DOI 10.26724 / 2079-8334-2018-2-64-33-39
UDC 611.43/47-018.1:577.213-06:616.5-001.17]:615.384-092.9

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INFLUENCE OF LACTOPROTEINUM SOLUTION WITH SORBITOL ON DNA CONTENT OF CELLS OF ENDOCRINE GLANDS ON THE BACKGROUND OF SKIN BURN IN RATS

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Damage to the endocrine glands is one of the key pathogenetic factors in skin burns, but intracellular mechanisms of the effect of burn disease and its therapy on these organs continue to be poorly understood. The article presents the results of the study of DNA content in adenohypophysis, adrenal and thymus cells of rats by flowing DNA-cytometry against the background of thermal skin burn and correction of it with solutions of 0.9% NaCl or Lactoproteinum with sorbitol. The study was performed 1, 3, 7, 14, 21 and 30 days after the thermal burn of 2-3 degrees of 21-23% of the body surface and its correction. The statistical processing of the obtained results was carried out in the license package "STATISTICA 6.1" using nonparametric estimation methods. Against the backdrop of applying 0.9% NaCl solution in adenohypophysis cells, occurs a significant decrease in the parameters of the synthetic S-phase (the percentage ratio of the DNA synthesis phase to all cells of the cell cycle) already from 1 day of the experiment, which were restored to the control level only 21 days after the skin burn. The index of the interval SUB-G0G1 (DNA fragmentation index) against the background of applying 0.9% NaCl solution increased significantly from 3 days, and the decrease in the indicator in adenohypophysis cells was observed from the 14th day of the study. In adrenal cells, a significant increase in the S-phase index was observed with a 0.9% NaCl solution correction followed by a decrease from the 3 days of the experiment, and the SUB-G0G1 interval also increased from 1 day, followed by a decrease in this index. Against the background of correction with 0.9% NaCl solution, a significant decrease in the S-phase index of thymus cells was observed 1 day after the skin burn, and on the 3 day there was an increase in this index with its normalization after 14 days from the beginning of the experiment. The parameters of the SUB-G0G1 interval of thymus cells were elevated from 1 day, but after 7 days did not differ from those of the control group. With the use of a solution of Lactoproteinum with sorbitol, the amplitude of the S-phase and the SUB-G0G1 interval of adenohypophysis, adrenal and thymus cells decreased, indicating a cytoprotective effect of this drug. It was concluded that correcting by the 0.9% NaCl solution not sufficiently compensated the DNA damage of the endocrine glands after thermal skin burn, and the use of Lactoproteinum with sorbitol significantly improves the studied DNA content in these organs.

Key words: DNA-cytometry, thermal damage to the skin of rats, adenohypophysis, adrenal glands, thymus, Lactoproteinum with sorbitol; 0.9% NaCl solution.

Burn illness and its therapy remains a topical issue of modern medicine in connection with a significant increase in the number of thermal injuries in the world and in Ukraine, as well as inadequate efficacy of existing medicines recommended for the treatment of this pathology [6, 8-10]. This may be explained by insufficiently studied mechanisms of the influence of drugs on the factors of burn disease [23, 25]. The use of plasma replacement solutions, in particular Lactoproteinum with sorbitol, in the treatment of burn disease is one of the fundamental and main methods of therapy [8]. The effectiveness of this group of drugs is based on a number of factors affecting the main pathogenetic links of burn disease [22]. The solution of Lactoproteinum with sorbitol is characterized by the following mechanisms of action: plasmo-substituting activity of a solution that stores fluid in the bloodstream and increases arterial pressure, detoxification and neutralization of metabolic acidosis [1]. These properties are due to the active substances of the drug - albumin, sorbitol and sodium-lactate. The oncotic property of this drug is due to the influence of albumin, and the improvement of microcirculation and perfusion of tissues - sorbitol, which is also an energy substance, and sodium lactate has a slow sedative effect. Consequently, a solution of Lactoproteinum with sorbitol is an active means of pathogenetic therapy of burn disease, which has long been recommended for use in this pathology [8]. However, recently appeared a number of publications [7], which indicate the existence of intracellular mechanisms of the effect of infusion drugs on the parameters of the cell cycle and the fragmentation of DNA cells of tissues of different organs in the treatment of burn disease.

Especially important is the study of intracellular mechanisms of the effects of drugs on the cells of the endocrine glands, taking into account their key role in the pathogenesis of burn disease. It has been established [3] that dysregulation of adenohypophysis plays an important role in the implementation of remote complications of burn disease, and data on adrenal depletion [11, 17] with thermal damage to the skin point to a possible pathway for the development of secondary insufficiency against the background of this pathology. Also, damage to thymus cells [13, 15, 27], which develops within a few days after thermal damage to the skin, is a prerequisite for the development of an immunodeficiency, which is accompanied by the subsequent damage to T-dependent cells [19, 21]. That is, complex lesions of the

endocrine glands on the background of burn disease, cellular mechanisms of which remain not detailed. One of the most accurate methods for verifying DNA damage is the method of cytometric flow DNA, which today is universally recognized in the study of apoptosis, which plays one of the major roles in the pathogenesis of burn disease [4, 5, 14].

The purpose of the study is to analyze the data on the multiorgan effect of Lactoproteinum with sorbitol on the content and DNA fragmentation of endocrine glands cells: adenohypophysis, adrenal glands and thymus on the background of burn disease with the determination of the laws of the effect of the drug.

Material and methods. Experimental studies on 108 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 were conducted on the basis of the research laboratory of functional morphology and genetics of the research center of the National Pirogov Memorial Medical University, Vinnytsya, certified by the Ministry of Health of Ukraine (ID number 003/10 dated 11.01.2010).

Rats were in the conditions of the scientific and experimental clinic of the National Pirogov Memorial Medical University, Vinnytsya on a standard water and food ration with free access to water and food in the form of balanced feed in accordance with established norms. The temperature in the room where the animals were kept was kept at a level of 24-25 ° C, humidity of air - within 40-60%. Animal retention and manipulation were conducted in accordance with the "General Ethical Principles of Animal Experiments" adopted by the First National Congress on Bioethics (Kyiv, 2001), and also guided by the recommendations of the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, 1985) and the provisions of the "Rules for preclinical safety assessment of pharmacological agents (GLR)" During the work with laboratory animals, they adhered to: rules of humane attitude towards experimentation and approved by the Committee on Bioethics of the National Pirogov Memorial Medical University, Vinnytsya (№ 1, 14.01.2010); International requirements for the humane treatment of animals, following the rules of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (1984); methodical recommendations of the State Pharmacological Center MoH Ukraine on pre-clinical research of drugs [2].

Before modeling skin burns, all animals were shaved lateral surfaces of the body with a mechanical type and a safe razor. The trauma was caused by applying to the lateral surfaces of the body of the animals four copper plates for 10 s (two plates on each side, the surface area of each plate was 13.86 cm^2) which were pre-held for 6 minutes in water at a constant temperature of 100ºC [12, 20]. To calculate the surface area of the skin of the rat, the formula by M. O. Lee [16] was used. Accordingly, the masses, the average area of the body surface of the rats was 240 ± 26 cm^2, and consequently, the burn from the exposure of the four heated plates with a total area (S = 55.44 cm^2) corresponded to 21-23% of the body surface of the animal.

The depth of burns was set according to the four-level classification adopted in Ukraine. According to it, 1% of 1-2 degree burns are taken for 1 unit of the injury severity index; 1% burn of 3A degree - for 2 units of severity index damage; 1% burn of 3B degree - for 3 units of severity index damage; 1% burns 4 degrees - for 4 units of severity index damage. Having established the found value, determined the degree of severity of burn shock based on the depth of the damage. It should be noted that the value of the index of severity of damage in the range up to 30 units determined a burn shock of a mild degree; the value of the index of the severity of damage in the range from 31 to 60 units - a burn shock of moderate severity; the value of the index of the severity of damage in the range from 61 to 90 units - severe burn shock; with an index of severity of damage of more than 90 units - an extremely severe burn shock. In the studies conducted, the magnitude of the index of gravity of the damage ranged from 52 to 56 units, which corresponds to a burn injury of moderate severity.

An infusion of a solution of 0.9% solution of NaCl or Lactoproteinum with sorbitol in a volume of 10 ml/kg body weight of the animal was carried out into the lower vena cava after its catheterization in aseptic conditions through the femoral vein. The catheter was applied under the skin, and its clearance throughout the length was filled with titrated heparin solution (0,1 ml of heparin per 10 ml of 0.9% NaCl solution) after each substance administration. Infusions were performed once a day during the first 7 days. It should be emphasized that the method of administration and dosage of solutions containing hydroxyethyl starch involves the use of drugs at doses ranging from 7 (average dose) to 15 ml/kg body weight (high dose). In view of this, a dose of 10 ml/kg body weight selected is appropriate.

Shaving of rats, burns, catheterization of major vessels and decapitation (after 1, 3, 7, 14, 21 and 30 days) were carried out under conditions of propofol anesthesia (60 mg/kg mass i/v).

The content of DNA in the nuclei of adenohypophysis, adrenal glands and thymus of rats was determined by flow cytometry. In animals, after decapitation, the data were removed from the glands, deprived of the capsule (if necessary) and from all their contents were prepared nucleic suspensions for flow cytometry. Cell suspensions from these cell cultures were prepared using a CyStain DNA nuclear DNA sample from Partec, Germany, according to the manufacturer's protocol. This solution allows rapid extraction of nuclei and the labeling of nuclear DNA by diamino phenylindole (DAPI), which is part of its composition. CellTrics 50 μm disposable filters (Partec, Germany) were used for the production of nucleic suspensions. The flow analysis was performed on a multi-functional flow-through cytometer "Partec PAS" from Partec, Germany, in the research center of the National Pirogov Memorial Medical University, Vinnytsya. UV radiation was used to stimulate DAPI fluorescence. From each sample of the nucleic suspension of the analysis, 10 thousand events were subject to. The cell cycle analysis was performed by FloMax software (Partec, Germany) in full numeric matching according to the mathematical model, which determined: G0G1 - percentage ratio of cells of the G0G1 phase to all cells of the cell cycle (DNA content = 2 c); S phase is the percentage of the phase of DNA synthesis to all cells of the cell cycle (DNA content> 2c and <4c.). Determination of DNA fragmentation (apoptosis) is accomplished by isolating the sub-G0G1 site on the RN1 DNA histograms before the peak G0G1, indicating cell nuclei containing DNA <2c.

The statistical processing of the obtained results was carried out in the license package "STATISTICA 6.1" with the use of nonparametric methods for evaluating the obtained results. Evaluated the correctness of the distribution of characteristics for each of the variation series received, the mean of each studied feature, and the standard quadratic deviation. The reliability of the difference between independent quantitative values was determined using the Man-Whitney U-criterion.

Results and its discussion. According to the results of a dynamic study of DNA content in adenohypophysis cells in rats and in the background of correction with 0.9% solution of NaCl or solution of Lactoproteinum with sorbitol, we found a degree change (Table 1). In the background of burn skin injury and the use of 0.9% NaCl solution in rats, smaller values of the S-phase are recorded starting from 1 day after burn injury with its gradual increase in 3 days, reaching the maximum after 21 days; and after 30 days, this figure is reduced, but remains higher than the level recorded in the group where the infusion of this drug was conducted in the absence of burn injury. Accordingly (Table 2), it was found that the mean values of the interval of the SUB-G0G1 increase from 3 days after burn injury, reaching the maximum value after 14 days. However, after 21 and 30 days, the average value of this indicator decreases relative to the previous ones, not reaching the level that was established in the group of intact animals against the background of infusion of 0.9% NaCl solution.

Table 1

Dynamics of S-phase indices (%) of cells of adenohypophysis, adrenals and thymus of rats on the background of skin burn injury and correction with 0.9% NaCl solution and Lactoproteinum with sorbitol (M±σ)

Day of research	Adenohypophysis			Adrenals			Thymus		
	0,9 % NaCl without burn	0,9 % NaCl + burn	LP - SB + burn	0,9 % NaCl without burn	0,9 % NaCl + burn	LP - SB + burn	0,9 % NaCl without burn	0,9 % NaCl + burn	LP - SB + burn
1	0,588±0,075	0,110±0,016*	0,240±0,023*, **	0,240±0,054	0,662±0,197*	0,514±0,096*	8,925±2,654	4,275±1,846#	4,608±1,295*
3	0,558±0,074	0,220±0,021	0,326±0,036	0,250±0,056	1,202±0,439*	0,606±0,127*	7,782±3,357	12,54±3,48#, *	8,843±2,437**
7	0,518±0,066	0,374±0,030	0,564±0,303	0,222±0,087	0,658±0,162	0,386±0,075	8,250±2,444	11,16±2,94*	9,635±2,013
14	0,550±0,090	1,186±0,215*	1,088±0,436*	0,230±0,073	0,498±0,099*	0,326±0,063*, #	8,315±2,861	6,317±2,977	8,245±0,921
21	0,568±0,101	1,734±0,399*	1,218±0,078*, **	0,216±0,073	0,298±0,141	0,258±0,111	8,480±1,269	6,662±2,086	7,367±1,488
30	0,528±0,084	1,036±0,093*	0,880±0,085*, **	0,206±0,078	0,246±0,188	0,232±0,089	7,635±2,416	6,642±2,195	6,998±2,822

Notes: here and in the following table, LP + SB - Lactoproteinum with sorbitol; * - a significant (p <0,01) difference with the parameters of a group of 0.9% NaCl solution without burn; ** - a significant (p <0,01) difference with the parameters of the group of 0.9% solution NaCl + burn; # - is a significant (p <0,05) difference with the parameters of the group of 0.9% NaCl solution without burn; ## - reliable (p <0,05) difference with the parameters of the group of 0.9% solution of NaCl + burn.

Table 2

Dynamics of the parameters of the interval of SUB-G0G1 (%) of cells of adenohypophysis, adrenals and thymus of rats on the background of burn skin trauma and correction with 0.9% NaCl solution and Lactoproteinum with sorbitol (M±σ)

Day of	Adenohypophysis			Adrenals			Thymus		
	0,9 % NaCl without burn	0,9 % NaCl + burn	LP - SB + burn	0,9 % NaCl without burn	0,9 % NaCl + burn	LP - SB + burn	0,9 % NaCl without burn	0,9 % NaCl + burn	LP - SB + burn
1	0,558±0,084	0,594±0,047	0,600±0,029	1,846±0,187	3,362±0,237*	3,012±0,135*	2,608±0,536	11,90±4,46 #	8,458±1,178#
3	0,534±0,071	0,740±0,042*	0,730±0,111#	1,832±0,267	5,480±0,851*	4,114±0,773*	2,608±0,536	12,03±3,20#	7,960±3,612#
7	0,548±0,118	0,918±0,167*	0,846±0,129*	1,906±0,339	4,120±0,571*	2,816±0,373*	2,608±0,536	5,515±0,780	4,712±0,988
14	0,540±0,083	1,114±0,199*	0,974±0,236#	1,938±0,313	3,248±0,866	2,348±0,415#	2,608±0,536	3,672±0,928	3,388±1,237
21	0,590±0,108	0,976±0,193*	0,784±0,194	1,846±0,279	2,332±0,251#	2,116±0,571	2,608±0,536	3,233±0,998	3,085±0,693
30	0,568±0,052	0,792±0,169	0,562±0,074	1,986±0,248	2,344±0,236#	1,948±0,668	2,608±0,536	2,428±0,736	2,383±0,930

The use of a solution of Lactoproteinum with sorbitol following a burn injury to the skin causes similar changes in the S-phase and SUB-G0G intervals in adenohypophysis cells, but their amplitude was

significantly lower, indicating the protective effect of this drug over a long period of experimental study (30 days). In particular, it was found that the magnitude of the S-phase after 1 day after burning of the skin after administration of Lactoproteinum with sorbitol on 53.3% lower compared to control (without burn injury of the skin) in groups of rats receiving similar solutions; after 3 days - by 41,2% ($p < 0,01$), and after 7 days practically does not differ from the level of control groups. Accordingly, after 14 days - 85.0% ($p < 0.05$) is higher than in control groups; after 21 days it reaches a maximum - by 108.6% ($p < 0.01$), higher than in control groups, and after 30 days it decreases, but remains 61.8% ($p < 0.01$) higher than in control group. Indicators of the interval of SUB-G0G1 in adenohypophysis cells 3 days after skin burning against the background of administration of Lactoproteinum with sorbitol were 31.3% ($p < 0.05$) higher than in control (without burn) groups of animals receiving a similar solution, and after 7 days - by 58,4% ($p < 0,01$) larger. After 14 days this indicator reaches a maximum - by 71.5% ($p < 0.05$), higher than in control groups. After 21 days in group using Lactoproteinum with sorbitol, the value of the SUB-G0G1 interval was 42.0% ($p = 0.076$) higher than in the corresponding control group, and after 30 days, the given index did not differ from that of the control animals.

It has also been established that at the background of burn disease in the course of infiltration with a 0.9% NaCl solution, the synthetic processes in adrenal cortical cells in the form of an increase in S-phase parameters from 1 day after burn injury increase with a maximum after 3 days, with a gradual decrease up to 14 days, and after 21 days, these indicators are approaching the level of indicators of the group, which introduced this solution without burning the skin. The dynamics of the change in the interval of the SUB-G0G1 was similar to that of the S-phase, but after 21 and even 30 days after the skin burn, the figure remained significantly higher than in the non-burn skin group.

The use of Lactoproteinum with sorbitol throughout the experiment significantly reduces the elevated levels of the SUB-G0G1 and S-phase of the adrenal cortical cells. Moreover, starting from the 14th day, these indices have no reliable or trend differences from the groups without burn injury to the skin. Correction of a 0.9% solution of NaCl in 1 day after burn skin damage results in a significant violation of the cell cycle of thymus cells, which consists of a statistically significant increase in the number of cell events in the G0G1 phase ($p < 0.05$), and, in particular, an increase in the number of events in the range of SUB-G0G1 ($p < 0.01$), which probably indicates the determining role of apoptosis in damaging the thymus in conditions of burn disease from the first day after burning the skin. In addition, the number of cells in the range S ($p < 0,01$) decreases, indicating a lack of recovery of the population of damaged cells. After 3 days there is a statistically significant decrease in the number of cells in the G0G1 phase ($p < 0,01$) due to the increase in cells in the S phase ($p < 0,01$), however, the parameters of the interval of SUB-G0G1 remain statistically significantly higher than those of the group without burns ($p < 0.05$). After 7 days of study, all cell cycle indices did not differ significantly from those observed in the non-burning group (ie, the effective compensation for the damage of thymus cells in a burn disease after 7 days was performed after DNA cytometry). After 14, 21, and 30 days, the core cell cycle rates are not statistically different from those of the control group.

On the background of burns, with the use of Lactoproteinum with sorbitol, significant differences in cell cycle indices in rats' thymus after 1 day after burning of the skin were not detected. After 3 days, with the use of Lactoproteinum with sorbitol, the S-phase showed statistically significant differences ($p < 0,05$) from the burn group + 0,9% NaCl solution, which indicates a more positive effect on the synthetic function of the thymus cells of this preparation. Regarding the effect on apoptosis of the drug in the aforementioned terms, only the tendency ($p = 0,055$) to the decrease of the indicator of the interval SUB-G0G1 is established. 7 days after burning of the skin with the application of 0.9% NaCl solution and in the subsequent periods of the experiment, the S-phase and SUB-G0G1 intervals did not differ significantly from similar indicators established in the group of animals without burn injury. For the group of burn + Lactoproteinum with sorbitol, statistically significant differences (or tendencies of difference) with indicators of burn group + 0.9% NaCl solution were not detected after 14, 21 and 30 days after thermal damage to the skin.

Analyzing the obtained experimental data we can state that intracellular damage to the DNA of cells of adenohypophysis, adrenal glands and thymus on the background of correction with 0.9% NaCl solution develops from the first days after thermal damage and consists in amplification of apoptosis in the form of increase of parameters of the interval SUB-G0G1 and decrease of indicators S-phases in all investigated organs. However, in each organ there are certain features that, in our opinion, reflect not only the effects of burn disease, but also adaptive mechanisms of protection against damage in this organ and its cells. It is known that apoptosis is a mechanism for updating the cell population in many pathological conditions [18] and burns in particular [7, 26]. Summing up the results of the study of the

content of DNA, we can note certain regularities and the hierarchy of changes in the parameters of the cell cycle of cells of various endocrine organs against the background of thermal damage to the skin. If synthetic processes in the adenohypophysis at the subcellular level significantly decrease from 1 day and then constantly increase, reaching the peak values after 21 days, the processes of apoptosis acquire a maximum after 14 days. In our opinion, this is consistent with the data on the clinical manifestations of hormonal insufficiency in the distant periods after the thermal damage [11].

In adrenal cells, using 0.9% NaCl solution, in contrast to cells of the adenohypophysis, the maximum of the S-phase was established after 3 days followed by a decrease in this index, while the parameters of the interval of SUB-G0G1 appeared to be increased in all terms of observation, indicating more pronounced damage to this group of cells in comparison with the adenohypophysis. The data we receive show that there is a long-lasting negative effect on the functioning of the cortical substance of the adrenal glands after thermal burn injuries of the skin, even with short-term damage. We have established hyperactivity of the cortical substance of the adrenal glands in the form of enhanced intracellular synthesis and simultaneously elevated cell apoptosis, which contributes to the depletion of the functioning of the glands, which, in turn, can cause the adrenal insufficiency inherent in the burn disease in this period. These results correlate with the data of other researchers about the development of adrenal insufficiency and the effectiveness of the use of corticosteroids in burn disease in different periods of its development [17, 24].

Thymus cells appeared to be more reactive with respect to the processes of synthesis and apoptosis on the background of thermal burn and correction with a 0.9% solution of NaCl - the normalization of the parameters occurred 7 days after the burn of the skin. However, these violations of the first days are likely to be responsible for further clinical and laboratory manifestations of damage to the thymus and T-dependent cells observed by experimental data, both in the early and in the long-term period of burn disease [15, 19, 21].

The influence of the Lactoproteinum with sorbitol on the cell cycle parameters of the cells of the three investigated organs was quite stereotyped and unidirectional. The data obtained, in our opinion, indicate the predominant effect of Lactoproteinum with sorbitol on the cell cycle in these organs against the background of burn inflicted skin due to action on the S-phase, that is, due to the stimulation of synthetic processes. In one or another degree, the stimulation of synthetic processes, albeit in somewhat different terms, is noted in the background of the use of the drug. In our opinion, this indicates a different level of involvement of the studied cells in the pathogenetic mechanism of the implementation of the burn disease, but the use of Lactoproteinum with sorbitol proved to be quite effective in correcting cell cycle disorders on the background of this pathology.

Conclusion

1. Thermal damage to the skin at the background of correction with 0.9% NaCl solution is accompanied by damage to the DNA of adenohypophysis, adrenal and thymus cells in the form of an increase in the percentage of cells with signs of apoptosis (fragmentation of DNA) and a violation of their proliferative activity. DNA damage of cells has peculiarities inherent in a certain organ and reflect the hierarchy of the inclusion of endocrine glands in response to a thermal damage.
2. The effect of the Lactoproteinum with sorbitol on the cell cycle indexes of the adenohypophysis, adrenal glands and thymus cells has a unidirectional cytoprotective character and consists of reducing the amplitude of the S-phase and the interval of SUB-G0G1. Preferably, the drug affects the S-phase, stimulating synthetic processes.

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Реферати

ВПЛИВ РОЗЧИНУ ЛАКТОПРОТЕЇНУ З СОРБІТОЛОМ НА ВМІСТ ДНК КЛІТИН ЕНДОКРИННИХ ЗАЛОЗ НА ФОНІ ОПІКУ ШКІРИ У ЩУРІВ

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Пошкодження ендокринних залоз є одним з ключових патогенетичних факторів при опіку шкіри, але продовжують залишатися маловивченими внутрішньо-клітинні механізми впливу опікової хвороби і її терапії на дані органи. У статті представлені результати дослідження вмісту ДНК в клітинах аденогіпофізу, надниркників і тимусу щурів методом проточної ДНК-цитометрії на тлі термічного опіку шкіри і корекції розчинами 0,9% NaCl або лактопротеїну з сорбітолом. Дослідження проведено через 1, 3, 7, 14, 21 і 30 діб після термічного опіку 2-3 ступеня 21-23% поверхні тіла і його корекції. Статистика обробка отриманих результатів проведена в ліцензійному пакеті "STATISTICA 6.1" з використанням непараметричних методів оцінки. На тлі використання 0,9% розчину NaCl в клітинах аденогіпофізу відбувається істотне зниження показників синтетичної S-фази (відсоткове співвідношення фази синтезу ДНК до всіх клітин клітинного циклу) вже з 1 доби експерименту, які відновлювалися до рівня контролю тільки через 21 добу після опіку шкіри. Показник інтервалу SUB-G0G1 (показник фрагментації ДНК) на тлі

ВЛИЯНИЕ РАСТВОРА ЛАКТОПРОТЕИНА С СОРБИТОЛОМ НА СОДЕРЖАНИЕ ДНК КЛЕТОК ЭНДОКРИННЫХ ЖЕЛЕЗ НА ФОНЕ ОЖОГА КОЖИ У КРЫС

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Повреждения эндокринных желез являются одним из ключевых патогенетических факторов при ожоге кожи, но продолжают оставаться малоизученными внутриклеточные механизмы влияния ожоговой болезни и ее терапии на данные органы. В статье представлены результаты исследования содержания ДНК в клетках аденогипофиза, надпочечников и тимуса крыс методом проточной ДНК-цитометрии на фоне термического ожога кожи и коррекции растворами 0,9 % NaCl или лактопротеина с сорбитолом. Исследование проведено через 1, 3, 7, 14, 21 и 30 суток после термического ожога 2-3 степени 21-23 % поверхности тела и его коррекции. Статистическая обработка полученных результатов проведена в лицензийном пакете "STATISTICA 6.1" с использованием непараметрических методов оценки. На фоне примененния 0,9 % раствора NaCl в клетках аденогипофиза происходит существенное снижение показателей синтетической S-фазы (процентное соотношение фазы синтеза ДНК ко всем клеткам клеточного цикла) уже с 1 суток эксперимента, которые восстанавливались до уровня контроля только через 21 сутки после ожога кожи. Показатель интервала SUB-G0G1 (показатель

застосування 0,9% розчину NaCl суттєво збільшується з 3 доби, а зниження даного показника в клітинах аденогіпофізу спостерігали з 14 доби дослідження. У клітинах надниркових залоз на тлі корекції 0,9% розчином NaCl встановлено істотне збільшення показника S-фази з наступним його зниженням починаючи з 3 доби експерименту, а інтервал SUB-G0G1 також підвищувався з 1 доби з подальшим зниженням цього показника. На тлі корекції 0,9% розчином NaCl спостерігається істотне зниження показника S-фази клітин тимусу через 1 добу після опіку шкіри, а на 3 добу спостерігалося збільшення цього показника з його нормалізацією через 14 діб від початку експерименту. Показники інтервалу SUB-G0G1 клітин тимусу були підвищеними починаючи з 1 доби, але вже через 7 діб не відрізнялися від аналогічних показників групи контролю. При застосуванні розчину лактопротеїну з сорбітолом зафіксовано зниження амплітуди показників S-фази і інтервалу SUB-G0G1 клітин аденогіпофізу, надниркників і тимусу, що вказує на цитопротективний ефект даного препарату. Зроблено висновок, що при корекції 0,9% розчином NaCl недостатньо компенсується пошкодження ДНК ендокринних залоз після термічного опіку шкіри, а застосування лактопротеїну з сорбітолом істотно покращує досліджувані показники вмісту ДНК в цих органах.

Ключові слова: ДНК-цитометрія, термічне ушкодження шкіри щурів, аденогіпофіз, наднирники, тимус, лактопротеїн з сорбітолом; 0,9 % розчин NaCl.

Стаття надійшла 21.05.18р.

фрагментации ДНК) на фоне применения 0,9 % раствора NaCl существенно увеличивается с 3 суток, а снижение даного показателя в клетках аденогипофиза наблюдали с 14 суток исследования. В клетках надпочечников на фоне коррекции 0,9 % раствором NaCl установлено существенное увеличение показателя S-фазы с последующим его снижением начиная с 3 суток эксперимента, а интервал SUB-G0G1 также повышался с 1 суток с последующим снижением этого показателя. На фоне коррекции 0,9 % раствором NaCl наблюдается существенное снижение показателя S-фазы клеток тимуса через 1 сутки после ожога кожи, а на 3 сутки наблюдалось увеличение этого показателя с его нормализацией через 14 суток от начала эксперимента. Показатели интервала SUB-G0G1 клеток тимуса были повышенными начиная с 1 суток, но уже через 7 суток не отличались от аналогичных показателей группы контроля. При применении раствора лактопротеина с сорбитолом зафиксировано снижение амплитуды показателей S-фазы и интервала SUB-G0G1 клеток аденогипофиза, надпочечников и тимуса, что указывает на цитопротективный эффект даного препарата. Сделан вывод, что при коррекции 0,9 % раствором NaCl недостаточно компенсируется повреждение ДНК эндокринных желез после термического ожога кожи, а применение лактопотеина с сорбитолом существенно улучшает изучаемые показатели содержания ДНК в данных органах.

Ключевые слова: ДНК-цитометрия, термическое повреждение кожи, аденогипофиз, надпочечники, тимус, лактопротеин с сорбитолом, 0,9 % раствор NaCl.

Рецензент Шепітько В.І.

DOI 10.26724 / 2079-8334-2018-2-64-39-43
UDC 616.314-084

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SEXUAL DIMORPHISM OF NORMATIVE CEPHALOMETRIC PARAMETERS DETERMINED BY THE HOLDAWAY METHOD IN BOYS AND GIRLS OF PODILLIA

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When studying individual facial harmony, one must take into account both ethnic characteristics of morphometric indices and age and sexual differences inside of the ethnic group itself. However, there are no data on the manifestations of sexual dimorphism of the cephalometric indices of soft tissues by the Holdaway method in Ukrainians. The purpose of the work is to establish sexual differences in cephalometric parameters determined by the Holdaway technique in boys and girls of Podillia region of Ukraine with orthognathic bite. With the Veraviewepocs 3D device, Morita (Japan), 38 boys (aged from 17 to 21) and 55 girls (aged from 16 to 20 years) with normal occlusion close to orthognathic bite, received side telerentgenograms and analyzed. Cephalometric points and measurements were carried out in accordance with the recommendations of R. A. Holdaway and taking into account the recomendations of A. E. Athanasiou and S. I. Doroshenko and Y. A. Kulginsky. The statistical processing of the obtained results was carried out in the licensed package "Statistica 6.0" using nonparametric methods for evaluating the obtained results. The juveniles have significantly higher or tended to higher values than girls with the following cephalometric parameters determined by the Holdaway method: Basic Upper Lip Thickness, Upper Lip Strain, H Angle, Inferior Sulcus to H Line, Soft Tissue Thickness Chin and Subnasale to H Line. Other cephalometric parameters are determined by Holdaway method (Soft tissue Facial Angle, Nose Prominence, Superior Sulcus Depth, Skeletal profile Convexity and Lower Lip's to H line) have no reliable or biased tendencies between the boys and girls.

Keywords: cephalometry, sexual dimorphism, Holdaway analysis, Ukrainian boys and girls.

Despite the immense amount of accumulated information about the structure of the human body and the perception of anatomical science as fundamental and unchanging, technological progress puts more and more complex issues and tasks for anatomists, creating a huge space for the appearance and transformation into a fundamentally new kind and quality of all branches of anatomy. Global world trends are aimed at creating a virtual world and require a huge amount of accurate information not only of a static nature, but also a description of the nature of the relationships of all elements in spatial and temporal dependence. And the dental industry, which can change the elements of soft and bone tissues of the face, constantly needs new, more accurate and improved diagnostic approaches. After all, the orthodontist practically is the only specialist who has the opportunity to influence the form and aesthetic