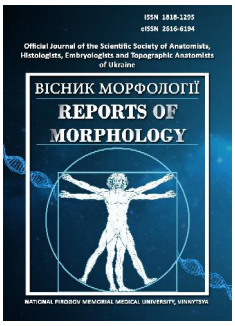
DOI: 10.31393/morphology-journal-2023-29(4)-06 Reports of Morphology, Vol. 29, №4, Pages 41-49

ISSN 1818-1295 eISSN 2616-6194

REPORTS OF MORPHOLOGY

Official Journal of the Scientific Society of Anatomists, Histologists, Embryologists and Topographic Anatomists of Ukraine

journal homepage: https://morphology-journal.com



Rats' thyroid gland histological and ultrastructural changes throughout the experimental thermal injury dynamics on the background of HAES-LX 5 % colloid-hyperosmolar solution injection

Tiron O. I., Vastyanov R. S.
Odesa National Medical University, Odesa, Ukraine

ARTICLE INFO
Received: 20 July 2023
Accepted: 28 September 2023

UDC: 616.441:599.323.4:615.459

CORRESPONDING AUTHOR
e-mail: chekina.o@ukr.net
Tiron O. I.

CONFLICT OF INTEREST
The authors have no conflicts of interest to declare.

FUNDING
Not applicable.

DATA SHARING
Data are available upon reasonable request to corresponding author.

The urgency of the burn injury problem is determined by frequent thermal injuries of patients of different ages, the complexity and duration of treatment, long-term disability and relatively high mortality. Depending on the area and depth of the lesion, a burn wound causes multiple and long-lasting disturbances in homeostasis, which cause organs and systems dysfunction. We are interested in the intrathyroid changes that occur during thermal burns, as thyroid gland plays one of the leading roles in the endocrine regulation of organisms' majority functions. When researching the issue of pharmacological correction of thyroid gland damage after a burn injury, we proceed from the classical fundamental concept regarding its pathogenetic validity. Taking into account the known pathogenetic mechanisms of burn disease with consecutive (and sometimes simultaneous) hypoproteinemia and haemoconcentration manifestations, intoxication formation, inflammatory and autoimmune reaction, we came to a conclusion regarding the reasonability of colloid solutions efficacy testing to attempt the pharmacocorrection in case of thyroid gland both structure and function burning. The purpose of the work is to establish histological and ultrastructural changes in the thyroid gland of experimental rats that were injected with colloidal hyperosmolar solution HAES-LX 5 % in the dynamics of skin thermal damage. Experimental studies were conducted on 90 white male rats. Skin thermal burns were simulated using four copper plates application to previously depilated lateral surfaces of the rats' body for 10 s. Rats were injected with colloidal hyperosmolar solution HAES-LX 5 % into the vena cava inferior during the first 7 days of the post-burn period. Thyroid gland pieces were fixed in a 10 % neutral formalin solution, dehydrated in alcohols of increasing concentration and embedded in paraffin blocks. The prepared sections of 5-6 μm thickness were stained with hematoxylin-eosin. For electron microscopic studies, pieces of the thyroid gland were taken, fixed in a 2.5% glutaraldehyde solution, and postfixed with a 1% osmium tetroxide solution in a phosphate buffer. Semi-thin sections were stained with methylene blue. Ultrathin sections were contrasted with uranyl acetate, lead citrate according to the Reynolds method and studied in a PEM-125K electron microscope. Colloidal hyperosmolar solution HAES-LX 5 % administration within 7 days of the post-burn period to correct the thermal injury effects has an expressed positive effect on burned animals thyroid gland histo- and ultrastructure. A significant improvement of the structural state of the stromal and parenchymal components of the organ and their relative normalization in the late period under the influence of the applied solution was established in the dynamics of the experiment. The colloidal hyperosmolar solution HAES-LX 5 % positive effects were expressed by cellular walls of the vessels and follicles dystrophic and destructive changes reduction the structural components of the organ restoration during the entire period of the study up to the 30th day of the trial. The first signs of the intraglandular environment recovery after colloidal hyperosmolar solution HAES-LX 5 % use were proved to start registered from the 7th day of the post-burn period and were maximally expressed from the 21st day until the end of the experiment. The authors are sure that colloidal hyperosmolar HAES-LX 5 % solution protective action possible mechanism is the generalized catabolic reaction

inhibition and the membrane-protective effect development. A complex of colloidal hyperosmolar solution HAES-LX 5 % protective, adaptive, adaptive, compensatory and regenerative effects were realized throughout the 30 days of the post-burn period, which efficacy exceeds the thyroid gland parenchyma and surrounding tissues destructive, decompensatory and necrotic changes. The authors consider the use of colloidal hyperosmolar solution HAES-LX 5 % to be one of the burn treatment regimen components as a restorative therapy drug and secondary cytoprotection aimed at the vascular wall and tissue defects integrity restoring.
Key words: *thyroid gland, thermal burn, post-burn period, morphological changes, ultrastructural changes, colloid-hyperosmolar solution HAES-LX 5 % restorative processes, pathogenetically based paharmacological correction.*

Introduction

Burn injuries are among the most common and severe diseases in humans, second only to transport injuries [10, 14, 20]. The urgency of the burn injury problem is determined by frequent thermal injuries of patients of different ages, the complexity and duration of treatment, long-term disability and relatively high mortality. Depending on the area and depth of the lesion, a burn wound causes multiple and long-lasting disturbances in homeostasis, which cause organs and systems dysfunction [3, 9, 13].

We are interested in the intrathyroid changes that occur during thermal burns, as thyroid gland plays one of the leading roles in the endocrine regulation of organisms' majority functions [15]. The thyroid gland, taking into account the wide range of thyroid hormones physiological activity, its structural and functional organization and morphofunctional features, as well as large-scale redundant regulatory feedback mechanisms, is one of the first to be subject to damaging thermal effects [9, 20]. Thyroid gland and other organs of the body dysfunction or pathological dysregulation arising as a result of thermal exposure "triggers" systemic dysfunctions via the "vicious circle" mechanisms, positive feedback and systemic-antisystemic regulation, outside of which there cannot be disorders of most organs and organ systems functioning, the pathogenetic mechanisms of which, firstly, are initiated by the general fundamental mechanisms of hypoxic and/or free radical cell death, secondly, are chains of pathophysiological processes provoked by thyroid pathology, and, thirdly, have not been sufficiently studied [9].

Despite significant advances achieved in the treatment of this pathology, mortality among severely burned victims remains high, especially with critical (40-50 % of the body surface) and supercritical (more than 50 %) deep burns [3, 17]. Therefore, while investigating the idea of thyroid gland burning pharmacological correction we used the classical fundamental concept of its pathogenetic validity. For this purpose, the pathophysiological mechanisms of the formation of endocrine disorders of the thyroid gland, pituitary gland and adrenal glands, the intensification of lipid peroxidation processes with the antioxidant system functional activity inhibition, blood rheological properties disruption with pronounced changes in red blood cells, as well as parenchymal organs involvement in this pathological process mediation were established.

Additionally, we carefully studied the morphological changes in the thyroid gland and adjacent tissues, starting from the first day of the postburn period, during the 30th day of the trial. Thyroid gland structural changes during the early post-burn period were concerned mainly the structure of its vascular component, its stroma and parenchyma and were predominantly of the nature of adaptation and/or compensation. Thyroid gland pathomorphological changes trend starting from the 21st day until the end of the trial was complex, on the one hand, with destructive and decompensatory nature, and, on the other hand, having an adaptive-compensatory, restorative and regenerative character. These data allowed us to believe the development of compensatory and restorative morphological changes in the thyroid gland and in surrounding organs and systems when prescribing pathogenetically based pharmacological correction.

According to fundamental concepts, hypohydration is one of the thermal damage leading clinical manifestation. Taking this into account, we tried to eliminate the thyroid gland parenchyma and cellular composition damage using 0.9 % physiological NaCl solution, which turned out to be unsuccessful. Taking into account the known pathogenetic mechanisms of burn disease with consecutive (and sometimes simultaneous) hypoproteinemia and haemoconcentration manifestations, intoxication formation, inflammatory and autoimmune reactions [18], we came to a conclusion regarding the reasonability of colloid solutions efficacy testing to attempt the pharmacocorrection in case of thyroid gland both structure and function burning.

The aim of the research is to establish histological and ultrastructural changes in the thyroid gland of experimental rats that were injected with HAES-LX 5 % colloidal hyperosmolar solution in the dynamics of skin thermal damage.

Materials and methods

Experimental trials were performed on 90 white male rats weighing 160-180 g (obtained from the vivarium of the Institute of Pharmacology and Toxicology of the National Academy of Medical Sciences of Ukraine) on the basis of the Research Center of National Pirogov Memorial Medical University. Animals keeping, handling and manipulation was carried out in accordance with the "General Ethical Principles of Animal Experiments" adopted by the "General

Ethical Principles of Animal Experiments" adopted by the Fifth National Congress on Bioethics (Kyiv, 2013) and was guided by the recommendations of the European Convention for the Protection of Vertebrate Animals for Experimental and Other Scientific Purposes (Strasbourg, 1985) and guidelines of the State Pharmacological Center of the Ministry of Health of Ukraine on "Preclinical studies of drugs" (2001) as well as rules of humane treatment of experimental animals and conditions approved by the Committee on Bioethics of National Pirogov Memorial Medical University (protocol № 1 from 14.01.2010).

Thermal skin burns of 2-3 degrees were modeled by four copper plates (each surface area equal to 13.86 cm^2) preheated for 6 min in water with a temperature of 100 °C applying to rats depilated side surfaces for 10 sec [5]. Rats were infused with hyperosmolar colloidal HAES-LX 5 % solution (10 ml/kg) into the lower femoral vein via catheter once per day throughout the first 7 days (the first administration was done 1 hr after the skin burn) after the skin burn during 5-6 min. Shaving, venous catheterization, skin burns and decapitation of rats were performed under propofol (i.v., 60 mg/kg) anesthesia.

Tissues for microscopic studies were collected 1, 3, 7, 14, 21 and 30 days after the skin thermal injury according to accepted methods [8]. The thyroid gland samples were fixed in a 10 % neutral formalin solution, dehydrated in alcohols of increasing concentration, and embedded in paraffin blocks. The prepared sections, 5-6 μm thick, were stained with hematoxylin-eosin [8].

The histological sections were examined under the MIKROmed SEO SCAN light microscope ("Sumy Electron Optics", Sumy, Ukraine), the photomicrographs were taken with the Vision CCD Camera with an image output system for histological specimens. The thyroid gland samples collected for electron microscopic examination were fixed with 2.5 % glutaraldehyde solution, and then post-fixed with 1 % osmium tetroxide prepared with phosphate buffer. Further processing was done according to used method [8]. Semi-thin sections were stained with methylene blue. Ultrathin sections made on an LKB-3 ultramicrotome were contrasted with uranyl acetate and lead citrate according to Reynolds method and then studied using PEM-125K electron microscope.

All morphological researches were performed under the Agreements on Scientific Cooperation among the Histology, Cytology and Embryology Department of Odesa National Medical University and Research Center of National Pirogov Memorial Medical University (from 01.01.2018) and Histology and Embryology Department of I. Horbachevsky Ternopil National Medical University (from 01.01.2019).

Results

Light-optical studies of micropreparations of the animals` thyroid gland on first day after experimental thermal injury and injection of colloid-hyperosmolar HAES-LX 5 % solution showed presence of interstitial swelling both in the capsule of the organ and in the interstitial septa; stasis in small calibre vessels and hyperemia in the arteries and veins. The follicles were polymorphic, some were in the active stage, others were overextended, lined with flat thyrocytes in the stage of hypofunction (Fig. 1A).

Histological examination of the thyroid gland after 3 days after HAES-LX 5 % injections for thermal injury correction showed a decrease both of stasis of the thyroid vessels and in interstitial and perivascular swelling in the organ. A majority of the follicles is lined with flat thyrocytes (see Fig. 1B).

Submicroscopic changes in the thyroid gland during three days of HAES-LX 5 % colloidal hyperosmolar solution usage to correct the effects of thermal injury were manifested by minor changes in the ultrastructure of the vessel wall, especially of small caliber, which were more pronounced on the first day and gradually subsided until

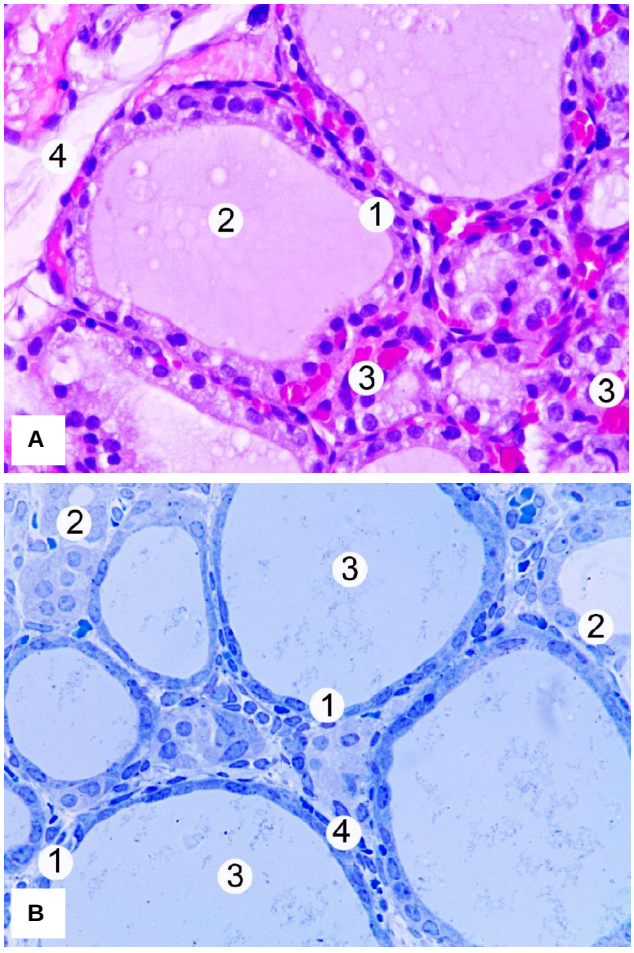


Fig. 1. Histological changes in the animal's thyroid gland after 1day (fragment A) and after 3 days (fragment B) after the cutaneous burn was treated with HAES-LX 5 % solution use. **A**: 1 - thyrocytes, 2 - colloid, 3 - capillary stasis, 4 - interstitial swelling. Hematoxylin-eosin staining. Increase x400. **B**: 1 - flat thyrocytes, 2 - cubic thyrocytes, 3 - colloid, 4 - hemocapillaries. Semi-thin cut. Methylene blue staining. Increase x400.

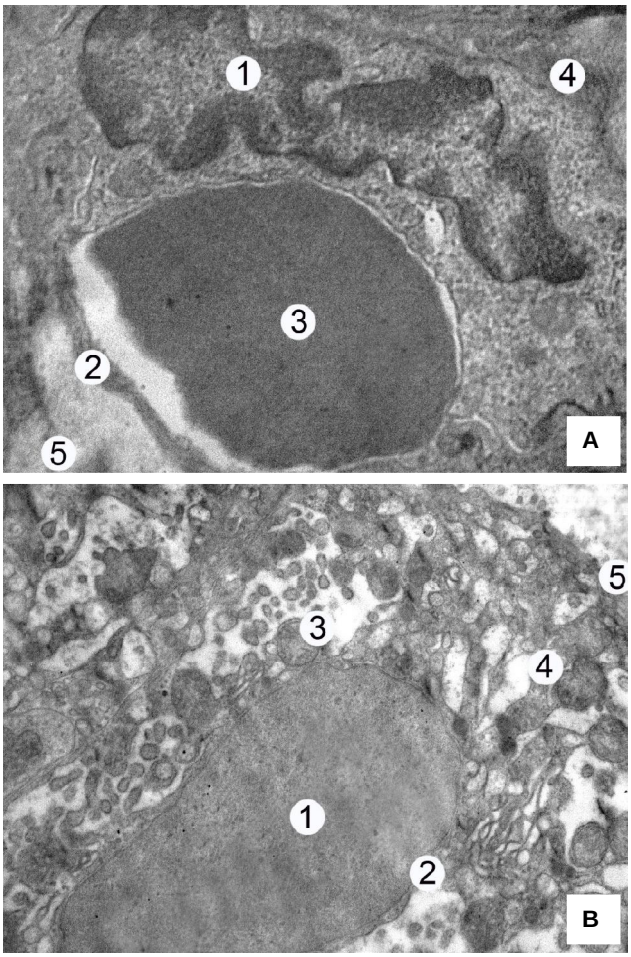


Fig. 2. Submicroscopic changes in the hemocapillary of the thyroid gland of an animal (fragment A) and thyrocytes of the thyroid gland (fragment B) after 1 day and 3 days, respectively, after experimental thermal skin injury with HAES-LX 5 % solution use. **A**: 1 - endotheliocyte nucleus, 2 - peripheral zone of endotheliocyte cytoplasm, 3 - erythrocyte in capillary lumen, 4 - unevenly thickened basement membrane, 5 - perivascular edema. Electronogram. Magnification x9000. **B**: 1 - thyrocyte nucleus, 2 - swelling of the perinuclear space, 3 - mitochondrion, 4 - hypertrophied tubules of the granular endoplasmic reticulum, 5 - apical surface with microvilli. Electronogram. Magnification x15000.

the third day. Locally thickened basement membrane, narrowing of fenestrae and a small number of microvesicles and caveolae in the peripheral zone of endotheliocytes were presented in electronograms analysis at these times of the trial (Fig. 2A).

Submicroscopically, on the 1st - 3rd days of the experiment, the HAES-LX 5 % solution was used as a corrective factor after thermal injury, and swelling of the perinuclear space was observed in thyrocytes. Large vacuole-like structures were visible in their cytoplasm, some mitochondria were characterized by disorganization of cristae, and tubules of the granular endoplasmic reticulum were characterized by hypertrophy. On the apical surface of the cells, the number of microvilli was insignificant (see Fig. 2B).

The analysis of histological preparations of the thyroid

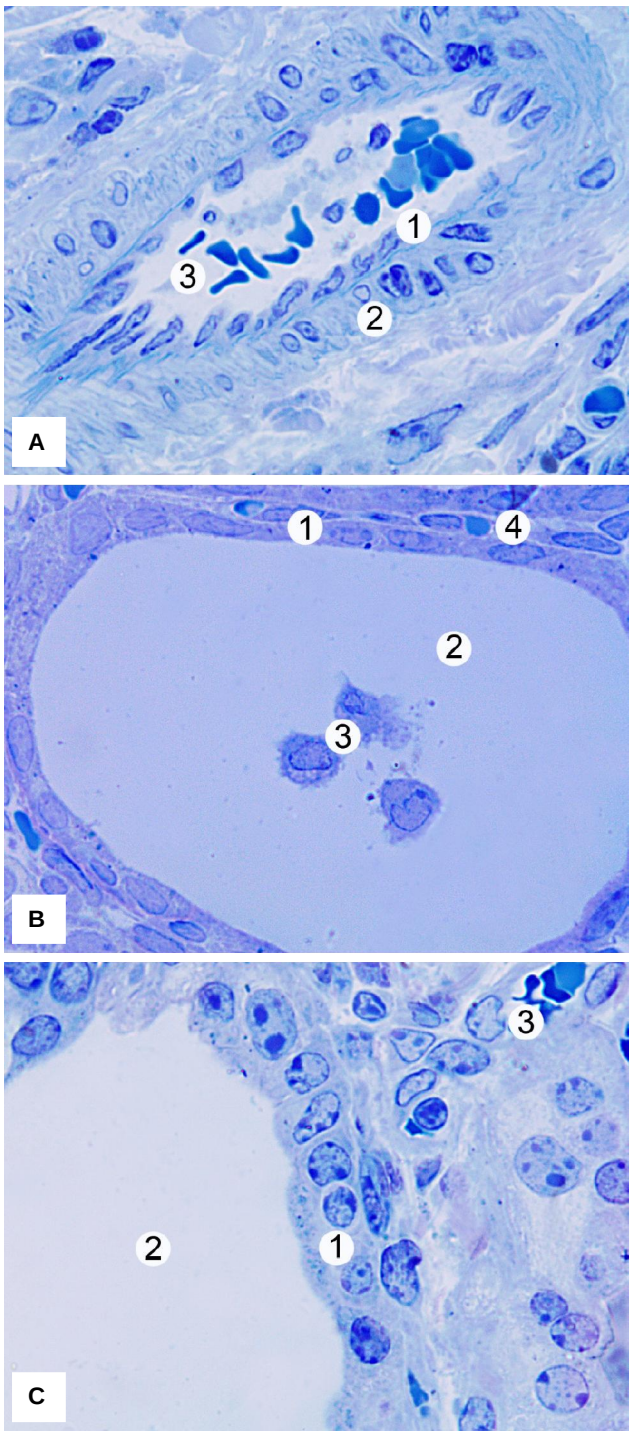


Fig. 3. Microscopic changes in the vessels of the thyroid gland of an animal in 7 days (fragments A B) and in 14 days (fragment C) after experimental thermal skin injury under the conditions of HAES-LX 5 % solution use. Semi-thin cut. Staining with methylene blue. Magnification x1000. **A**: 1 - endothelium, 2 - smooth myocytes of the media, 3 - lumen of arteriole. **B**: 1 - flat thyrocytes, 2 - colloid, 3 - desquamated thyrocytes. **C**: 1 - prismatic thyrocytes, 2 - colloid, 3 - hemocapillary.

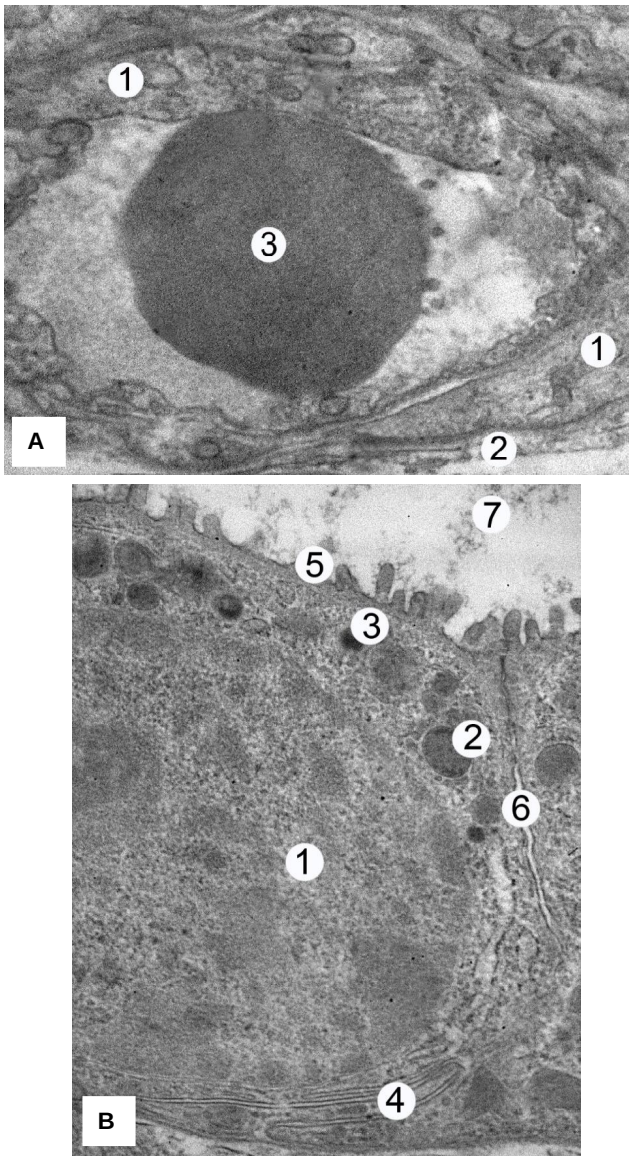


Fig. 4. Submicroscopic changes in the hemocapillary of the thyroid gland of an animal (fragment A) and thyrocytes of the thyroid gland (fragment B) after 7 days and 14 days, respectively, after experimental thermal skin injury with HAES-LX 5 % solution use. **A**: 1 - peripheral zone of endotheliocyte cytoplasm, 2 - basement membrane, 3 - erythrocyte in capillary lumen. Electronogram. Magnification x9000. **B**: 1 - thyrocyte nucleus, 2 - mitochondria, 3 - lysosome, 4 - tubules of granular endoplasmic reticulum, 5 - apical surface with microvilli. Electronogram. Magnification x17000.

gland 7-14 days after the seven-day administration of the HAES-LX 5 % solution for the correction of thermal injury consequences showed the absence of edematous manifestations in the stroma of the organ. The vessels in the stroma were moderately moderately blood-filled vessel (Fig. 3A).

Majority of the follicles in these terms of the experiment are lined with cubical or prismatic epithelium with clearly contoured basophilic nuclei. Mostly, on the 7th day, isolated overstretched follicles on the periphery of the organ and follicles with the manifistation of desquamation of thyrocytes in their lumen were detected (see Fig. 3B, 3C).

Submicroscopically, on the 7-14th day of the experiment, after a seven-day usage of the HAES-LX 5 % solution for the thermal injury effects correction, it was found that the capillaries of the organ have a preserved ultrastructure. The nuclei of endotheliocytes are oval in shape with shallow invaginations of the karyolemma and small lumps of heterochromatin located marginally. The peripheral zone of the cytoplasm of these cells was in some degree thickened, and a large number of micropinocytotic vesicles and vesicles were observed in it, which indicates the processes of active transendothelial exchange (Fig. 4A).

Ultrastructurally, thyrocytes of the thyroid gland at 7-14 days after experimental thermal injury for the seven-day usage of colloid-hyperosmolar injection of HAES-LX 5 % solution for its correction were characterized by the presence of a round or oval nucleus with the predominance of euchromatin and structured mitochondria, osmiophilic lysosomes, clearly contoured granular tubules of endoplasmic reticulum, microvesicles in the cytoplasm. At the apical pole of the follicular cells there was a significant number of microvilli, which were involved in the process of endocytosis of thyroglobulin (see Fig. 4B). These signs of the morphology preservation of follicular cells on a submicroscopic level indicate the expression of the cytoprotective effect of HAES-LX 5 % solution.

Microscopic studies of the thyroid gland of animals in 21-30 days after experimental thermal injury under the conditions of a seven-day injection of colloidal hyperosmolar HAES-LX 5 % solution for its correction showed that the histostructure of the organ is close to the normal state. No signs of connective tissue edema were recorded in the stromal component, and the vessels of the capsule and interlobular trabeculae corresponded to their

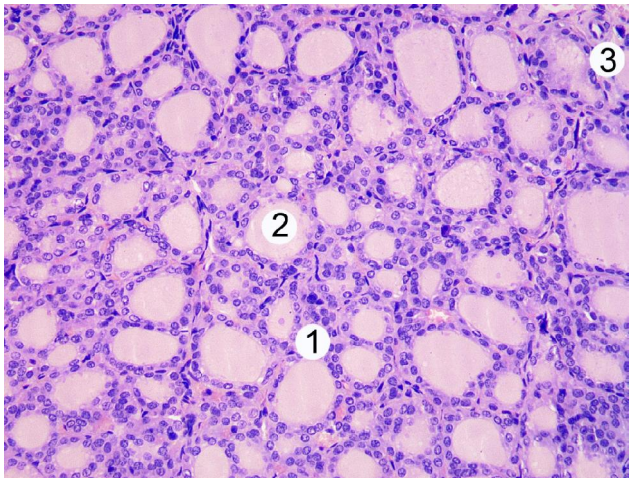


Fig. 5. Microscopic changes in the thyroid gland of an animal in 30 days after experimental thermal skin injury under the conditions of HAES-LX 5 % solution use. Hematoxylin-eosin staining. Magnification x200. 1 - thyrocytes, 2 - colloid, 3 - arteriole.

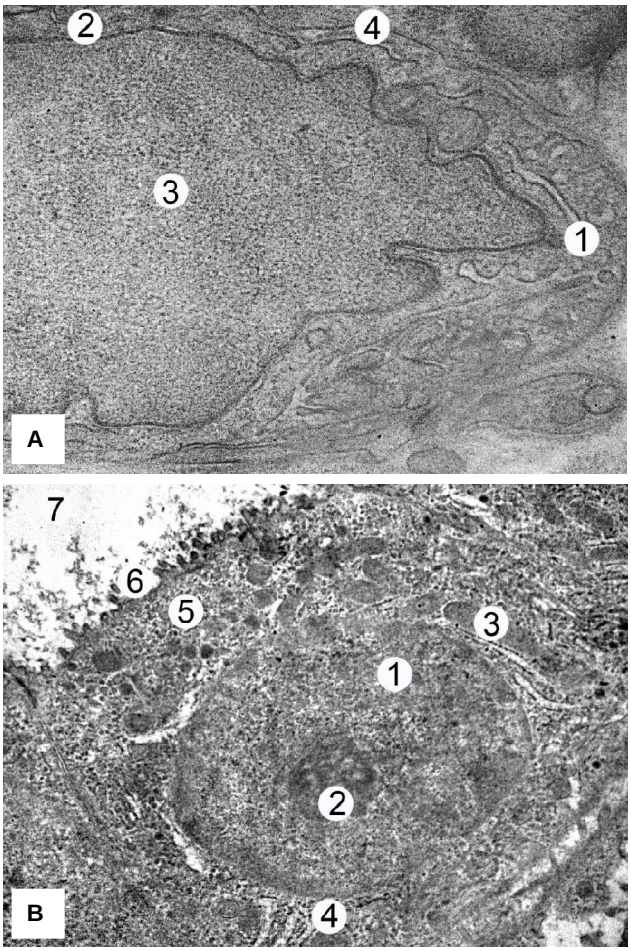


Fig. 6. Submicroscopic changes in the hemocapillary of the thyroid gland of an animal (fragment A) and thyrocytes of the thyroid gland (fragment B) in 21 days and 30 days, respectively, after experimental thermal skin injury under the conditions of HAES-LX 5 % solution use. **A**: 1 - organelle zone of endotheliocyte cytoplasm, 2 - peripheral zone of endotheliocyte cytoplasm, 3 - capillary lumen, 4 - basement membrane. Electronogram. Magnification x12000. **B**: 1 - nucleus and 2 - nucleolus of thyrocyte, 3 - mitochondrion, 4 - tubules of granular endoplasmic reticulum, 5 - microvesicles, 6 - apical surface with microvilli, 7 - colloid. Electronogram. Magnification x14000.

typical morphology. The blood supply of the vascular bed of the thyroid gland is moderate. Follicles in the composition of the lobes were mostly isomorphic and lined with cuboidal epithelium. A significant number of interfollicular islands were observed (Fig. 5).

Electromicroscopic studies of the structure of hemocapillaries of the thyroid gland on 21-30 days of the experiment in the conditions of correction of thermal injury with infusions of HAES-LX 5 % solution established the integrity of the endothelial lining of the wall, the clear contouring of the cells` plasmolemma, and the moderate thickness of the basement membrane. In the peripheral zone of the cytoplasm of endotheliocytes, numerous micropinocytotic vesicles and caveolae were detected, and in the zone of organelles - well-structured general purpose organelles (Fig. 6A).

The ultrastructure of thyrocytes in these terms of the experiment, under the conditions of correction of thermal injury by the introduction of HAES-LX 5% solution, corresponded to the normal state. The predominantly cubic-shaped cells contained a centrally located rounded nucleus with an osmiophilic structured nucleolus. In their cytoplasm, organelles of protein-synthesizing and energy apparatus were well developed. The apical pole was profusely filled with small microvesicles, and the plasmalemma formed numerous microvilli, which indicates the manifistation of active endocytosis of thyroglobulin and synthesis of thyroid hormones (see Fig. 6B).

Discussion

Thus, the obtained data indicate that the HAES-LX 5 % colloidal hyperosmolar solution administration within 7 days of the post-burn period to correct the thermal injury consequences has an expressed positive influence on burned animals thyroid gland histo- and ultrastructure. A significant improvement of the structural state of the stromal and parenchymal components of the organ and their relative normalization in the late period under the influence of the applied solution was established in the dynamics of the experiment. The colloidal hyperosmolar solution HAES-LX 5 % positive effects were expressed by cellular walls of the vessels and follicles dystrophic and destructive changes reduction the structural components of the organ restoration during the entire period of the study up to the 30th day of the trial.

The first signs of intraglandular environment recovery were proved to start from the 7th day of the post-burn period, and the maximally expressed HAES-LX 5 % colloidal hyperosmolar solution influence was observed from the 21st day until the end of the trial. Making parallels with the stages of burn disease classification, we note that the correction we applied showed effectiveness starting from the toxemia stage, and this positive histological dynamic lasted throughout the 30 days.

We conducted trials with thyroid gland and its microenvironment morphological state pharmacological corrections taking into account the pathogenetic mechanisms of burn disease. Our choice of HAES-LX 5 % colloidal hyperosmolar solution was due to the ineffectiveness of hypovolemia and oxygen deficiency correction by 0.9 % physiological NaCl solution introduction [19].

We believe that we have chosen a sufficiently effective compound for thyroid gland parenchyma, stroma and vascular environment thermally induced morphological disorders correction - HAES-LX 5 % colloidal hyperosmolar solution, created on the basis of HAES-LX 5 % hydroxyethylated starch, which influence on the body revealed the encouraging results in experimental [12] and clinical conditions [16]. HAES-LX 5 % colloidal-hyperosmolar solution (Institute of Blood Pathology and

Transfusion Medicine of the National Academy of Medical Sciences of Ukraine) contains as a colloid base poly (0-2-hydroxyethyl) starch - 5 %, as well as xylitol - 5 %, sodium lactate - 1.5 %, sodium chloride - 0.8 %, potassium chloride - 0.03 %, calcium chloride - 0.02 %, magnesium chloride - 0.01 %. The drug has a multiionic composition: Na^+ - 270.7 mmol/l, K^+ - 4.0 mmol/l, Ca^{2+} - 1.8 mmol/l, Mg^{2+} - 1.1 mmol/l, Cl^- - 146.6 mmol/l, $CH_3CH(OH)COO^-$ - 133.8 mmol/l [11].

Both small intestine and thymus morphological structure case of a burn injury were shown to be restored under the influence of HAES-LX 5 % colloidal-hyperosmolar solution [2, 4]. Stimulation of thymus cells synthetic processes according to the main indicators of the cellular cycle were proved under the influence of this drug in burn injury conditions [1]. Also in the studies of Gunas I.V. et al. [6] it was found that the administration of HAES-LX-5% solution for 7 days in rats after a burn injury of the skin reduces pathological changes in the stroma and parenchyma of the lungs in the early period of burn disease.

Our experiments on HAES-LX 5 % colloidal hyperosmolar solution use together with lactoprotein with sorbitol hyperosmolar solution as corrective compounds in case of thyroid gland burning, which are currently ongoing, highlight a practically comparable profile of their protective action in terms of thyroid morphological changes normalization, pituitary gland, thyroid gland, parathyroid gland and adrenal glands hormonal activity recovery as well as in the aspect of lipoperoxidation inhibition in the tissue of the thyroid gland, pancreas and liver.

An important aspect of this work and the obtained data analysis we consider not only to receive the array of encouraging pathomorphological results, but also to establish the mechanism of positive/protective effect of the applied colloid-hyperosmolar solution realization under the conditions of thyroid gland and the whole body burning. Taking into account the applied solution multicomponent ionic composition and the complete predominance of catabolic and necrotic processes in the post-burn period dynamics, we consider the inhibition of the generalized catabolic reaction to be one of the mechanisms of HAES-LX 5 % colloidal hyperosmolar solution protective effect. In this case, the efficacy of the applied solution we suppose to be identical to the membrane-protective effect.

The proven thyroid gland structure almost complete cytomorphological restoration within 30 days of the post-burn period is not final, given the thermal factor powerful alterating effect, which is why we assume the implementation of self-sustaining functional cellular activity under the influence of the HAES-LX 5 % solution. This type of activity lasts for 30 days. We believe that under these conditions a complex of protective, adaptive, adaptive, compensatory and regenerative effects are realized, the total efficacy of which exceeds destructive, decompensatory and necrotic changes within the thyroid gland parenchyma and surrounding tissues. This probably occurs due to the excessive permeability restoration of histo-hematic barrier, which functional breakdown occurs under the investigated pathological conditions [17, 18].

Abovementioned speculations cannot fully explain the 30-day long-term protective effect of HAES-LX 5 % colloidal hyperosmolar solution use in conditions of thyroid gland thermal damage. Therefore, upon ascertaining the fact of the thyroid gland follicles and the vascular component integrity histological and ultrastructural signs restoration, we stress the necessity of experiments continuation aimed at HAES-LX 5 % colloidal hyperosmolar solution protective effects mechanisms implementation in case of thyroid gland burning.

The obtained data analysis allows recommending the HAES-LX 5 % colloidal hyperosmolar solution use as one of the components of the burn treatment regimen as a restorative therapy drug, secondary cytoprotection aimed at restoring the integrity of the vascular wall and tissue defects.

Conclusions

1. Colloidal hyperosmolar solution HAES-LX 5 % administration within 7 days of the post-burn period to correct the thermal injury effects has an expressed positive effect on burned animals thyroid gland histo- and ultrastructure.

2. A significant improvement of the structural state of the stromal and parenchymal components of the organ and their relative normalization in the late period under the influence of the applied solution was established in the dynamics of the experiment.

3. The colloidal hyperosmolar solution HAES-LX 5 % positive effects were expressed by cellular walls of the vessels and follicles dystrophic and destructive changes reduction the structural components of the organ restoration during the entire period of the study up to the 30th day of the trial.

4. The first signs of the intraglandular environment recovery after colloidal hyperosmolar solution HAES-LX 5 % use were proved to start registered from the 7th day of the post-burn period and were maximally expressed from the 21st day until the end of the experiment.

5. Colloidal hyperosmolar HAES-LX 5 % solution protective action possible mechanism is the generalized catabolic reaction inhibition and the membrane-protective effect development.

6. A complex of colloidal hyperosmolar solution HAES-LX 5 % protective, adaptive, adaptive, compensatory and regenerative effects were realized throughout the 30 days of the post-burn period, which efficacy exceeds the thyroid gland parenchyma and surrounding tissues destructive, decompensatory and necrotic changes.

7. Colloidal hyperosmolar solution HAES-LX 5 % use seems to be one of the burn treatment regimen components as a restorative therapy drug and secondary cytoprotection aimed at the vascular wall and tissue defects integrity restoring.

References

[1] Cherkasov, E. V. (2015). Клітинна смерть і клітинний цикл в тимусі при експериментальній опіковій хворобі у щурів в умовах її лікування інфузією комбінованих гіперосмолярних розчинів [Cell death and cell cycle in the thymus during experimental burn disease in rats under the conditions of its treatment by infusion of combined hyperosmolar solutions]. *Український науково-медичний молодіжний журнал - Ukrainian scientific and medical youth magazine*, (2), 68-75.

[2] Cherkasov, V. G., Dzevulska, I. V., Cherkasov, E. V., Kaminsky, R. F., Pastukhova, V. A., Kovalchuk, O. I., & Trofimenko, Yu. Yu. (2017). Influence of HAES-LX-5 % infusion solution on the DNA content of endocrine glands cells against the background of thermal burn of skin in rats. *Світ медицини та біології - World of Medicine and Biology,* 4(62), 168-173. doi: 10.26724/2079-8334-2017-4-62-168-173

[3] Chernyakova, H. M., Minukhin, V. V., & Voronin, Ye. P. (2016). Сучасний погляд на місцеве лікування опіків з інфекційною складовою [A modern view of the local treatment of burns with an infectious component]. *Вісник проблем біології і медицини - Herald of problems of biology and medicine,* 4(133), 68-72.

[4] Gavryluk, A. O., Galunko, G. M., Chereshniuk, I. L., Tikholaz, V. O., Cherkasov, E. V., Dzevulska, I. V., & Kovalchuk, O. I. (2018). Indicators cell cycle and DNA fragmentation in cells of small intestine mucosa 14, 21 and 30 days after skin burns on the background of preliminary infusion of solution lactoprotein with sorbitol or HAES-LX 5 %. *Світ медицини та біології - World of Medicine and Biology,* 1(63), 104-108. doi: 10.26724/2079-8334-2017-4-62-104-108

[5] Gunas, I., Dovgan, I., & Masur, O. (1997). *Method of thermal burn trauma correction by means of cryoinfluence. Abstracts are presented in zusammen mit der Polish Anatomical Society with the participation of the Association des Anatomistes Verhandlungen der Anatomischen Gesellschaft, Olsztyn*. Jena - Munchen : Der Urban & Fischer Verlag, 105.

[6] Gunas, I. V., Yakovleva, O. O., & Ocheretniuk, A. O. (2012). Корекція гістологічних змін в легенях щурів при застосуванні інфузійного розчину HAES-LX-5% в перші 7 діб після опіку шкіри [Correction of histological changes in rats' lungs with HAES-LX-5% infusion solution usage in the period of 7 days after skin burn]. Світ медицини та біології - World of Medicine and Biology, 8(4), 73-76.

[7] Hamblin, M. R. (2019). Novel pharmacotherapy for burn wounds: what are the advancements. *Expert Opin Pharmacother,* 20(3), 305-321. doi: 10.1080/14656566.2018.1551880

[8] Horalskyi, L. P., Khomych, V. T., & Kononskyi, O. I. (2019) *Основи гістологічної техніки і морфофункціональні методи досліджень у нормі та при патології [Basics of histological technique and morphofunctional research methods in normal and pathological conditions].* Житомир : ЖНАЕУ - Zhytomyr: ZhNAEU, 286.

[9] Jeschke, M. G., Gauglitz, G. G., Kulp, G. A., Finnerty, C. C., Williams, F. N., Kraft, R., … & Herndon, D. N. (2011). Long-Term Persistance of the Pathophysiologic Response to Severe Burn Injury. *PLoS One,* 6(7), e21245. doi: 10.1371/journal.pone.0021245

[10] Jeschke, M. G., van Baar, M. E., Choudhry, M. A., Chung, K. K., Gibran, N. S., & Logsetty, S. (2020). Burn injury. *Nat Rev Dis Primers*, 6(1), 11. doi: 10.1038/s41572-020-0145-5

[11] Kondratskyi, B. O., Novak, V. L., & Kondratskyi, Ya. B. (2011). Комплексний колоїдно-гіперосмолярний інфузійний препарат [Complex colloid-hyperosmolar infusion preparation]. Патент України №93776 - Patent of Ukraine N 93776. Бюл. № 5 - Byul N5, 12.

[12] Maievskyi, O. Ye., Mironov, Ye. V., Bobruk, S. V., & Gunas, I. V. (2018). Dynamics of histochemical changes in the skin of rats within a month after the burning of II-III degrees on the background of the injection first 7 days HAES-LX-5% solution. *Світ медицини та біології - World of Medicine and Biology,* 4(66), 180-184. doi: 10.26724/2079-8334-2018-4-66-180-184

[13] Mehta, K., Arega, H., Smith, N. L., Li, K., Gause, E., Lee, J., & Stewart, B. (2022). Gender-based disparities in burn injuries, care and outcomes: A World Health Organization (WHO) Global Burn Registry cohort study. *Am J Surg,* 223(1), 157-163. doi: 10.1016/j.amjsurg.2021.07.041

[14] Opriessnig, E., Luze, H., Smolle, C., Draschl, A., Zrim, R., Giretzlehner, M., … & Nischwitz, S. P. (2023). Epidemiology of burn injury and the ideal dressing in global burn care - Regional differences explored. *Burns,* 49(1), 1-14. doi: 10.1016/j.burns.2022.06.018

[15] Sawicka-Gutaj, N., Zawalna, N., Gut, P., & Ruchala, M. (2022). Relationship between thyroid hormones and central nervous system metabolism in physiological and pathological conditions. *Pharmacol Rep,* 74(5), 847-858. doi: 10.1007/s43440-022-00377

[16] Semenenko, A. I., Khrebtii, H. I., Malyk, S. L., Dmytriiev, D. V., Bodnar, R. Y., Zheliba, L. M., … & Alsalama, M. W. O. (2020). Influence of different qualitative composition of infusion solutions on cerebral hemodynamics in patients with acute ischemic stroke. *Wiad Lek,* 73(2), 272-277. doi: 10.36740/WLek202002112

[17] Smolle, C., Cambiaso-Daniel, J., Forbes, A. A., Wurzer, P., Hundeshagen, G., Branski, L. K., … & Kamolz, L. P. (2017). Recent trends in burn epidemiology worldwide: A systematic review. *Burns,* 43(2), 249-257. doi: 10.1016/j.burns.2016.08.013

[18] Stanojcic, M., Abdullahi, A., Rehou, S., Parousis, A., & Jeschke, M. G. (2018). Pathophysiological Response to Burn Injury in Adults. *Ann Surg,* 267, 576-584. doi: 10.1097/SLA.0000000000002097

[19] Wang, Y., Beekman, J., Hew, H., Jackson, S., Issler-Fishe, A., Parungao, R., … & Maitzet, P. K. M. (2018). Burn injury: challenges and advances in burn wound healing, infection, pain and scarring. *Adv Drug Deliv Rev,* 123, 3-17. doi: 10.1016/j.addr.2017.09.018

[20] Zarutskyi, Ya. L., & Bilyi, I. Ya. (2018). *Воєнно-польова хірургія [Military field surgery].* Київ : ФЕНІКС - Kyiv: PHOENIX, 544.

ГІСТОЛОГІЧНІ ТА УЛЬТРАСТРУКТУРНІ ЗМІНИ ЩИТОПОДІБНОЇ ЗАЛОЗИ ЩУРІВ В ДИНАМІЦІ ЕКСПЕРИМЕНТАЛЬНОЇ ТЕРМІЧНОЇ ТРАВМИ ПРИ ВВЕДЕННІ КОЛОЇДНО-ГІПЕРОСМОЛЯРНОГО РОЗЧИНУ HAES-LX 5 %

Тірон О. І., Вастьянов Р. С.

Актуальність проблеми опікової травми визначається частими термічними ураженнями різних вікових контингентів пацієнтів, складністю та тривалістю лікування, довготривалою втратою працездатності та порівняно високою летальністю. Залежно від площі та глибини ураження, опікова рана викликає множинні й тривалі порушення гомеостазу, які спричиняють дисфункції органів і систем. Нас зацікавили зміни, що виникають при термічному опіку, в щитоподібній залозі,

оскільки їй відводиться одна з провідних ролей в ендокринній регуляції більшості функцій організму. При дослідженні питання фармакологічної корекції ураження щитоподібної залози після опікової травми ми виходимо із класичної фундаментальної концепції стосовно її патогенетичної обґрунтованості. Зважаючи на відомі патогенетичні механізми опікової хвороби з послідовними (а інколи - із одночасними) проявами гіпопротеїнемії, гемоконцентрації, формуванням інтоксикаційного синдрому, запальної та аутоімунної реакції, ми дійшли висновку стосовно доцільності тестування колоїдних розчинів з намаганнями фармакокорекції індукованих термічним подразненням структури та функції щитоподібної залози. Мета роботи - встановлення гістологічних та ультраструктурних змін щитоподібної залози щурів, яким в динаміці термічного ураження шкіри вводили колоїдно-гіперосмолярний розчин HAES-LX 5 %. Експериментальні дослідження проводили на 90 білих щурах-самцях. Термічні опіки шкіри моделювали шляхом притискання чотирьох мідних пластин до завчасно депільованих бокових поверхонь тіла щурів протягом 10 с. Протягом перших 7 діб післяопікового періоду щурам у нижню порожнисту вену вводили колоїдно-гіперосмолярний розчин HAES-LX 5 %. Шматочки щитоподібної залози фіксували в 10 % нейтральному розчині формаліну, проводили дегідратацію в спиртах зростаючої концентрації, заливали у парафінові блоки. Виготовлені зрізи, товщиною 5-6 мкм, забарвлювали гематоксиліном-еозином. Для електронномікроскопічних досліджень вилучали шматочки щитоподібної залози, фіксували їх у 2,5 % розчині глютаральдегіду, постфіксували 1 % розчином тетраокису осмію на фосфатному буфері. Напівтонкі зрізи забарвлювали метиленовим синім. Ультратонкі зрізи контрастували уранілацетатом, цитратом свинцю згідно методу Рейнольдса та вивчали в електронному мікроскопі ПЕМ-125К. Введення протягом 7 діб післяопікового періоду колоїдно-гіперосмолярного розчину HAES-LX 5 % для корекції наслідків термічної травми спричиняє виражений позитивний ефект на гісто- та ультраструктуру щитоподібної залози обпечених тварин. В динаміці досліду встановлено суттєве покращення структурного стану стромального та паренхіматозного компонентів органу та їх відносну нормалізацію у пізні терміни під впливом застосованого розчину. Позитивні ефекти застосування колоїдно-гіперосмолярного розчину HAES-LX 5 % були виражені зменшенням дистрофічних і деструктивних змін клітин стінок судин та стінки фолікулів у період інфузій з відновленням та нормалізацією морфології структурних компонентів органу протягом всього терміну дослідження до 30-ї доби досліду. Доведено, що перші ознаки відновлення внутрішньозалозистого оточення виникають, починаючи з 7-ї доби післяопікового періоду, а максимально виражений проективний ефект від застосування колоїдно-гіперосмолярного розчину HAES-LX 5 % спостерігався, починаючи з 21-ї доби і до кінця досліду. Ймовірним механізмом реалізації захисної дії колоїдно-гіперосмолярного розчину HAES-LX 5 % є гальмування генералізованої катаболічної реакції та розвиток мембранопротекторного ефекту. Протягом 30 діб післяопікового періоду реалізується комплекс захисних, адаптаційних, пристосувальних, компенсаторних та регенераторних ефектів колоїдно-гіперосмолярного розчину HAES-LX 5 %, ефективність яких перевищує деструктивні, декомпенсаторні та некротичні зміни в паренхімі щитоподібної залози та оточуючих тканинах. Застосування колоїдно-гіперосмолярного розчину HAES-LX 5 % доцільно як одного із компонентів схеми лікування при опіках в якості препарату відновлювальної терапії, вторинної цитопротекції, спрямованої на відновлення цілісності судинної стінки та дефектів тканин.

Ключові слова: *щитоподібна залоза, термічний опік, післяопіковий період, морфологічні зміни, ультраструктурні зміни, колоїдно-гіперосмолярний розчин HAES-LX 5 %, відновлювальні процеси, патогенетично обумовлена фармакологічна корекція.*

Author's contribution

Tiron O. I.: conceptualization, research, methodology and writing of the original draft, formal analysis and validation, data visualization, resources.

Vastyanov R. S.: conceptualization, review writing and editing, supervision, project administration.