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HYPEROSMOLAR SOLUTIONS IN THE CORRECTION OF DEGENERATIVE CHANGES IN THE ADENOHYPOPHYSIS AT THERMAL BURNS IN RATS

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Summary. *The article describes the ultrastructural changes of adenohypophysis in experimental burn. The dynamics of microcirculation changes and the consequences of its violation also discovered. Between 1-14 days after the burn we observed of blood stasis, at 21-30 day observed recovery microcirculation and endocrine cells. Hyperosmolar infusion solutions enhance structural recovery of adenohypophysis.*

Key words: *adenohypophysis, burn, microcirculation.*

Introduction. Burn disease includes both local skin lesions and complex secondary changes in the internal systems. The development of multiple organ failure often becomes self-importance, determining the course and outcome of thermal damage [1, 7, 13].

In a complex and poorly understood pathogenesis of burn disease importance is held by the nervous and endocrine systems [2]. Hormones are involved not only in the trigger, but also in the development of compensatory adaptive responses and mobilize the protective properties of the body. Especially important role in this complex process belongs to the pituitary-adrenal cortex, pituitary-thyroid gland [4, 9, 11, 12]. They are not only intermediate efferent pathways in the nervous regulation, but are peripheral endocrine effectors, providing a balance of metabolic and regenerative processes.

In this regard, of particular relevance acquire ultrastructural study adenohypophysis after thermal burns, especially changes in hemodynamics and their recovery hyperosmolar infusion solutions.

The purpose of this research was to study the ultrastructural changes microcirculation and cell injury in rat adenohypophysis at different stages of experimental burns.

Materials and methods. Experimental study of changes in the adenohypophysis at burn disease (after 1, 3, 7, 14, 21 and 30 days) were conducted in Wistar rats weight 150-160 g. Maintenance and manipulation of the animals were carried out in accordance with the recommendations "European Convention for the Protection of Vertebrate Animals used for experimental and other scientific purposes".

The male Wistar rats were divided into 4 groups of 8 rats each. Group 1: intact (control) rats; group 2: modeling burn injury in rats (only 0,9% NaCl solution); group 3: burn model with Lactoprotein-S application; group 4: burn model with joint application of Lactoprotein-S and HAES-LX-5%.

Burn modeled by applying to the side surfaces of the body of animals four copper plates (2 plates on each side) that previously kept for six minutes in water at a constant temperature of 100°C. The total area of the burn in rats indicated weight was 21-23% with an exposure of 10 sec., which is sufficient to form a second degree burn – superficial dermal burns (former A third degree) and shock of moderate severity.

For electron microscope study of adenohypophysis fixed in 2,5% solution of glutaraldehydein phosphate buffer with 1% OsO_4. Dehydration was performed in increasing concentrations of alcohol (70%, 80%, 90%, 100%) and acetone. Impregnated and poured into a mixture of epon-araldite under conventional methods. Ultrathin slices contrasted in 2% solution uranyl acetate and lead citrate. Slices examined and photographed under an electron microscope TEM-125K. Semi-thin slices stained in

methylene blue and photographed on microscope Olympus BX51 (Japan).

Results and discussion. Electron microscopic results showed that the general marker of pathological changes in the adenohypophysis burn disease were blood vessel stasis, tissue edema and necrotic processes in chromophil cells.

At the first 2 weeks after burn injury we observed blood stasis without acute perivascular edema and structural changes in endothelial cells. In endothelium localized pinocytotic vesicles, granular endoplasmic reticulum, mitochondria with intact membranes, indicating their functional activity. Around vessels localized stromal cells separating chromophil and chromophobe cells into groups. In chromophil adenohypophysis cells were established processes of organelle degradation and intracellular edema. Manifestations of ultrastructural changes of hemodynamics were swelling tanks endoplasmic reticulum (ER) and mitochondria matrix, cariopicnosis and organelles destruction in cells. The most common pathological changes we found in the somatotropes; marked a significant number of cells with signs of apoptosis. Acute edema and vacuolization of endoplasmic reticulum caused sharp somatotropes, increase perinuclear space, which in some cases led to degradation of organelles and necrosis. The stromal elements adenohypophysis remained structurally intact.

At 21-30 days after burn modeling in adenohypophysis found recovery processes in structural and functional elements of the injured gland. Continued to record signs of hemodynamic disorders (blood stasis, sludge syndrome), watched some chromophil cells in a state of acute vacuolization, but in the last term research perivascular and interstitial edema seen only as a focal changes and haven't generalized nature. In functionally active endocrine cells recorded numerous autophagosomes, indicating that the elimination of damaged organelles.

In animal group with injected solution HAES-LX-5% and Lactoprotein-S after burn modeling also established pathological changes in adenohypophysis. The main manifestations of the pathological process were erythrocytes stasis in blood vessels and swelling of organelles chromophil cells. At 1-3 day term recorded intact haemocapillare with moderate erythrocyte stasis. The endothelial cells hadnon-injured organization and localized organelles in cytoplasm, nuclei without swelling and degradation of chromatin, mitochondria with intact cristae, pinocytotic vesicles and endoplasmic reticulum elements. Around capillaries localized pericytes and collagen fibers; perivascular edema is not established. At the same time capillaries dilatation reduce by 20% (Table 1).

Stromal cells in adenohypophysis at 1-3 days after burn did not suffer severe damage. In osmiophilic cytoplasm localized intact mitochondria with cristae, single vesicles and endoplasmic reticulum elements; stromal cells edema unchecked, recorded only a few apoptotic cells.

The ultrastructural study chromophil cells revealed that the degree of cytoplasm swelling in applying the solution HAES-LX-5% and Lactoprotein-S is significantly lower than in animals treated with 0,9% NaCl solution. Common pathological changes in burn disease were swelling and destruction of mitochondria, abnormal formation of vesicles, endoplasmic reticulum edema. In somatotropes localized numerical elements of granular endoplasmic reticulum, secretion granules and lysosomes. At 1 day set gonadotropes degranulation without signs of structural injuries, but recorded cells with the number of vacuoles in the cytoplasm. At 3 day set accumulation of secretory granules in chromophil cells.

Alteration processes in chromophil cells realized by apoptosis. Significant differences in density of apoptotic cells between 1 and 3 day not observed, but in 3 day recorded swelling and vacuolization some somatotropes.

In group with Lactoprotein-S application pathological changes were found at 3 day after burn modeling: erythrocyte stasis, ultrastructural defects perivascular space, numerous injured cells, apoptotic pericytes. At 30 day established recovery both organelles of the secretory cells and elimination of degenerative cells. Regenerative processes dominated in endocrine then stromal cells that morphologically recorded as a reduction cytoplasm swelling, increasing density of endoplasmic reticulum and ribosomes. Nuclei somatotropes, corticotropes and thyreotropes significantly recovered.

Conclusion. Ultrastructural studies of rat adenohypophysis in experimental burn disease showed major pathogenetic factors of systemic damage during burn

Table 1.

Capillary cross-sectionalarea in adenohypophysis after thermal burns (μm²).

Group/term	NaCl	LP	HAES-LX-5%
Control	254,8±39,2		
1 day	404,1±50,9*	361,9±60,2*	295,6±39,5*,**
3 day	736,5±130,8*	707,0±101,8*	656,3±86,9*
7 day	530,8±106,5*	454,3±51,7*	577,2±73,6*
14 day	492,2±65,8*	399,2±46,3*	367,2±50,9*,**
21 day	589,2±65,1*	381,7±57,1*,**	438,7±115,0*,**
30 day	549,2±77,2*	335,5±40,7*,**	397,0±52,8*,**

Note: * – to the control (p<0,05); ** – to burn group (p<0,05).

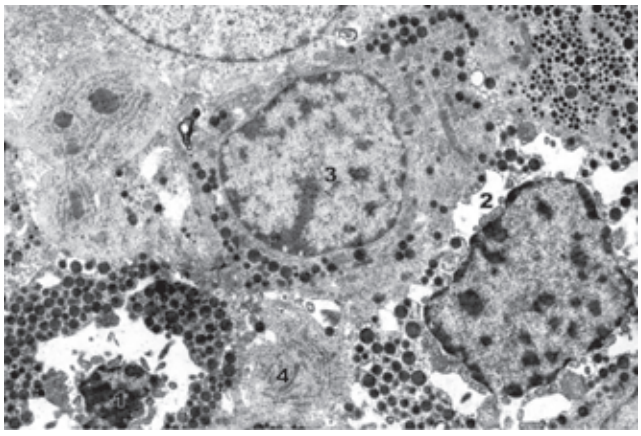

Figure 1. Electron microphotograph of structural changes adenohypophysis after burn disease modeling. Somatotropes swelling, organelles destruction. Note: 1 – apoptosis; 2 – ER swelling; 3 – non-injured somatotropes; 4 – granular ER. ×10000.

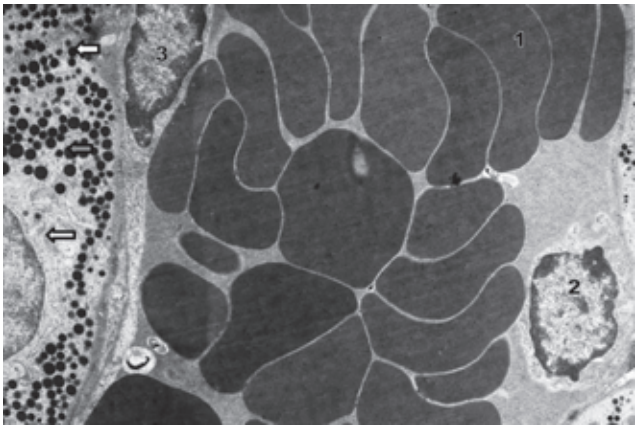

Figure 2. Electron microphotograph of rats adenohypophysis after burn and Lactoprotein-S application. Blood stasis: erythrocytes(1), inactive lymphocyte (2), endothelial cell (3). Swelling of mitochondria (⇦) in somatotropes, granule secretion (⇦), ER (⇦). ×9800.

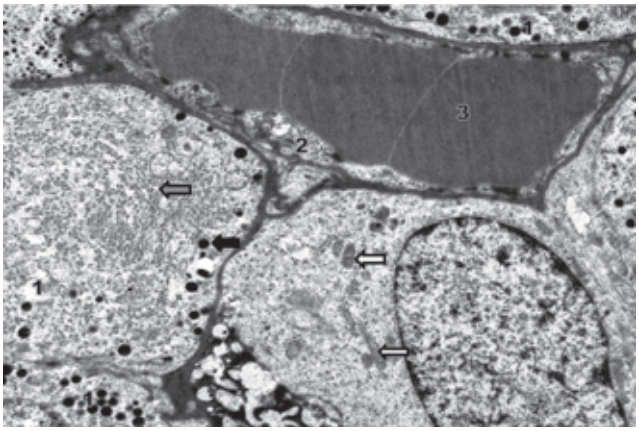

Figure 3. Electron microphotograph of rats adenohypophysis after burn and HAES-LX-5% application. Blood stasis, non-injured perivascular somatotropes. Note: 1 – somatotropes; 2 – endothelial cells; 3 – erythrocytes; secretory granules (⇦); granular endoplasmic reticulum (⇦); intact mitochondria (⇦). ×10000.

shock, toxemia period and initial recovery. At hemodynamic disorders in adenohypophysis progresses perivascular edema, causing structural and functional abnormalities in chromophil cells. Destructive changes endocrine cells occurin first 21 days and ends spontaneously recovery. The obtained results are a prerequisite to the study of pharmacological correction of tissue edema in burn disease that will lead to prevent the serious consequences of the disease.

Our electron microscopic results showed that burn is due to or exacerbated by altered control of endothelial permeability. Defects in endothelial permeability can lead to edema and increase in interstitial pressure, which in turn induces compression and altered tissue perfusion. Necrosis of somatotropesis also associated with increases in vascular permeability. Edema is usually a reversible condition and the control of vascular permeability may be restored once the triggering cause is removed. Vascular permeability is mediated by at least two broad mechanisms, called the paracellular and transcellular pathways. The first is controlled by the dynamic opening and closing of endothelial junctions, while the second includes vesicular transport systems, fenestrae and biochemical transporters.

During the past few years, our knowledge of the molecular organization of endothelial junctions has been increased substantially. Several new junction components have been identified, although their precise functions and reciprocal interactions remain to be understood in detail [3]. However, a lot of work is needed before we understand how the defects in junction structure and function act as the underlying cause of pathology. It will be important to integrate these different approaches to achieve a better understanding of the etiology of vascular pathology and of junction integrity disorders in burn disease in order to develop more effective therapies.

Summarizing the experimental study we can argue that the use of hyperosmolar infusion solutions Lactoprotein-S and HAES-LX-5% had positive effect on recovery of adenohypophysis after local thermal skin burn. After thermal injury in the circulating blood dramatically increases level of intermediate metabolites, products of necrotic tissues causing changes in the rheological blood properties and the functioning of microcirculation [6, 8, 10, 12, 13]. Application in such circumstances studied pharmacological solutions in the acute phase of burn injury restores microcirculation, which has a positive impact on the reduction of degenerative changes after burn shock. In our opinion expressed by the pharmacological effect of Lactoprotein-S and HAES-LX-5% especially due to the influence of drugs on the rheological parameters of blood, but it requires the approval of relevant research.

Reviewer: Corresponding Member NAMS Ukraine, professor Yu.B. Tchaikovskyi

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ГІПЕРОСМОЛЯРНІ РОЗЧИНИ В КОРЕКЦІЇ ДЕГЕНЕРАТИВНИХ ЗМІН В АДЕНОГІПОФІЗІ ПРИ ТЕРМІЧНИХ ОПІКАХ У ЩУРІВ

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Резюме. Наведені дані про ультраструктурні зміни аденогіпофіза при експериментальному опіку шкіри щурів. Виявлені динаміка змін мікроциркуляції і наслідки її порушення. З 1 по 14 добу після опіку ми спостерігали стаз крові, на 21-30 добу спостерігалося відновлення мікроциркуляції і ендокринних клітин адено-гіпофіза. Гіперосмолярні інфузійні розчини сприяють структурному відновленню аденогіпофіза.

Ключові слова: аденогіпофіз, опік, мікроциркуляція.

ГИПЕРОСМОЛЯРНЫЕ РАСТВОРЫ В КОРРЕКЦИИ ДЕГЕНЕРАТИВНЫХ ИЗМЕНЕНИЙ В АДЕНОГИПОФИЗЕ ПРИ ТЕРМИЧЕСКИХ ОЖОГАХ У КРЫС

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Резюме. Приведены данные об ультраструктурных изменениях аденогипофиза при экспериментальном ожоге кожи у крыс. Выявлены динамика изменений микроциркуляции и последствия ее нарушения. С 1 по 14 сутки после ожога мы наблюдали стаз крови, на 21-30 сутки наблюдалось восстановление микроциркуляции и эндокринных клеток аденогипофиза. Гиперосмолярные инфузионные растворы способствуют структурному восстановлению аденогипофиза.

Ключевые слова: аденогипофиз, ожог, микроциркуляция.