2,3 | 220,7±10,6 |
| Aspartate aminotransferase, mmol/l | 139,6±10,1 | 323,6±10,5 |
| Alkaline phosphatase, mmol/l | 673,2±10,7 | 338,3±10,4 |
| Note - * accurate compared to control p<0,05,* -p<0,01** | | |

lilumis a specific synthetic thyreostatic that inhibits the activity of thyroid body hormones involved in the synthesis and also inhibits thyroxinsynthesis, lowers the synthesis of basic metabolism [16, 17]. Research has shown that at Thyroid-stimulating (TSH) level in blood has risen, $T_3$ and $T_4$ level has decreased. We have showed a prevailing amount of thyroid hormones in the lymph than in the blood of experimental animals.

The amount of thyroid hormones in the body of animals has decreased in parallelat mercazolilum management, both in the blood and in the lymph, but the amount of hormones in the lymph was inhibited. Thus, it can be concluded that hypothyroidism in rats has been developed at mercazolilum managementin an average daily dose of 20 mg / 100 g within 30 days with water. It is characterized by features of the general state of rats, wool in the tail area of some individuals has lost, body weight has decreased, aggressive and hormonal, biochemical composition of lymph and blood, changes in physico-chemical and rheological properties of blood and lymph have been observed in the behavior of rats.

**Conclusion.** The results obtained in the presented research data, especially the results in the lymph can have important theoretical implications to understand the biochemical mechanisms at experimental hypothyroidism. Thus, we obtained experimental hypothyroidism in rats that showed a decrease in the level of thyroid hormones in the blood and lymph.

The level of thyroid hormones in the lymph slightly exceeded their level in the blood, both in normal conditions and also at hypothyroidism. Lymph flow has decreased and hormonal, biochemical, rheological lymph parameters have changed dramatically at hypothyroidism. Our findings suggest that experimental hypothyroidism in rats has been obtained. Thyroid body disturbance in animals occurs at mercazolilum management, it shows by a decrease of hormonal state both in the lymph and in the blood.

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## ЕГЕУҚҰЙРЫҚТАРДА ГИПОТИРЕОЗ КЕЗІНДЕГІ ЛИМФА МЕН ҚАНДАҒЫ ГОРМОНДАР КОНЦЕНТРАЦИЯСЫНЫҢ ӨЗГЕРІСТЕРІ ЖӘНЕ БИОХИМИЯЛЫҚ КӨРСЕТКІШТЕРІНІҢ ЕРЕКШЕЛІКТЕРІ

**Аннотация.** Мақалада егеуқұйрықтардың лимфасы мен қанының гормоналды көрсеткіштеріне мерказолил препартының әсері қарастырылған. Зерттеуде көрсетілгендей, мерказолилді енгізгенен кейін егеуқұйрықтарда гипотиреоз белгілері байқалғанда кеуде арнасында лимфа ағысының төмендегені байқалады. Лимфа құрамында гормоналды және биохимиялық өзгерістер байқалды. Зат алмасу өзгерісі тек лимфада емес, сонымен бірге организмнің функционалды жағдайында байқалды. Эксперименталды гипотиреоз кезінде егеуқұйрықтардың лимфасы мен қанында реологиялық және физика-химиялық көрсеткіштердің өзгеретіндігі байқалды: тұтқырлық артты, қанның ұюы мен эритроциттер санының төмендеуі, қанда тромбоциттер мен лейкоциттер мөлшері артты. 2-ші тәжірибелік топтағы гипотиреозды егеуқұйрықтардың лимфасы мен қанында $T_3$, $T_4$ мөлшерінің төмендеуі және ТТГ артуы, яғни оларда гипотиреоз белгісінің пайда болғандығын көрсетті. Эксперимент нәтижесінде, гипотиреозды егеуқұйрықтар лимфасында $T_3$ мөлшері 45,7% және $T_4$ 35,6%-ға төмендегені, ал қанда бұл көрсеткіштер бақылау тобы жануарларымен салыстырғанда $T_3$ 43,5% және $T_4$ 41,6%-ға төмендегенін көрсетті.

**Түйін сөздер:** гормондар, қан, егеуқұйрық, лимфа, лимфа ағысы, тироксин, трийодтиронин.

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## ИЗМЕНЕНИЕ КОНЦЕНТРАЦИИ ТИРЕОИДНЫХ ГОРМОНОВ И ОСОБЕННОСТИ БИОХИМИЧЕСКИХ ПОКАЗЕТЕЛЕЙ ЛИМФЫ И КРОВИ У КРЫС ПРИ ГИПОТИРЕОЗЕ

**Аннотация.** В статье рассмотрено влияние препарата мерказолила на гормональный статус в лимфе и крови у крыс. В исследовании показано, что после ведения мерказолила и появление признаков гипотиреоза

у крыс наблюдалось снижение лимфотока из грудного лимфатического протока. Наблюдались изменения в гормональном и биохимическом составе лимфы. Наблюдались нарушения не только обмен веществ в лимфе, но и функциональной состоянии организма. При экспериментальном гипотиреозе у крыс наблюдались нарушения реологических и физико-химических показателей лимфы и крови: повышалось вязкость, снижалась свертываемость и число эритроцитов, увеличилась тромбоцитов и лейкоцитов в крови. У крыс 2-ой опытной группы с гипотиреозом приводило к возникновению снижению в содержании $T_3$, $T_4$ и повышение ТТГ в лимфе и крови, которые отражали возникновение у них состояния гипотиреоза. Эксперименты показали, что у крыс с гипотиреозом содержание $T_3$ снижалось на 45,7% и $T_4$ на 35,6% в лимфе, а крови $T_3$ на 43,5% и $T_4$ на 41,6% понижалось по сравнению с контрольной группой животных.

**Ключевые слова:** гормоны, кровь, крысы, лимфа, лимфоток, тироксин, трийодтиронин.

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