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RENAL DYSFUNCTION PATHOGENETICALLY BASED PHARMACOLOGICAL CORRECTION USING LIPOPROTEIN WITH SORBITOL AND HAES-LX-5 % HYPEROSMOLAR COLLOIDAL SOLUTIONS IN CONDITIONS OF THYROID GLAND BURNING

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The purpose of the study was to investigate the lipoprotein with sorbitol and HAES-LX 5 % hyperosmolar colloidal solutions impact on kidney functioning peculiarities in the dynamics of thyroid gland burning. The expressed kidney function disorders manifested by their filtrative, excretory and detoxicative functions disturbances occur throughout the 30 days of the postburn process together with lipoperoxidative processes acceleration and antioxidant protection suppression within the kidneys parenchyma. Kidneys functional activity disturbances were proved to reach their maximal expression on the 3rd – 14th days of the study. Lipoprotein with sorbitol and HAES-LX 5 % hyperosmolar colloidal solutions revealed nephroprotective effects in terms of nephrocyte damage free radical mechanism prevention, the antioxidant protection enzymatic link activation and kidney specific functions recovery. Used hyperosmolar colloidal solutions optimal protective activity occurs on the 7th – 14th day of the trial and lasts until the end of the experiment. Thus, the scheme of thyroid gland burning pharmacological correction including the lipoprotein with sorbitol and HAES-LX 5 % hyperosmolar colloidal solutions administration is pathogenetically justified and be able not only to restore the nephrocytes functional activity but also to prevent their damage throughout the post-burn process dynamics.

Key words: thyroid gland, thermal injury, kidneys, hyperosmolar colloid solutions pathogenetic mechanisms, pathological dysregulation.

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ПАТОГЕНЕТИЧНО ОБҐРУНТОВАНА ФАРМАКОЛОГІЧНА КОРЕКЦІЯ НИРКОВОЇ ДИСФУНКЦІЇ ПРИ ТЕРМІЧНОМУ УРАЖЕННІ ЩИТОПОДІБНОЇ ЗАЛОЗИ ЗАСТОСУВАННЯМ ГІПЕРОСМОЛЯРНИХ КОЛОЇДНИХ РОЗЧИНІВ ЛІПОПРОТЕЇНУ З СОРБІТОЛОМ ТА HAES-LX-5 %

Метою дослідження є дослідження впливу гіперосмолярних колоїдних розчинів ліпопротеїну з сорбітолом та HAES-LX 5 % на особливості функціонування нирок в динаміці термічного ушкодження щитоподібної залози. Протягом 30 діб післяопікового періоду відбуваються виражені порушення функції нирок, які проявляються порушенням їх фільтраційної, екскреторної та дезинтоксикаційної функції, а також прискоренням процесів ліпопероксидації та пригніченням активності антиоксидантного захисту в їх паренхімі. Доведено, що порушення функціональної активності нирок набуває максимуму на 3-й – 14-й добах дослідження. Застосування гіперосмолярних колоїдних розчинів ліпопротеїну з сорбітолом та HAES-LX 5 % виявилося ефективним в аспектах запобігання вільнорадикального механізму ураження нефроцитів, активації ферментативної ланки антиоксидантного захисту та відновлення специфічної функції нирок. Оптимум захисної активності застосованих гіперосмолярних колоїдних розчинів приходиться на 7–14 доби досліду і триває до кінця експерименту. Таким чином, схема фармакологічної корекції термічного ураження щитоподібної залози із введенням гіперосмолярних колоїдних розчинів з багатоіонним складом ліпопротеїну з сорбітолом та HAES-LX 5 % є патогенетично обґрунтованою та такою, яка не лише здатна відновити функціональну активність нефроцитів, але й запобігти їх ураженню в динаміці постопікового процесу.

Ключові слова: щитоподібна залоза, опікова травма, нирки, гіперосмолярні колоїдні розчини, патогенетичні механізми, патологічна дизрегуляція

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Burn injuries belong to most common and severe diseases in humans, second only to traffic injuries [1, 10, 11]. Taking into account the ongoing military aggression against Ukraine with the use of weapons of both mass destruction and indiscriminate action, the significance of human body burning investigation is imperative [1]. Burn wound causes multiple and long-lasting disturbances in homeostasis, depending on the area and depth of the lesion, which cause dysfunction of numerous organs and systems [2, 12, 14].

The thyroid gland due to its structural and functional organization, morpho-functional peculiarities features, thyroid hormones wide range of physiological activity and regulatory feedback massive duplicative mechanisms is one of the first to fall under the alterative thermal influence [6, 13]. Thyroid gland and other organs dysfunction or pathological dysregulation, which occurs as a result of thermal exposure, "triggers" systemic dysfunctions via the "vicious circle" mechanisms, positive feedback and systemic-antisystemic regulation. The named systemic dysfunctions stimulate the majority of organs and organ systems functional disorders, which pathogenetic mechanisms, firstly, are initiated by hypoxic and/or free radical cell death fundamental mechanisms secondly, are chains of pathophysiological cascades induced by thyroid pathology, and, thirdly, are insufficiently researched.

Parenchymatic organs were proved to be involved in the burning pathological process mediation [3]. The blood system, erythrocytes together with thyroid gland, liver and pancreatic parenchyma were shown to be involved into the pathophysiological mechanisms of thyroid dysfunction caused by excessive thermal exposure. Resuming, we checked the fact of kidneys involvement into the thermally affected thyroid gland pathological process mediation [4].

We use the classical fundamental concept regarding the pathogenetic validity of thyroid burning pharmacological correction [13, 15]. Fundamentally, hypohydration is considered to be one of the thermal damage leading clinical manifestations but saline solution injections failed to be effective in thyroid parenchyma and cellular composition damages elimination [13]. Taking into account the known burn disease pathogenetic mechanisms with consecutive (and sometimes simultaneous) hypoproteinemia, hemoconcentration, endotoxemia development together with inflammatory and autoimmune reaction we decided to check the colloid solutions efficacy trying to achieve the thyroid burning pharmacological correction.

The purpose of the study was to investigate the lipoprotein with sorbitol and HAES-LX 5 % hyperosmolar colloidal solutions impact on kidney functioning peculiarities in the dynamics of thyroid gland burning.

Materials and methods. Experimental trials were performed on 350 white male rats weighing 180–220 g. The animals were kept in standard vivarium conditions. Experimental 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 Odesa National Medical University (Prot. N17-C from 12.11.2021).

Experimental animals were randomized as follows. Group 1 – intact rats (n=48); group 2 – rats with thyroid gland burning (n=66); group 3 – rats with thyroid gland burning injected with saline (n=66); group 4 – intact rats injected with lipoprotein with sorbitol (LPS) solution (n=42); group 5 – rats with thyroid gland burning injected with LPS (n=42); group 6 – intact rats injected with HAES-LX-5 % solution (n=42); group 7 – rats with thyroid gland burning injected with HAES-LX-5 % solution (n=42). Thermal skin burns of 2–3 degrees were modelled by four copper plates (each surface area equal to 13.86 cm^2) previously preheated with a temperature of 100 °C during 6 min applying to pre-depilated side surfaces of the rats' body for 10 sec [8]. The total area of skin lesions was 21-23 %.

Rats were infused i.v. with saline, LPS and HAES-LX 5 % (both 10 ml/kg) hyperosmolar solutions once per day during the first 7 days (the first administration was done 1 hr the skin burn) into the lower femoral vein. Animals were euthanized by decapitation (after 1, 3, 7, 14 and 21 days). Shaving, venous catheterization, skin burns and decapitation of rats were performed under propofol (i.v., 60 mg/kg) anesthesia.

Colloidal hyperosmolar LPS solution ("Biopharma", Ukraine) is a protein-salt solution containing donor albumin as a colloid base, sorbitol, sodium lactate, sodium chloride, calcium chloride, potassium chloride and sodium bicarbonate. The drug has multiionic composition including Na^+, K^+, Ca^{2+}, Cl^-, HCO_3^- and $CH_3CH(OH)COO^-$ ions.

Colloidal hyperosmolar HAES-LX 5 % solution (Institute of Blood Pathology and Transfusion Medicine of the National Academy of Medical Sciences of Ukraine, Ukraine) contains starch, xylitol, sodium lactate, sodium chloride, potassium chloride, calcium chloride and magnesium chloride as a colloid base. The drug also has a multiionic composition – Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^- and $CH_3CH(OH)COO^-$.

Kidneys were removed from rats 1, 3, 7, 14, 21, and 30 days after the skin burning and their homogenate was prepared. The malonic dialdehyde (MDA) and diene conjugates (DC) concentration as well as the activity of antioxidant enzymes glutathione, superoxidedismutase (SOD), glutathioneperoxidase (GPR) and glutathionereductase (GTR) were determined in kidney homogenates in the indicated time intervals after thermal burns of the skin with the help of conventional methods.

Intact rats were i.p. injected with water for injections in the other part of the trial, and the model of water-induced diuresis was performed 2 hrs after. Rats with the model of water induced diuresis were administered with hydrous water (intragastric injection, equal to 5 % of the rats' body weight, 37 ºC) 1, 3, 7, 14, 21, and 30 days after the skin burning. Urine was collected for 2 hrs after that. Total protein and creatinine concentrations were determined in the urine samples of rats at the indicated time intervals.

Table 1

The influence of PLS and HAES-LX 5 % on changes in lipid peroxidation in rats' kidney parenchyma after thyroid gland burning during the 7 days of trial

N	Experimental groups	The amount of the substances investigated (M±m)					
		MDA, µmole/g	DC, µmole/g	Glutathione, мМ	SOD, unit/g	GTP, unit/g	GTR, unit/g
	Day 1						
1	Control (intact rats), n=8	2.07±0.17	0.26±0.03	11.4±1.1	1.14±0.11	1.89±0.16	2.03±0.17
2	Rats with a burn, n=11	3.82±0.31	0.67±0.07	6.8±0.7	0.71±0.07	1.08±0.11	1.17±0.11
3	Rats with a burn+NaCl, n=11	3.91±0.32	0.63±0.08	6.9±0.7	0.74±0.07	1.03±0.12	1.21±0.09
4	LPS, n=7	2.01±0.19	0.23±0.03	11.7±1.2	1.17±0.11	1.96±0.17	2.12±0.18
5	Rats with a burn + LPS, n=7	3.71±0.33	0.61±0.07	7.1±0.7	0.73±0.07	1.12±0.11	1.24±0.11
6	HAES-LX 5 %, n=7	2.07±0.18	0.29±0.03	10.9±1.1	1.19±0.12	1.87±0.16	2.08±0.19
7	Rats with a burn + HAES-LX 5 %, n=7	3.63±0.31	0.66±0.07	7.3±0.7	0.72±0.08	1.06±0.11	1.19±0.11
		$P_{1-2}<0.001$ $P_{1-3}<0.001$ $P_{1-5}<0.001$ $P_{1-7}<0.001$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}<0.001$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}<0.001$	$P_{1-2}<0.001$ $P_{1-3}<0.001$ $P_{1-5}<0.001$ $P_{1-7}<0.001$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}<0.001$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}<0.001$	$P_{1-2}<0.01$ $P_{1-3}<0.01$ $P_{1-5}<0.01$ $P_{1-7}<0.01$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}<0.01$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}<0.01$	$P_{1-2}<0.01$ $P_{1-3}<0.01$ $P_{1-5}<0.01$ $P_{1-7}<0.01$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}<0.01$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}<0.01$	$P_{1-2}<0.05$ $P_{1-3}<0.05$ $P_{1-5}<0.05$ $P_{1-7}<0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}<0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}<0.05$	$P_{1-2}<0.01$ $P_{1-3}<0.01$ $P_{1-5}<0.01$ $P_{1-7}<0.01$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}<0.01$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}<0.01$
	Day 3						
1	Control (intact rats), n=8	2.11±0.19	0.27±0.04	11.3±1.2	1.21±0.12	1.84±0.14	2.11±0.19
2	Rats with a burn, n=11	3.19±0.29	0.51±0.06	8.1±0.6	0.84±0.07	1.26±0.12	1.23±0.13
3	Rats with a burn+NaCl, n=11	2.96±0.26	0.46±0.06	9.2±0.8	0.91±0.08	1.33±0.14	1.36±0.13
4	LPS, n=7	2.07±0.18	0.23±0.03	11.6±1.2	1.27±0.12	1.87±0.17	2.16±0.18
5	Rats with a burn + LPS, n=7	2.38±0.21	0.34±0.04	10.3±1.1	1.11±0.09	1.62±0.16	1.66±0.16
6	HAES-LX 5 %, n=7	2.12±0.19	0.26±0.04	11.4±1.2	1.19±0.13	1.81±0.16	2.13±0.19
7	Rats with a burn + HAES-LX 5 %, n=7	2.31±0.21	0.37±0.04	10.8±1.1	1.07±0.08	1.69±0.17	1.71±0.16
		$P_{1-2}<0.01$ $P_{1-3}<0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}<0.05$ $P_{4-5}>0.05$ $P_{2-7}<0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}<0.05$ $P_{1-3}<0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}<0.05$ $P_{4-5}>0.05$ $P_{2-7}<0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}<0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}<0.05$ $P_{4-5}>0.05$ $P_{2-7}<0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}<0.05$ $P_{1-3}<0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}<0.05$ $P_{4-5}>0.05$ $P_{2-7}<0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}<0.05$ $P_{1-3}<0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}<0.05$ $P_{4-5}>0.05$ $P_{2-7}<0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}<0.01$ $P_{1-3}<0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}<0.05$ $P_{4-5}<0.05$ $P_{2-7}<0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$
	Day 7						
1	Control (intact rats), n=8	2.04±0.18	0.22±0.03	10.9±1.3	1.17±0.13	1.94±0.16	2.07±0.18
2	Rats with a burn, n=11	2.67±0.24	0.39±0.05	8.9±0.7	0.98±0.07	1.51±0.13	1.42±0.14
3	Rats with a burn+NaCl, n=11	2.48±0.23	0.32±0.03	9.6±0.9	1.03±0.08	1.59±0.16	1.71±0.18
4	LPS, n=7	2.11±0.17	0.19±0.02	11.2±1.2	1.23±0.12	1.91±0.18	2.13±0.19
5	Rats with a burn + LPS, n=7	2.27±0.26	0.29±0.04	10.8±1.1	1.11±0.11	1.67±0.17	1.67±0.17
6	HAES-LX 5 %, n=7	2.03±0.19	0.21±0.02	10.7±1.1	1.14±0.13	1.88±0.17	2.02±0.19
7	Rats with a burn + HAES-LX 5 %, n=7	2.33±0.24	0.26±0.03	9.9±1.0	1.08±0.09	1.56±0.16	1.88±0.19
		$P_{1-2}<0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}<0.05$	$P_{1-2}<0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}<0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}<0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}<0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$

The data obtained were calculated statistically using one-way variant ANOVA parametric criterion accompanied by a post-hoc Newman-Keuls test. The minimum statistical probability was determined at $p<0.05$.

Results of the study and their discussion. On the 1st day after thyroid gland burning the MDA and DC concentrations in the kidney tissue was 1.9 times and 2.6 times, respectively, higher than these indicators in the control group ($p<0.001$, Table 1). The antioxidant enzymes activity was significantly lower than in the control rats. Glutathione activity in the kidney parenchyma was 1.7 times less ($p<0.01$), SOD activity – 1.6 times less ($p<0.01$, GTP activity – 1.8 times ($p<0.05$) and GTR – 1.7 times ($p<0.01$) less pertaining with the corresponding control measurements. None of the lipoperoxidation and antioxidant defence investigated indexes were changed due to saline and both LPS and HAES-LX-5 % hyperosmolar colloidal solutions administration.

The expressed changes were also recorded on the 3rd day of the trial concerning the MDA ($p<0.01$) and DC ($p<0.05$) content increase and the activity of the investigated antioxidant enzymes inhibition ($p<0.05$) in kidney parenchyma. LPS administration resulted in both MDA and DC content decrease by 25.4 % and by 33.3 %, respectively, and in glutathione (by 27.2 %), SOD (by 32.1 %), GTP (by 28.6 %) and GTR (by 35 %) activity increase when compared with similar indexes in rats with thyroid gland burning without treatment (in all cases $p<0.05$). The analogous data connected with lipoperoxidation intermediate products content decrease and the investigated antioxidant enzymes activity increase we registered after the HAES-LX 5 % colloidal hyperosmolar solution injection on the 3rd day of the trial.

The values of all investigated indexes in rats with thyroid gland burning without treatment and with NaCl, LPS and HAES-LX 5 % solutions administration did not differ significantly from similar data recorded in intact rats till the end of the trial ($p>0.05$; Table 2).

The content of protein and creatinine in urine of burned rats significantly exceeded the initial parameters during the whole trial ($p<0.01$). At the same time, protein excretion rates increased significantly (in the range from 2.83 times on the 30th day to 8 times on the 14th day of the trial; $p<0.001$) and creatinine excretion rates decreased (in the range from 13.3 % the 30th day to 27.4 % on the 14th day; $p<0.05$).

Under the LPS and HAES-LX 5 % solutions influence, the indexes of urine protein level and its excretion, remaining significantly increased, were lower pertaining the same indexes in rats with thermal injury that were not treated on the 7th day of the trial ($p<0.05$).

Creatinine excretion rate on the 3rd day of the trial after LPS and HAES-LX-5 % hyperosmolar colloidal solutions administration was equal to 1.76±0.09 μmol/l and 1.79±0.09 μmol/l, respectively, which failed to have statistical difference from similar control indexes ($p>0.05$).

Creatinine content in urine on the 21st day of the experiment under the influence of LPS and HAES-LX-5 % solutions was by 35.2 % and by 27.7 % lower, respectively, when compared with similar indexes in burned rats without treatment ($p<0.05$).

The revealed kidney function changes induced by LPS and HAES-LX 5 % solutions in conditions of water induced diuresis in rats with thyroid gland burning continued till the end of the observation period.

Thermal damage of the body was accompanied by diuresis marked decrease in rats, which lasted throughout the whole period of observation. Under these conditions, only on the 14th day of the trial, the LPS and HAES-LX 5 % solutions administration contributed to all studied indexes of diuresis increase comparing them with the same indexes in rats with thyroid gland burning without treatment ($p<0.05$). We registered a diuresis gradual increase until the end of the experiment.

Thus, the data obtained indicate the expressed kidney function disorders manifested by their excretory and detoxicative functions disturbances throughout the 30 days of the postburn process together with lipoperoxidative processes acceleration and antioxidant protection suppression within the kidneys' parenchyma. Kidneys functional activity disturbances which we consider as the pathological dysregulation standpoint, according to used criteria, reach their maximal expression on the 3rd – 14th days of the study.

Massive hypohydration in conditions of thyroid gland burning explains kidneys involvement into the pathological process mediation [4, 13]. Other explanations stem from the burn process pathophysiological mechanisms and relate to endotoxinemia alterative impact on nephrocytes. We proved another argument in favour of kidney damage during the burn process by clarifying the breakdown of the functional system "lipid peroxidation – antioxidant defence" in the kidney parenchyma towards the lipoperoxidation acceleration and the coupled antioxidant defence suppression. Free radical mechanism traced by us is well known to be one of the apparent mechanisms of cell death.

The given pathophysiological mechanisms explain the kidneys involvement into the thyroid gland burning mediation. Summarizing the renal array of the obtained data, we note the pronounced renal dysfunction under model conditions in the form of kidneys excretory (reduced diuresis) and filtrative (proteinuria and decreased glomerular filtration rate based on creatinine) functions disorder.

Table 2

The influence of PLS and HAES-LX 5 % on changes in lipid peroxidation in rats' kidney parenchyma after thyroid gland burning from the 14th to 30th days of trial

N	Experimental groups	The amount of the substances investigated (M±m)					
		MDA, nmole/g	DC, μmole/g	Glutathione, мM	SOD, unit/g	GTP, unit/g	GTR, unit/g
	Day 14y						
1	Control (intact rats), n=8	2.09±0.19	0.17±0.04	11.3±1.4	1.24±0.14	1.88±0.17	2.17±0.17
2	Rats with a burn, n=11	2.41±0.22	0.27±0.03	9.8±0.8	1.09±0.09	1.66±0.17	1.68±0.17
3	Rats with a burn+NaCl, n=11	2.27±0.19	0.21±0.04	10.4±1.1	1.17±0.11	1.71±0.18	1.82±0.16
4	LPS, n=7	2.03±0.18	0.21±0.02	10.7±1.1	1.26±0.13	1.82±0.18	2.13±0.18
5	Rats with a burn + LPS, n=7	2.18±0.21	0.22±0.03	10.8±1.1	1.21±0.12	1.68±0.17	1.89±0.18
6	HAES-LX 5 %, n=7	2.08±0.17	0.16±0.02	11.7±1.2	1.23±0.13	1.79±0.18	2.11±0.19
7	Rats with a burn + HAES-LX 5 %, n=7	2.16±0.18	0.18±0.03	10.3±1.1	1.22±0.13	1.77±0.18	1.83±0.17
		$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$
	Day 21						
1	Control (intact rats), n=8	2.04±0.21	0.21±0.03	11.8±1.3	1.31±0.14	1.74±0.16	2.23±0.21
2	Rats with a burn, n=11	2.19±0.23	0.19±0.04	10.9±1.1	1.16±0.11	1.57±0.17	1.81±0.19
3	Rats with a burn+NaCl, n=11	2.09±0.18	0.16±0.03	11.4±1.2	1.24±0.12	1.46±0.16	2.02±0.18
4	LPS, n=7	2.11±0.19	0.23±0.03	11.9±1.2	1.26±0.13	1.69±0.17	2.17±0.18
5	Rats with a burn + LPS, n=7	2.06±0.21	0.14±0.02	11.3±1.3	1.26±0.13	1.49±0.16	2.11±0.21
6	HAES-LX 5 %, n=7	2.01±0.18	0.17±0.02	11.4±1.2	1.34±0.13	1.77±0.16	2.27±0.23
7	Rats with a burn + HAES-LX 5 %, n=7	2.07±0.17	0.18±0.02	10.9±1.3	1.21±0.12	1.38±0.14	1.89±0.19
		$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$
	Day 30						
1	Control (intact rats), n=8	2.11±0.18	0.23±0.06	10.9±1.3	1.09±0.11	1.87±0.19	1.98±0.19
2	Rats with a burn, n=11	2.21±0.19	0.16±0.05	11.6±1.2	1.04±0.12	1.72±0.18	1.77±0.16
3	Rats with a burn+NaCl, n=11	2.14±0.21	0.24±0.04	10.7±1.4	1.12±0.11	1.96±0.17	2.11±0.19
4	LPS, n=7	2.13±0.19	0.21±0.03	10.6±1.1	1.13±0.11	1.81±0.17	2.03±0.18
5	Rats with a burn + LPS, n=7	2.13±0.23	0.22±0.03	11.1±1.2	1.09±0.09	1.79±0.18	2.07±0.19
6	HAES-LX 5 %, n=7	2.04±0.18	0.19±0.02	11.3±1.2	1.06±0.09	1.87±0.17	1.91±0.19
7	Rats with a burn + HAES-LX 5 %, n=7	2.04±0.19	0.21±0.04	10.4±1.1	1.07±0.11	1.84±0.19	1.98±0.21
		$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$	$P_{1-2}>0.05$ $P_{1-3}>0.05$ $P_{1-5}>0.05$ $P_{1-7}>0.05$ $P_{2-3}>0.05$ $P_{2-5}>0.05$ $P_{4-5}>0.05$ $P_{2-7}>0.05$ $P_{5-7}>0.05$ $P_{6-7}>0.05$

Our results regarding the erythrocyte membranes pathological changes, acceleration of lipoperoxidation processes in blood and erythrocytes together with proven renal dysfunction complement the concept of pathological dysregulation in conditions of excessive thermal exposure to thyroid gland and confirm the systemic nature of burn-induced functional disorders.

We consider fundamental the data which highlighted the LPS and HAES-LX 5 % hyperosmolar colloidal solutions nephroprotective effects. It is important that, first of all, the use of LPS and HAES-LX 5 % hyperosmolar colloidal solutions proved to be effective in terms of nephrocyte damage free radical mechanism prevention and the antioxidant protection enzymatic link activation. Secondly, LPS and HAES-LX 5 % hyperosmolar colloidal solutions in conditions of thyroid gland thermal damage contributed kidney specific functions recovery. Thirdly, the conducted studies did not reveal any difference both colloidal solutions efficacy and terms of their nephroprotective activity implementation – they are identical in terms of overall protective activity. Similarly, these two compounds showed protective activity in thymus, spleen and small intestine mucosa burning [5, 7, 9]. Fourthly, the temporal aspect of LPS and HAES-LX 5 % solutions nephroprotective activity realization is interesting. We remind that these compounds were administered systemically during the first 7 days after thyroid gland burning. It's important that their protective effect is postponed which indicates the individual peptidergic components with a multiionic composition induction under their influence. The applied LPS and HAES-LX 5 % hyperosmolar colloidal solutions optimal protective activity occurs on the 7^{th} – 14^{th} day of the trial and lasts until the end of the experiment, which, in our opinion, is an advantage in their probable clinical use.

Taking into account the applied solution multicomponent ionic composition and the complete predominance of both catabolic and necrotic processes in the post-burn period dynamics, we consider the generalized catabolic reaction inhibition to be one of the mechanisms of colloidal solutions protective effect. In this case, the applied solution efficacy is identical to their membrane-protective effect. The data we obtained regarding the LPS and HAES-LX 5 % solutions nephroprotective effectiveness in thermally damaged thyroid gland are consistent with their positive impact on thyrocytes and surrounding tissues morphological structure under similar conditions.

Thus, the data obtained we consider to be an experimental evidence of a correctly formulated and effective scheme for organ dysfunctions (in our case, renal dysfunction) prevention in case of thyroid gland burning. The scheme of thyroid gland burning pharmacological correction includes the LPS and HAES-LX 5 % hyperosmolar colloidal solutions with a multiionic composition injection for 7 days during which the postponed "synthetic" effects are initiated. We consider the developed scheme of thyroid gland burning pharmacological correction to be pathogenetically justified and to be able not only to restore the nephrocytes functional activity but also to prevent their damage throughout the post-burn process dynamics. We hope for both the therapeutic and prophylactic effects formation as a result of LPS and HAES-LX 5 % solutions administration, which requires further verification.

Conclusions

1. The expressed kidney function disorders manifested by their excretory and detoxicative functions disturbances occur throughout the 30 days of the postburn process together with lipoperoxidative processes acceleration and antioxidant protection suppression within the kidneys' parenchyma.

2. Kidneys functional activity disturbances reach their maximal expression on the 3^{rd} – 14^{th} days of the study.

3. LPS and HAES-LX 5 % hyperosmolar colloidal solutions revealed nephroprotective effects in terms of nephrocyte damage free radical mechanism prevention and the antioxidant protection enzymatic link activation.

4. LPS and HAES-LX 5 % hyperosmolar colloidal solutions in conditions of thyroid gland thermal damage contributed kidney specific functions recovery.

5. LPS and HAES-LX 5 % hyperosmolar colloidal solutions optimal protective activity occurs on the 7^{th} – 14^{th} day of the trial and lasts until the end of the experiment.

6. The scheme of thyroid gland burning pharmacological correction including the LPS and HAES-LX 5 % hyperosmolar colloidal solutions administration considered to be pathogenetically justified and to be able not only to restore the nephrocytes functional activity but also to prevent their damage throughout the post-burn process dynamics.

Prospects for further research include a further study of the thyroid gland burning pathogenetically based pharmacological correction efficacy using the lactoprotein with sorbitol and HAES-LX 5 % hyperosmolar colloidal solutions administration in the aspect of inherent in pathological dysregulation processes restoration as well as the biological organism sanogenetic systems activation.

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