Features of the thyroid gland structural components remodeling in the toxemia stage after experimental thermal injury

Koritskiy V.G., Nebesna Z.M.
SHEI "I. Horbachevsky Ternopil State Medical University Ministry of Health of Ukraine“, Ternopil, Ukraine

Thermal injury causes severe structural and metabolic disturbances not only of the skin itself, but also of all organs and systems of the affected organism, and is the manifestation of a complex symptom complex - a burn disease. Of particular importance in patients with burns are changes in the endocrine system. The aim of the study was to establish the microscopic and electron-microscopic reorganization of the components of the thyroid gland of animals after thermal damage on 14 day after experimental thermal injury. A III degree burn was applied under ketamine anesthesia with copper plates heated in boiled water to a temperature of 97-100°C. The size of the lesion area was 18-20% of the epilated surface of the body of rats. An experimental study of the structural components of the thyroid gland after a burn injury was performed on laboratory white male rats weighing 160-180 g. Rats euthanasia was performed after ketamine anesthesia by decapitation. In the experiment, the study of the microscopic and submicroscopic state of the follicles and hemocapillaries of the thyroid gland after thermal injury of the III degree. It has been established that in the toxemia stage after the application of the burn injury on 14 day (late toxemia stage), significant destructive and degenerative changes are found in the thyrocytes of the wall of the follicles and hemocapillaries, the organ acquires a macrofollicular structure. The height of thyrocytes decreases, the nuclei and organelles of cytoplasm are significantly damaged, the number and height of microvilli on their apical surface decreases, which negatively affects the cell's secretory cycle and transcapillary organ metabolic processes. The established destructive changes in the blood capillaries and thyrocytes of the follicles are the morphological manifestation of the suppression of the secretory activity of the thyroid gland during thermal injury and corresponds to the hypofunctional state of the organ.

Keywords: thyroid gland, microscopic and submicroscopic changes, thermal skin injury.

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CORRESPONDING AUTHOR
E-mail: nebesna_zm@tdmu.edu.ua
Nebesna Z.M.

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Introduction
The study of the pathogenesis of organs in the composition of the body systems after severe thermal trauma is an urgent problem of combustiology [12, 15, 21]. Today, the frequency of burns in developed countries is 1: 1000 per year, and the mortality, despite the use of modern treatments, remains fairly high and ranges from 5.9% to 21.2% [12, 13, 15, 17, 21, 24, 25, 26]. In the case of severe thermal trauma, there is a number of factors that lead to sepsis and multiple organ failure: microcirculation disorder, presence of necrotic tissues inhabited by wounds, endogenous intoxication, activation of lipid peroxidation, development of syndrome of systemic inflammatory response, DIC, etc. [2, 3, 5, 6, 7, 10, 13, 14, 20]. It has been established that in the complicated and inadequately studied pathogenesis of burn disease one of the main places has endogenous intoxication, which is the result of proteolysis of damaged tissues and alteration of histo-hematological barriers. Hormonal changes are involved not only in triggering mechanisms of the pathogenesis of burn disease, but also in the development of compensatory-adaptive responses and the mobilization of protective functions of the organism [4, 11, 16, 19, 23]. Particularly important role in this complex process belongs to the systems of the pituitary gland - adrenal cortex, the pituitary gland - thyroid gland. They represent not only an intermediate link in the efferent pathways of the nerve regulation, but also are peripheral endocrine effector that provides a balance of metabolic and regenerative processes.

Today, we know about the ability of the thyroid gland to...
morphofunctional reorganization under the influence of endo- and exogenous factors [1, 18, 19]. However, the status of this organ in the process of adaptation processes remains poorly understood.

The aim of the work was to establish microscopic and electron microscopic reorganization of the components of the thyroid gland of animals after thermal lesions in the stage of toxemia after an experimental thermal trauma.

Materials and methods

Experiments were conducted on 20 sexually mature white male rats. The animals were kept on a standard diet by the vivarium of the State Higher Educational Institution "I. Horbachevsky Ternopil State Medical University Ministry of Health of Ukraine". Animal care and all manipulations were conducted in accordance with the provisions of the "European Convention for the Protection of Vertebrate Animals Used for Experiments and for Other Scientific Purposes" (Strasbourg, 1986), as well as in accordance with the provisions of the "General Ethical Principles of Experiments on animals", adopted by the First National Congress on Bioethics (Kyiv, 2001).

Burns of the third degree were applied under ketamine anesthesia with copper plates heated in boiled water to a temperature of 97-100°C [7, 22]. The size of the lesions was 18-20% of the shaved surface of the body of rats. At daily inspection, we monitored their overall condition, the degree of manifestation of local changes in the area of burn wound, body weight and mortality. The object of the study was thyroid gland. To study micro and submicroscopic changes, animals were decapitated under ketamine anesthesia at 14 day, which, according to presentations, corresponds to the stage of late toxemia of burn disease [21].

Material for microscopic research was taken according to the generally accepted method [8]. Sections of the thyroid gland were fixed in a 10% neutral formalin solution, dehydrated in alcohols of increasing concentration, poured in paraffin blocks. The cut-offs of 5-6 microns thickness were stained with hematoxylin-eosin and methylene blue [8]. The histological preparations were studied using MIKROmed SEO SCAN light microscope and photo-documented with a Vision CCD Camera with a histologic image display system. For electron microscopic studies, we took pieces of the thyroid gland, fixed them in a 2.5% solution of glutaraldehyde, fixed with a 1% solution of osmium tetroxide on phosphate buffer. Further processing was carried out in accordance with the generally accepted method [8]. Ultra-thin sections made on ultramicrotome UMPT-7 were contrasted with uranyl acetate, lead citrate according to the Reynolds method and studied in an electron microscope of PEM-125K.

Results

According to conducted histological studies of experimental animals, after an experimental thermal trauma in the organ, there are heterogeneous in shape and size follicle. Prevailing large over-stretched with a dense, oxyphilsic colloid, in which vacuole resorption is absent. Thyrocytes of such follicles have a flattened form and hyperchromic, picnotically altered nuclei. Desquamation of the thyroid gland epithelium is also revealed in the lumen of the follicle (Fig. 1, Fig. 2).

In the central parts of the lobules, also observed single deformed, medium and small follicles, in which the thyrocytes have cubic or prismatic form, light cytoplasm, normochromic, centrally located nuclei. The colloid in such follicles was not much, it was loose and acquired a disperse form, numerous and large vacuoles of resorption, which sometimes merged into illuminated strips, were found. Inter-follicular, interstitial of connective tissue is moderately swollen.

During this period of the experiment, changes in the organ vascular and microcirculatory system, manifested by plethora, stasis, are detected. The expansion capillaries are
densely surrounded by follicles and has expanded and narrowed areas of their lumens. In their wall there are hypertrophied, edematous endothelial cells, as well as densified, picnotic. Around the hemocapillaries there is significant perivascular space.

Submicroscopically in enlarged follicles, thyrocytes have a flattened form, poorly contoured borders between the cells. There are no microvilli on their luminal surface. In the swollen, enlightened cytoplasm, organelles are numb and significantly destructively altered. In the flat form of nuclei there is an electron-transparent karyoplasm, which includes small ectopic nucleoli. The outer membrane of nuclear membrane sometimes expands, increasing perinuclear space. Observed areas of a condensed osmophilic karyoplasm, which reduces the clarity of the nuclear membrane. Also decreases the number of nuclear pores. On the surface of the fragmented and thickened tubules, the granular endoplasmic net has little ribosomes, as well as free ribosomes and polysomes in the cell cytoplasm. Expansion and deformation of the granulosa endoplasmic mesh channels lead to the formation of large cavities of irregular shape, limited by unclearly contoured membranes (Fig. 3).

Circular vesicles of the Golgi complex sometimes expanding or vice versa considerably narrowing, their length extends. Available, primary and secondary lysosomes, which are freely located in the cytoplasm and near the Golgi complex. Damage to the mitochondria is accompanied by significant illumination of the matrix. A small number of cristae is contained in swollen electron-transparent mitochondria. Also, an irregular shape of the mitochondria with uneven contours of the outer membranes, which may be partially destroyed, is observed. Separate mitochondria have the appearance of large vacuoles. In the cytoplasm of the cells, an insignificant amount of apical grains is detected and large, irregularly shaped, vacuolic structures are filled with colloid (Fig. 4).

The need to intensify the metabolic processes of the affected organism causes the activation of the work of the synthetic apparatus of the thyrocytes: the tubules and circular vesicles of the granular endoplasmic net, which are concentrated at the basal pole, numerical polysomes, and the mitochondria have clearly contoured cristae, are expanding. The membranes of the basal part of the thyrocytes form a kind of labyrinth of branches, which are compensatory adapted changes to ensure the withdrawal of the hormone (Fig. 4).

It has been established that at separate sites in the follicles, the thyrocytes do not adhere tightly to the wall of the

Fig. 3. Submicroscopic organization of the wall of the follicles of the thyroid gland 14 days after the experimental thermal trauma. Enlargement of the follicle with dense colloid (1), flat nucleus (2) and cytoplasm of thyrocyte (3), single microvilli on the apical surface of the cell (4), branching of the basal surface of the thyrocyte (5), basement membrane (6). x9000.

Fig. 4. Submicroscopic organization of the thyroid gland 14 days after the experimental thermal trauma. Enlargement of the follicle with colloid (1), osmophilic, fused nucleus (2) and cytoplasm (3) of the thyrocyte, large vacuolic structures (4), endothelial cell (5), erythrocyte in the lumen of the capillary (6). x7000.

Fig. 5. Submicroscopic organization of the wall of the thyroid gland 14 days after the experimental thermal trauma. Enlargement of the capillary with erythrocytes (1), endothelial cell (2), capillary basement membrane (3), flat form of thyrocyte cytoplasm (4), primary and secondary lysosomes (5), microvilli on the apical surface of the cells (6), branching of the basal surface of the thyrocytes (7). x12000.
hemocapillaries, and separate from them by layers of connective tissue. Connective tissue strip looks edematous, has an electronically bright amorphous component and separate collagen fibrils.

The ultrastructure of blood capillaries is changing. Most of them have extensive erosions filled with erythrocytes. Endothelial cells are significantly altered, their nuclei are picnotically altered, they have elongated shape and deep invaginations of nuclear membrane. The perinuclear space between the membranes of the nuclear membrane is poorly expressed. The content of condensed heterochromatin increases, it forms large osmophilic clusters. In the cytoplasm there are few organelles and foamy cystic bubbles, their plasmalemma of the luminal surface is uneven and microvilli are single. In the cytoplasmic subtle areas, there is little fenestra. Such hemocapillaries are limited by narrow basal membranes (Fig. 4, Fig. 5).

**Discussion**

Histological studies have shown that changes in the structural components of the thyroid gland follicles during the experimental thermal trauma develop in the background of microcirculation disturbance, which is to some extent consistent with the studies [1, 7, 11, 21]. Significantly disturbed ultrastructure of the walls of perifollicular blood capillaries. Dystonia of blood vessels, which is detected on a burn injury on light optic and especially on submicroscopic levels, is manifested by enlargement, plethora, stasis and significant destructive changes in the walls of blood capillaries.

Activation of free-oxidation of lipids leads to the destruction of phospholipids of cell membranes. Such a statement about the mechanism of cellular membrane damage is consistent with the results of our research and [20, 21], which established a high level of toxic substances of lipid peroxidation in blood plasma of animals under investigation during thermal trauma. In this connection, it can be assumed that being in the blood, peroxides and free radicals primarily cause damage to the membranes of endothelial cells of the capillaries, and in the future, when they reach the bloodstream in the tissues, they lead to the destruction of the plasmalemma and organelles of the membranes of all organs of the affected organism, including thyroid gland. It is known that the mechanisms of adaptation to hypoxia are realized on the principle of stress reactions with the participation of the hypothalamic-pituitary-adenal system, the least explored is the role of the hypothalamic-pituitary-thyroid system [2, 3, 4, 10, 11, 23]. In the scientific literature, there is virtually no data on the participation of hormones in adapting to high temperatures. In the early stages of adaptation to hypoxia, hyperfunction of the thyroid gland and increased levels of thyroid hormones in the blood, which correlate with increased metabolism, is observed [1]. With prolonged action, hypofunction of the gland was noted under the conditions of "minimization" of metabolic functions and reduction of metabolism [1].

It is necessary to note the important role of thyroid hormones in the adaptation processes, since they have almost the widest spectrum of influence, since under their control are lipid, carbohydrate, protein and water-salt metabolism, as well as regeneration processes, permeability of cell membranes, etc.

In the scientific literature, the flow of compensatory and adaptive processes in the thyroid gland and its reorganization under conditions of stress, under the conditions of burn injury, have not been sufficiently studied. At morphological study of thyroid gland it is established that in the conditions of stress the volume of stromal elements of the organ increases, volume density of thyrocytes decreases, volume of colloid increases, the thyroid epithelium flings up. In some cases desquamation of thyrocytes occurs. If the stimulus is very strong or recurrent, then the resistance stage goes into the stage of exhaustion, there is a decrease in the function of the thyroid gland.

Thus, the results of histological studies correlate with the scientific data of other researchers [5, 14, 21] and indicate that in the stage of late toxemia after severe thermal trauma the destruction of membrane structural components of thyroid gland cells is significantly increased, which is necessarily accompanied by the development of dystrophic and necrobiotic processes in the body, a decrease in the secretory process.

In subsequent studies, it is planned to establish the degree of morphological changes in the structural components of the thyroid gland in the dynamics after the experimental thermal trauma under the use of corrective drugs.

**Conclusions**

In the stage of late toxemia after the thermal trauma in rats, deep irreversible destructive changes in thyrocytes in the follicles and hemocapillars of the thyroid gland develop, which are manifested by deep lesions of plasma, nuclear and intracellular membranes, leading to a decrease in secretion and excretion of hormones, a violation of transendothelial metabolism, and corresponds to the hypofunctional state of the organ.


**References**


**ОСОБЛІВОСТІ РЕМОДЕЛОВАННЯ СТРУКТУРНИХ КОМПОНЕНТІВ ЩИТОПОДІБНОЇ ЗАЛОЗИ В СТАДІЇ ТОКСЕМІЇ ПІСЛЯ ЕКСПЕРІМЕНТАЛЬНОЇ ТЕРМАНОЇ ТРАВМИ**

Корицький В. Г., Небесна З. М.

Термічна травма спричиняє тяжкі структурно-метаболічні порушення не тільки безпосередньо шкірного покриву, але й усіх органів та систем ураженого організму, що є проявом складного симптомокомплексу - олігової хвороби. Особливе значення у хворих з олігією відіграють зміни органів ендокрінної системи. Метою дослідження було встановлення мікроскопічної та електронно-мікроскопічної реєстрації компонентів щитоподібної залози тварин після термічного ураження на 14 добу після експериментальної термічної травми. Опік III ступеня наносили під кетаміновим наркозом мідними пластинами, навітря у куполічні води до температури 97-100°C. Розмір ділянки ураження становив 18-20% епільованої поверхні тіла щурів. Експериментальної вивчення структурних компонентів щитоподібної залози після олігієвої травми було виконано на лабораторних білих щурах-самцях масою 160-180 г. Експериментальні шкірні кольорові враження представлені зазначений хімічними ознаками - 14 доби (стадія пізньої токсемії) в мітохондрій фітооболіок та гемокапілярів виявляються значні деструктивні
та дегенеративні зміни, орган набуває макрофолікулярної будови. Знижується висота тироцитів, значно пошкоджуються ядра і органелли цитоплазми, зменшується кількість і висота мікроворсинок на їх апікальній поверхні, що негативно впливає на секреторний цикл клітин та транскапілярні обмінні процеси органу. Таким чином, встановлені деструктивні зміни кровоносних капілярів та тироцитів фолікулів є морфологічним проявом пригнічення секреторної активності щитоподібної залози при термічній травмі та відповідають гіпофункціональному стану органу.

Ключові слова: щитоподібна залоза, мікроскопічні та субмікроскопічні зміни, термічна травма шкіри.

ОСОБЕННОСТИ РЕМОДЕЛИРОВАНИЯ СТРУКТУРНЫХ КОМПОНЕНТОВ ЩИТОВИДНОЙ ЖЕЛЕЗЫ В СТАДИИ ТОКСЕМИИ ПОСЛЕ ЭКСПЕРИМЕНТАЛЬНОЙ ТЕРМИЧЕСКОЙ ТРАВМЫ

Корцикий В.Г., Небесная З.М.

Термическая травма вызывает тяжёлые структурно-метаболические нарушения не только непосредственно кожного покрова, но и всех органов и систем пораженного организма, является проявлением сложного симптомокомплекса - ожоговой болезни. Особое значение у больных с ожогами играют изменения органов эндокринной системы. Целью исследования было установление микроскопической и электронно-микроскопической реорганизации компонентов щитовидной железы животных после термического поражения на 14 сутки после экспериментальной термической травмы. Ожог III степени наносили под кетаминовым наркозом медными пластинами, нагретыми в кипящей воде до температуры 97-100°C. Размеры участка поражения составляли 15-20% эпилированной поверхности тела крыс. Экспериментальное изучение структурных компонентов щитовидной железы после ожоговой травмы были выполнены на лабораторных белых крысах-самцах массой 160-180 г. Эвтаназию крыс проводили после кетаминового наркоза путем декапитации. В эксперименте изучили микроскопическое и субмикроскопическое состояния фолликулов и гемокапилляров щитовидной железы после термической травмы III степени. Установлено, что в стадии токсемии после нанесения ожоговой травмы на 14 сутки (стадия поздней токсемии) в тироцитах стенки фолликулов и гемокапиллярах обнаруживаются значительные деструктивные и дегенеративные изменения, орган приобретает макрофолликулярное строение. Снижается высота тироцитов, значительно повреждаются ядра и органеллы цитоплазмы, уменьшается количество и высота микроворсинок на их апикальной поверхности, что отрицательно влияет на секреторный цикл клеток и транскапиллярные обменные процессы органа. Таким образом, установленные деструктивные изменения кровеносных капилляров и тироцитов фолликулов являются морфологическим проявлением подавления секреторной активности щитовидной железы при термической травме и соответствует гипофункциональному состоянию органа.

Ключевые слова: щитовидная железа, микроскопические и субмикроскопические изменения, термическая травма кожи.