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SUBSTANTIATION OF MORPHOLOGY AND METABOLISM OF SPINAL STRUCTURES IN RATS WITH EXPERIMENTAL HYPOTHYROIDISM

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✓ ***Resume***

The study was conducted on 34 white laboratory rats weighing 150-200 g. In experimental animals, we obtained an experimental model of hypothyroidism by intragastric administration of one of the thyrostatics – mercazolil at a dose of 3 mg/ kg of animal weight. It was noted that in hypothyroid rats, both the level of markers of bone resorption and the marker of bone formation — bone alkaline phosphatase, reflecting a slowdown in remodeling processes, which ultimately leads to a decrease in bone mass, significantly decreases. The detected morphological changes in the bone-ligamentous structures confirm the negative effect of hypothyroxinemia on the condition of soft tissue structures at the sites of attachment to vertebrae.

Key words: bone-ligamentous structures, morphometry, experimental hypothyroidism.

ЭКСПЕРИМЕНТАЛ ГИПОТИРЕОЗДА КАЛАМУШЛАР УМУРТҚА ПОҒОНАСИ ТУЗИЛМАЛАРИНИНГ МОРФОЛОГИЯСИ ВА МЕТАБОЛИТИК ЎЗГАРИШЛАРИНИ АСОСЛАШ

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✓ ***Резюме***

Тадқиқот оғирлиги 150-200 г вазндаги 34 та оқ лаборатор каламушларда ўтказилган. Жониворларида экспериментал гипотиреоз модели тиреостатиклардан ҳисобланган мерказолилни 3 мг/кг тана вазнига мувофиқ ошқозон ичига киритиш йўли билан чақирилган. Экспериментал гипотиреозда суяк резорбцияси ва суякланиш маркерлари миқдорининг статистик аҳамиятли даражада пасайиши ва охир оқибат суяк вазнининг сезиларли пасайиши кузатилган. Аниқланган морфологик ўзгаришлар суяк-бойлам тузилмалари ривожланишига, яъни умуртқаларга юмшоқ тўқималарнинг бирикиш жойларига гипотироксинэмиянинг сальбий таъсирини асослайди.

Калит сўзлар: суяк бойлам тузилмалари, морфометрия, экспериментал гипотиреоз.

ОБОСНОВАНИЕ МОРФОЛОГИИ И МЕТАБОЛИЗМА СТРУКТУР ПОЗВОНОЧНИКА У КРЫС ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ГИПОТИРЕОЗЕ

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✓ ***Резюме***

Исследование проведено на 34 белых лабораторных крысах весом 150-200 г. На подопытных животных получена экспериментальная модель гипотиреоза путем внутрижелудочного введения одного из тиреостатиков – мерказолила в дозе 3 мг/кг массы животных. Отмечалось, что у гипотиреоидных крыс статически значимо снижается как уровень маркёров костной резорбции, так и маркёра костеобразования, что в конечном итоге приводит к снижению костной массы. Обнаруженные морфологические изменения в костно-связочных структур подтверждают негативные влияние гипотироксинемии на состояние мягкотканных структур на местах прикрепления к позвонкам.

Ключевые слова: костно-связочные структуры, морфометрия, экспериментальный гипотиреоз.

Relevance

All over the world, thyroid diseases occupy one of the leading places in the pathology of endocrine organs. The need to study the subtle mechanisms of the pathogenesis of this disease, accompanied by a violation of all types of metabolism, is explained by the fact that substitution therapy used in the treatment of hypothyroidism does not fully provide the necessary balance of thyroid hormones and a full life. Apparently, hormonal correction alone is not enough to achieve optimal quality of life in patients with congenital or acquired hypothyroidism [1, 5, 6].

Hypothyroidism is associated with the risk of osteoporosis. Hypothyroidism leads to a decrease in the rate of bone remodeling with an increase in the cycle time of this process [2, 3, 4, 5]. The imbalance of remodeling cycles in hypothyroidism leads to a decrease in bone mass, a violation of the microstructure with a deterioration in bone quality and an increased risk of fractures.

All of the above allows us to conclude that the problem we are developing is poorly understood and its relevance due to the prevalence of deformities and injuries of bones and in particular vertebrae, the lack of their morphofunctional justification.

The purpose the study: Study of morphofunctional and metabolic features of the bone-ligamentous tissue of the spine in rats with experimental hypothyroidism.

Materials and methods

The study was conducted on 34 white laboratory rats weighing 150-200 g in strict accordance with ethical standards and recommendations for humane treatment of laboratory animals, reflected in the European Convention for the Protection of Vertebrates Used for Experimental and Other Scientific Purposes. The animals were kept in standard vivarium conditions under natural light, on a standard diet of laboratory animals. In experimental animals, we obtained an experimental model of hypothyroidism by intragastric administration of one of the thyrostatics – mercazolil at a dose of 3 mg/ kg of animal weight. Animals under light ether anesthesia were taken out of the experiment on the 30th day. The content of calcium, magnesium, phosphorus in blood serum was determined by colorimetric methods and sets of HUMAN reagents (Germany), markers of bone remodeling - C-terminal telopeptides of type I collagen, bone alkaline phosphatase (Metra BAF Kit reagents from Quidel Corporation), levels of thyrotropin, total T3 and thyroxine, testosterone (reagents of Vector-Best CJSC, Russia).

For histological examination, pieces of the bone-ligamentous structure of rats were taken in the area of attachment of soft tissues to the vertebrae. The pieces were fixed in 10% neutral formalin for 7 days, then passed through alcohols of increasing strength and poured into paraffin. Sections 5-6 microns thick were prepared. The obtained sections were stained with hematoxylin and eosin, picrofuxin according to Van Gieson.

Static processing of the results was carried out using the Statistica 6.0 software package (Stat Soft) with the calculation of the arithmetic mean (M), the standard error of the mean (m) with an assessment of the significance of group differences according to the Student's t-criterion.

Results and discussion

The obtained results of the analysis of thyrotropin, T3 and thyroxine in the blood serum of the experimental group of animals indicate the development of hypofunction of the thyroid gland. In the rats of the experimental group, a decrease in the secretion of T3 and thyroxine was observed against the background of an increase in the content of thyrotropin (Table 1).

The content of thyroid-stimulating and thyroid hormones in the blood serum of rats with experimental hypothyroidism

Hormones	Control group	Experimental group, n=24
Thyrotropin, mkME/l	1,12±0,098	1,89±0,092**
Total thyroxine nmol l	77,2±3,26	59,8±2, 38*
Total triiodothyronine, nmol/l	2,94±0,16	1,67±0,095**

*Note * - P < 0,05; ** - P < 0,005*

Pronounced changes in markers of bone metabolism in the blood serum of the experimental group of rats are determined (Table 2). Both the level of markers of bone resorption β-CTX and the marker of bone formation — bone alkaline phosphatase, significantly decreases, reflecting a slowdown in remodeling processes, which ultimately leads to a decrease in bone mass [3, 5].

Table 2

The content of indicators of mineral metabolism and markers of bone metabolism in experimental hypothyroidism in rats

Indicators	Control group, n=10	Experimental group, n=24
Ca total, mmol/l	2,25±0,090	2,02±0,085*
P, mmol/l	1,84±0,044	1,68±0,054*
Mg, mmol/l	0,92±0,058	0,81±0,041*
Bone alkaline phosphatase, ME/l	6,4±0,54	4,8±0,32**
β-CTX, ng/l	0,90±0,05	0,76±0,029**

*Note : *- P < 0,1; **- P < 0,5*

There were no statistically significant changes in the serum levels of calcium, phosphorus and magnesium in animals with hypothyroidism, although there was a tendency to decrease their levels.

As a result of morphological examination, the formation of bone tissue with solid architectonics was observed in animals of the control group. The compact substance is externally covered with a periosteum consisting of outer and inner layers. The outer layer is formed by dense fibrous tissue, the fibers are oriented parallel to the bone surface. The inner layer is formed by loose fibrous tissue. Fibroblasts and osteoblasts, as well as blood capillaries, are found among the thin collagen fibers. The outer common plate is located under the periosteum, the inner common plate is also deeper defined. On the side of the bone marrow there is an endost containing osteoblastic cells. In the spongy substance of the bone, the anastomosing bone trabeculae differ in a variety of thickness and stainability, mainly inactive osteoblasts. There are pronounced branching of bone trabeculae with detachment of the red bone marrow from bone structures. In trabeculae, basophilic wavelike lines are determined, resulting from the processes of demineralization and violation of mineralization of the intercellular substance of bone tissue.

The obtained morphological data indicate that with prolonged administration of mercazolil to experimental animals, changes in the histological structure are revealed in the bones, characterizing the development of destructive and degenerative processes with impaired mineralization of the intercellular matrix.

The presence of a boundary area between the ligamentous and fibrous-cartilaginous tissues is very characteristic. At the same time, the fibers of the first have a wavy configuration, and the cellular elements are represented by both fibrocytes and fibroblasts, the fibers of the second are rectilinear and oriented at an angle, and the oval-shaped cellular elements with dense cytoarchitectonics have a volumetric cytoplasm, an oval or oval-round nucleus. We have identified vascular glomeruli in the border region, whereas they are absent in the fibrous cartilage zone.

It can be assumed that due to the interaction of cells and intercellular matter, interstitial connections are carried out. Nevertheless, the results of the conducted studies show that with the development of hypothyroidism, there is a violation of bone remodeling and mineral metabolism.

The reason for the development of the described morphological changes is a violation of the basal metabolism. Thyroid hormone deficiency leads to the development of stromal vascular carbohydrate dystrophy. Changes occur in the walls of blood vessels due to the accumulation of glycoproteins and glucosaminoglycans in them, disorders develop in the microcirculatory system, which leads to

hypoxia. Hypoxia is the main pathogenetic factor in the development of dystrophic and destructive changes in fibroblastic cells of ligamentous structures.

Conclusions

1. Hypothyroid states in experimental animals lead to the development of structural changes in bones in general and vertebrae in particular. Signs of destructive and degenerative processes associated with a violation of the state of the intercellular matrix appear in the bones, which undoubtedly leads to a decrease in bone strength.
2. As a result of modeling experimental hypothyroidism, the content of thyroid hormones (triiodothyronine and thyroxine) in the blood serum decreases with an increase in the concentration of thyrotropin.
3. Experimental hypothyroidism is characterized by a violation of the processes of bone metabolism, which is reflected in a decrease in serum levels of Ca, P and Mg.
4. Severe destructive and dystrophic changes of immature cells are noted in the border areas where soft tissue structures are attached to the vertebrae. The detected morphological changes in tendons confirm the available literature data on the negative effect of hypothyroxinemia on the condition of tendons and ligaments at the sites of attachment to vertebrae.

LIST OF REFERENCES:

1. Kozlov V.N. Thyroid transformation in modeling the endemic effect in white rats in an experiment. //Siberian honey. w. 2006; (5): 27-30.
2. Nochvnaya L.B., Pavlenko O.A., Kalinina O.Yu., Stolyarov V.A. The state of bone tissue in patients with newly diagnosed hypothyroidism. //Siberian honey. w. 2011; 26 (4): 189-193.
3. Rasulov H.A., Khidirova G.O. Structural prerequisites for the formation of paraarticular structures of rats in experimental hypothyroidism. //”EDICATIO” Russia. Novosibirsk. № 3. (10).2015. – Pp. 28-30.
4. Rasulov H.A. Experimental hypothyroidism kalamushlar kalkonsimon bezi va oek pilaring morphofunctional hususiyatlarini solishtirma baoлolash //"Eurasian Bulletin of Pediatrics" tibbiy ilmiy-innovation journal. 2019; 100-107 betlar.
5. Rasulov H.H. Development of thyroid cells under thyroostatic load // "American Journal of Medicine and Medical Sciences" 2019. 9 (11) 453-456.
6. Bassett J.H., Boyd A., Howell P.G., et al. Optimal bone strength and bone mineralization require type 2 iodothyronine deiodysal in the osteoblast. Proc. Natl. US Academy of Sciences. 2010; 107 (6): 7604-7609.

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