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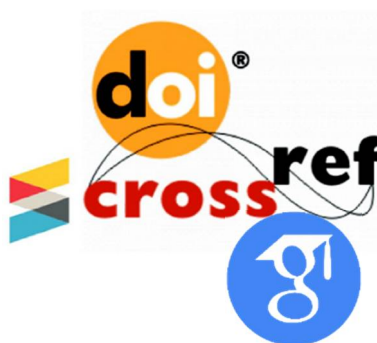
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MORPHOLOGICAL STRUCTURE OF THE THYROID GLAND OF WHITE RATS IN CHEMOTHERAPY OF BREAST CANCER



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ABSTRACT

Paclitaxel used in chemotherapy of breast cancer is an inhibitor of mitosis and is obtained from plants. They block cell division, disrupt the function of microtubules and some enzyme proteins. They change the metabolism of amino acids and some other substances, such as nucleic acids, fat synthesis, and also affect cellular respiration. When we modeled breast cancer in 6-month-old rats and carried out chemotherapy using paclitaxel, we encountered various pathomorphological changes.

Key words: Cancer, chemotherapy, follicle, thierocyte, hormone, B-cell, C-cell, thyroid substance, epithelium, stroma, parenchyma.

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МОРФОЛОГИЧЕСКАЯ СТРУКТУРА ЩИТОВИДНОЙ ЖЕЛЕЗЫ БЕЛЫХ КРЫС ПРИ ХИМИОТЕРАПИИ РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ

АННОТАЦИЯ

Паклитаксел используемый в химиотерапии рака молочной железы является ингибитором митоза и получена из растений. Они блокируют деление клеток, нарушают функцию микротрубочек и некоторых ферментных белков. Они изменяют метаболизм аминокислот и некоторых других веществ, таких как нуклеиновые кислоты, синтез жиров, а также влияют на клеточное дыхание. Когда мы моделировали рак молочной железы у 6-месячных крыс и проводили химиотерапию с использованием паклитаксела столкнулись с различными патоморфологическими изменениями.

Ключевые слова: Рак, химиотерапия, фолликул, териоцит, гормон, В-клетка, С-клетка, тиреоидное вещество, эпителий, строма, паренхима.

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SUT BEZI SARATONI KIMYOTERAPIYADA OQ ZOTSIZ KALAMUSHLAR QALQONSIMON BEZINING MORFOLOGIK TUZILISHI

ANNOTATSIYA

Sut bezi saraton kasalligi kimyoterapiyasida qo'llaniladigan paklitaksel dori vositasi mitoz ingibitorlari sanalib, ushbu guruh kimyoterapiya preparatlari o'simliklardan olinadi. Ular hujayra bo'linishini bloklaydi, mikronaychalar va ba'zi ferment oqsillari funktsiyasini buzadi. Ular aminokislotalar va ba'zi boshqa moddalar, masalan nuklein kislotalar, yog'lar sintezi almashinuvini o'zgartiradi va hujayra nafas olishiga ta'sir qiladi. 6 oylik kalamushlarda sut bezi saraton kasalligini modellashtirib, paklitaksel dori vositasi yordamida kimyoterapiya qo'llaganimizda turli ko'rinishdagi patomorfologik o'zgarishlarga duch keldik.

Kalit so'zlar: Saraton, kimyoterapiya, follikula, teriotsit, garmon, B-hujayra, C-hujayra, teroid modda, epitelii, stroma, parenxima.

Relevance. Over the past decades, the rapid increase in the incidence of cancer worldwide has changed the way scientists view cancer and its treatment. The increase in cancer incidence requires intensification of chemotherapy regimens in some cases and creates the basis for the development of new drugs, as well as methods of influencing tumor cells [2,7]. Damage to the thyroid gland in cancer is mainly due to a change or increase in the concentration of chemotherapeutic drugs, which increases their toxicity, as well as prolongs hospital stay and increases mortality rates [9,14].

The increase in the number of cancer cases in the world requires the development of new drugs and methods of influencing tumor cells, and in some cases, the intensification of chemotherapy regimens. Despite the successes achieved in the treatment of tumor diseases, treatment toxicity remains a serious problem [4,10,12]. The spectrum of thyroid diseases is very wide: from minimal structural changes to significant functional and morphological diseases that reduce the quality and duration of life of patients [1,5,13].

Currently, the incidence of thyroid cancer is growing worldwide. The growth rate of detection of this disease is 4% per year. Today, this pathology is one of the most common malignant tumors of the endocrine system, accounting for 2.2% of all oncological diseases [3,11].

The occurrence of thyroid diseases is explained by many endogenous and exogenous factors. Among the most studied environmental factors, a number of deficiencies in iodine consumption can be distinguished. However, even a slight increase in iodine consumption in previously iodine-deficient population groups changes the nature of the observed thyroid pathology in different directions [6,8].

The aim of the study. Study of morphological changes in the thyroid gland during chemotherapy for breast cancer.

Materials and methods of the study. The experiments were conducted on 70 white mongrel female rats in vivarium conditions. Six-month-old rats participated in the experiment. Ethical requirements for the use of animals were observed during the experiments. Before the experiments, all sexually mature rats underwent a week-long quarantine and, after excluding somatic and infectious diseases, were transferred to a vivarium with standard conditions. During the experiment, the behavior and physiological state of the animals in the standard and experimental groups were observed. The rats were divided into 2 groups (n = 70): control group 1 (n = 40); 2 (n = 30) - groups of experimental animals were exposed to the carcinogen 7,12-dimethylbenzanthracene in order to induce mammary gland cancer in the experimental groups from the age of 6 months. The achieved success rate was 68.9%, i.e., 21 rats were induced to have breast cancer by subcutaneous injection of the carcinogen 7,12-dimethylbenzanthracene at a dose of 0.1 mg into the mammary gland of 30 female rats. In the second group (n = 21), rats with cancer were intravenously injected with paclitaxel at a dose of 0.2 mg/kg.

During the experiment, the dynamics of the rats' body weight, their general condition and behavior were observed. No deviations in the general condition and behavior of the animals were

observed. After this, the experimental animals were weighed at the appropriate time in the morning, killed by decapitation under ether anesthesia. The animals were killed in accordance with international recommendations for conducting medical and biological research using laboratory animals.

The research methods included organometric, histological, microscopic and statistical methods.

Using organometric, histological and microscopic methods, the indices of thyroid gland morphogenesis at different levels of structure (organ, tissue and cellular) were studied in white rats of different ages. Statistical (methodological) information was used to process the research results.

After extraction, the thyroid gland was cleaned and after organometry, it was preserved in a 10% solution of neutral formalin. After fixation, the preparations were washed in running water for one hour. The materials were poured into paraffin blocks according to the standard method and dehydrated with a highly concentrated alcohol solution.

Results of the study. The thyroid gland was located in the front part of the neck of white male rats and with the help of connective tissue it is attached to the trachea and larynx. The thyroid gland consists of two lobes - right and left, as well as the neck connecting them. Macroscopically, the thyroid gland has the shape of a butterfly, while the upper edge of the thyroid lobes reaches the larynx, and the lower edge corresponds to the semicircles of the V-VII trachea.

From the outside, the thyroid gland is covered with a fibrous capsule and the capsule is thickened. And the capsule created trabeculae and they penetrated deep into the inner part of the gland. It is part of the stroma of the thyroid gland and contains blood vessels and nerves. Structural and functional unit of the thyroid gland follicles changed shape, acquired different outlines and follicles decreased in size.

Thyrocytes are the main cells of the organ, these cells have decreased in size and these follicular epithelial cells participate in the formation of the organ parenchyma. Follicular epithelial cells in their basal part are tightly surrounded by a dense network of capillary vessels and provide their connection. And the apical surfaces are facing the cavity of the follicle and their activity is reduced. The structures connecting the lateral surfaces with neighboring cells on the side have weakened, and the intercellular distances have increased. On the apical surface, the number of microvilli is reduced. These cells were attached to the wall of the basal membrane of the follicles and formed the wall of the follicles. In the thyroid gland, the follicles are located in different orders throughout the gland and the formation of colloidal substances in their cavities is absent.

Violation of the formation of colloidal substance in the spaces of the follicles indicates a violation of the secretion of thyroid hormones. Around the follicles, the capillary blood vessels have formed a mesh and they are damaged.

The shape of the thyrocyte cells appears as flat and cuboidal in accordance with the inactive state of the thyroid gland of white rats treated with paclitaxel at a dose of 0.2 mg / kg during chemotherapy for breast cancer. A decrease in the amount of colloidal substance in the cavity of the follicles is confirmed by the disruption of the formation of colloidal substance in the follicles. Micropreparations stained with hematoxylin and eosin showed white granular formations (Fig. 2).

In the experimental group of breast cancer chemotherapy, the diameter of thyroid capillaries in the central part of 6-month-old white rats ranged from 6.85 μm to 12.74 μm , an average of 9.48 ± 0.23 μm , and the diameter of capillaries in the peripheral part ranged from 5.47 μm to 10.39 μm , an average of 7.83 ± 0.1 μm . The density of the number of capillaries in the central part ranged from 94.76 to 29.45, an average of 112.34 ± 2.63 , the number of capillaries in the peripheral part ranged from 76.68 to 86.39, an average of 81.92 ± 2.43 . The surface of the thyroid gland in the central part of the capillary cross-section varied from 8.08 μm^2 to 12.67 μm^2 , on average 10.28 ± 0.82 μm^2 , the surface of the capillaries in the peripheral part varied from 5.69 μm^2 to 9.72 μm^2 , on average 7.76 ± 0.28 μm^2 . The height of the thyroid epithelium in the central part varied from 4.89 μm to 6.75 μm , on average 5.5 ± 0.24 μm , and the height of the thyroid epithelium in the peripheral part varied from 4.17 μm to 5.73 μm , on average 4.91 ± 0.15 μm . The number of interfollicular C-cells in the central part ranged from 5.93 to 9.89, with an average of 7.84 ± 0.25 , the number of C-

cells in the peripheral part ranged from 15.73 to 21.18, with an average of 18.43 ± 0.27 , the number of B-cells of the thyroid follicle in the central part ranged from 8.91 to 12.29, with an average of 10.23 ± 0.76 , the number of B-cells in the peripheral part ranged from 6.35 to 10.73, with an average of 8.47 ± 0.07 . The follicle diameter in the central part of the thyroid gland varied from 25.68 to 37.16 μm , with an average of $31.09 \pm 1.76 \mu\text{m}$, and in the peripheral part it varied from 33.57 to 39.96 μm , with an average of $36.74 \pm 0.19 \mu\text{m}$. The follicle surface in the central part of the gland varied from 706.97 μm^2 to 1256.43 μm^2 , with an average of $983.58 \pm 27.63 \mu\text{m}^2$, and in the peripheral part it varied from 1159.26 μm^2 to 1379.35 μm^2 , with an average of $1268.25 \pm 26.71 \mu\text{m}^2$.

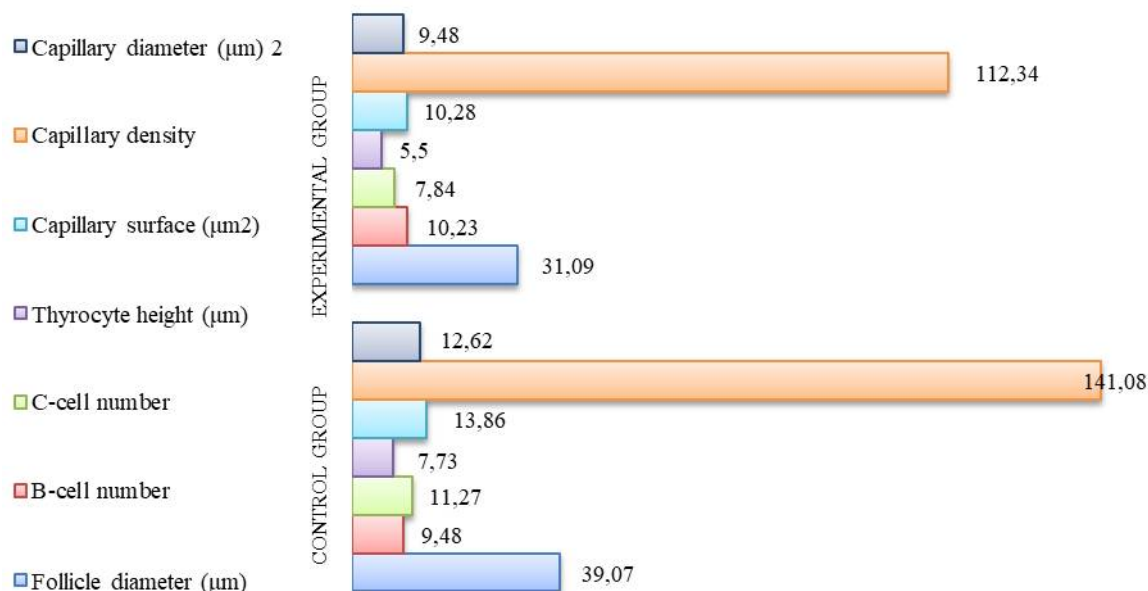


Figure 1. Dynamics of thyroid gland parameters in animals of the experimental group.

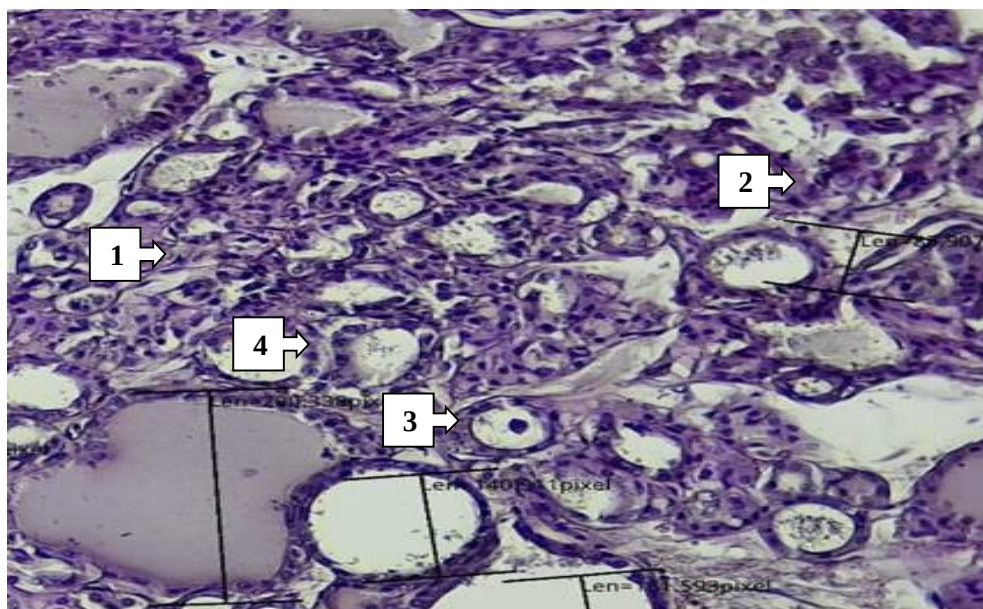


Figure 2. Microscopic image of the thyroid gland of 6-month-old white outbred rats of the experimental group. Hematoxylin and eosin staining (OK 10X40 OB). 1-islets of the thyroid gland, 2-follicular C-cells, 3-impaired formation of colloidal substance in the follicular space, 4-thyrocytes.

When analyzing the ratio of components of thyroid follicles during chemotherapy for breast cancer, thyrocyte cells in the central part ranged from 29.47% to 39.18%, an average of $34.04 \pm 1.74\%$, and in the peripheral part ranged from 27.05% to 35.07%, an average of $31.53 \pm 0.92\%$. The colloidal substance in the central part varied from 27.93% to 32.15%, with an

average of $30.02 \pm 0.7\%$, and in the peripheral part it varied from 32.63% to 38.51%, with an average of $35.48 \pm 0.7\%$. The thyroid stroma in the central part varied from 13.92% to 17.48%, with an average of $15.47 \pm 0.38\%$, and in the peripheral part it varied from 9.1% to 11.81%, with an average of $10.4 \pm 0.74\%$ (Table 1).

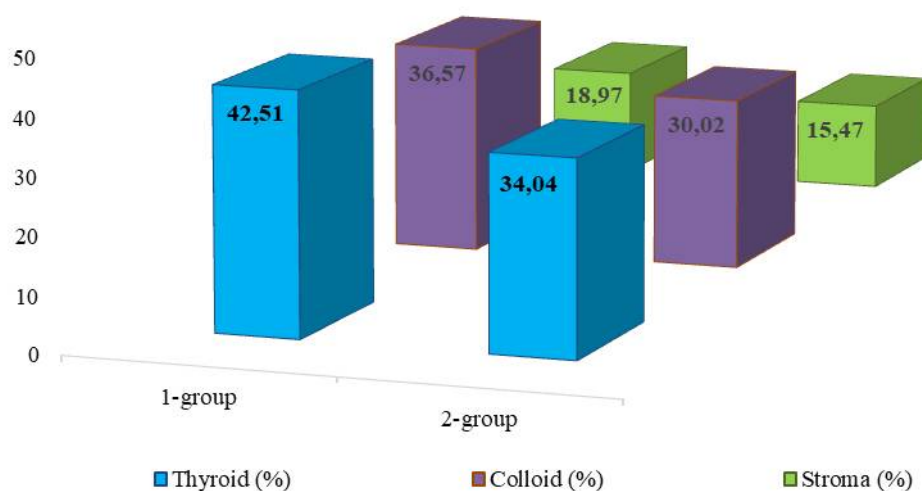


Figure 3. Dynamics of thyroid gland parameters in animals of the experimental group.

In the experiment, the size of parafollicular or C-cells in the thyroid gland of white rats decreased during chemotherapy with paclitaxel at a dose of 0.2 mg/kg during breast cancer. They produce protein hormones thyrocalcitonin, somatostatin and biogenic amines-serotonin. These cells are mainly located on the posterior surface of the lobes of the thyroid gland, which is adjacent to the pharynx. Their number decreased. The parathyroid gland, inferior thyroid artery and recurrent laryngeal nerve are located behind the lobes of the gland.

In addition, there is an increase in the number of interfollicular islets, where thyrocytes are collected in the parenchyma of the thyroid gland. They do not have a follicle cavity. The size of the thyrocytes of the islets decreases and the production of thyroid hormones decreases. As the functional activity of the thyroid gland decreases, the activity of the islets decreases and the ability of thyrocytes to form colloidal substance decreases. Thus, the formation of new follicles from the islets has ceased. Among the islet thyrocytes, we see that the number of C-cells is also reduced.

Table 1

Histomorphometric indices of the thyroid gland of white outbred rats of the experimental groups.

Parameters	6 month old rats	
	Central part	Peripheral part
Capillary diameter (μm)	$9,48 \pm 0,23$	$7,83 \pm 0,1$
Capillary density	$112,34 \pm 2,63$	$81,92 \pm 2,43$
Capillary surface (μm^2)	$10,28 \pm 0,82$	$7,76 \pm 0,28$
Thyrocyte height (μm)	$5,5 \pm 0,24$	$4,91 \pm 0,15$
C-cell number	$7,84 \pm 0,25$	$18,43 \pm 0,27$
B-cell number	$10,23 \pm 0,76$	$8,47 \pm 0,07$
Follicle diameter (μm)	$31,09 \pm 1,76$	$36,74 \pm 0,19$
Follicle surface (μm^2)	$983,58 \pm 27,63$	$1268,25 \pm 26,71$
Thyroid (%)	$34,04 \pm 1,74$	$31,53 \pm 0,92$
Colloid (%)	$30,02 \pm 0,7$	$35,48 \pm 0,7$
Stroma (%)	$15,47 \pm 0,38$	$10,4 \pm 0,74$

In practice, in breast cancer chemotherapy, we see that the blood supply is reduced by decreasing the diameter of the arteries, given the large and active blood supply to the thyroid gland due to its function. The cross-sectional area of the upper and lower pairs of thyroid arteries of the thyroid gland also decreases in accordance with the decrease in diameter. In some cases, we can also see the branches of the lower thyroid artery.

The thyroid gland is innervated by nerve fibers of the upper, middle and lower branches of the sympathetic trunk in the cervical region. The nerves of the thyroid gland penetrate the gland through the vein and form nerve glomeruli. At the same time, the nerve networks of the gland also function as part of the upper and lower laryngeal nerves of the parasympathetic nervous system.

In white rats with chemotherapy with paclitaxel at a dose of 0.2 mg / kg for breast cancer, the thyroid follicles are filled with a normal amount of keloids, but the interlobular connective tissue is poorly distinguishable when stained according to Van Gieson. Comparing the central and peripheral parts of the thyroid gland of rats of the experimental group, epithelial cells are more reduced in the central part, and the amount of colloid substance is less formed in the peripheral part.

Conclusion. The shape of the thyrocyte cells appears as flat and cuboidal in accordance with the inactive state of the thyroid gland of white rats under chemotherapy with paclitaxel at a dose of 0.2 mg / kg of breast cancer.

In the experiment, the number and size of parafollicular or C cells in the thyroid gland of white rats under chemotherapy of breast cancer.

The veins of the thyroid gland drain blood through the paired superior, middle and inferior thyroid veins and bleeding is observed through the lowest odd thyroid vein. In the thyroid gland, the lymphatic vessels are visible as a branched network. The lymphatic vessels were also damaged, starting as a three-dimensional network and forming connections with four to five follicles.

B cells or Ashkenazi-Hurtel cells of the thyroid gland, which are not foreign cells and are quite large thyrocyte cells. They differ from other thyrocytes and have granular nuclei that are well stained in the cytoplasm, are located in the center of the cell and have a round shape. These cells are usually found in the parenchyma of the thyroid gland in very small quantities. B cells are found in large quantities mainly in old organisms. In our experience, an increase in the number of B cells was observed when using chemotherapy for breast cancer. This indicates that the number of active thyrocytes has decreased and their function is performed by B cells.

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