EXPERIMENTAL INVESTIGATIONS

The Ukrainian Journal of Clinical Surgery. 2024 January/February; 91(3):54-61
DOI: 10.26779/2786-832X.2024.3.54

Experimental substantiation of the expediency of using hyperosmolar colloidal solutions for the correction of renal dysfunction in conditions of thermal skin damage

O. I. Tiron[1], I. P. Khomenko[2,3], I. A. Lurin[2], S. V. Tertyshny[1,4], G. F. Stepanov[1], R. S. Vastyanov[1]

[1]Odesa National Medical University,
[2]National Academy of Medical Sciences of Ukraine, Kyiv,
[3]Scientific and Practical Centre for Preventive and Clinical Medicine of the State Administration of Affairs, Kyiv,
[4]Military Medical Clinical Centre of the Southern Region, Odesa

Abstract

Objective. To study the effectiveness of hyperosmolar colloidal solutions of lactoprotein with sorbitol and HAES–LX 5% on changes in renal functional activity in the dynamics of thermal skin damage.

Materials and methods. The study was conducted under conditions of a chronic experiment on a model of skin burn injury. The concentration of lipoperoxidation intermediates and the activity of antioxidant enzymes in kidney homogenates was determined 1, 3, 7, 14, 21 and 30 days after thermal skin burn. The functional activity of the kidneys was determined using the model of induced water diuresis.

Results. We have demonstrated marked impairment of filtration, excretory and detoxification functions of the kidneys within 30 days of the post–burn period, as well as acceleration of lipoperoxidation and inhibition of antioxidant defence activity. The saline solution had no thermoprotective effect in the skin burn model. The use of hyperosmolar colloidal solutions of lactoprotein with sorbitol and HAES–LX 5% effectively prevented the free radical mechanism of nephrocyte damage and activation of the enzymatic link of antioxidant defence. The optimum protective activity of the hyperosmolar colloidal solutions of lactoprotein with sorbitol and HAES–LX 5% occurred on days 7–14 of the experiment and lasted until its completion.

Conclusions. The scheme of pharmacological correction of thermal damage to the thyroid gland with the introduction of hyperosmolar colloidal solutions with a multionic composition of lactoprotein with sorbitol and HAES–LX 5% is pathogenetically justified, can not only restore the functional activity of nephrocytes, but also prevent their damage in the dynamics of the postburn process.

Key words: skin burn; thyroid gland; kidneys; antioxidant protection; induced water diuresis; pathological dysregulation of organs and systems; hyperosmolar colloidal solutions of lactoprotein with sorbitol and HAES–LX 5%; pathogenetically based pharmacological correction.

The relevance of a comprehensive study of the problem of burns is undoubtedly due to the increasing number of patients with burn injuries, the insufficient effectiveness of existing therapies and the high incidence of systemic complications [1–4]. Unfortunately, this topic is also relevant because the Russian aggression against our country continues and leads to a significant proportion of victims with burn injuries [5].

Experts note the ineffectiveness of existing treatment methods, not least due to the complex pathogenesis of this pathological condition, numerous factors responsible for the cascade of pathological processes in thermal burns, the formation of multiorgan dysfunction and pathological dysregulation of organs and systems in thermal damage [4, 6, 7]. Our studies have shown the formation of thyroid dysfunction and pronounced pathomorphological changes in thyrocytes, thyroid parenchyma and surrounding tissue in thermal skin damage [8, 9], as well as the pathogenetic significance of kidney involvement and renal dysfunction in thermal thyroid damage [10].

The established chains of pathogenetic mechanisms initiated by excessive thermal exposure of thyroid lesions prompted us to attempt to develop a pathogenetically oriented correction of the pathological thermal changes reproduced in the experiment. The ineffectiveness of fluid volume restoration in the body of animals under these model conditions by the administration of 0.9% sodium chloride (NaCl) saline served as an impetus for the choice of hyperosmolar colloidal solutions as promising components of a comprehensive pathogenetic correction of burn damage to the thyroid gland. The positive effects of hyperosmolar colloidal solutions of lactoprotein with sorbitol (LS) and HAEX LX 5% in the restoration of the morphological structure of the thyroid gland [11] gave reason to hope for their protective functional effect under these model conditions.

The aim of the study was to investigate the effectiveness of the influence of hyperosmolar colloidal solutions of LS and HAES–LX–5% on changes in renal functional activity in the dynamics of thermal skin damage. As parameters of kidney function, we chose the processes of lipoperoxidation and antioxidant protection in the kidney parenchyma, which determine, among other things, the vital activity of nephrocytes, and transport processes in the kidney parenchyma, the severity of which was judged based on the content of protein and creatinine in blood and urine.

Materials and methods

Experimental studies were conducted on 350 male rats weighing 180 – 220 g, which were kept in vivarium conditions. The animals were kept, treated and manipulated in accordance with the General Ethical Principles for Animal Experiments approved by the First National Congress on Bioethics (20 September 2001, Kyiv), and guided by the recommendations of the European Convention for the Protection of Human Subjects, Kyiv), and were guided by the recommendations of the European Convention for the Protection of Vertebrate Animals Used for Scientific Experiments and

Table 1. **Effect of hyperosmolar colloidal solutions on the severity of changes in lipoperoxidation and antioxidant defence in the rat kidney parenchyma 1, 3 and 7 days after thermal damage of the thyroid gland**

Groups of rats	The content of the test substances ($\bar{x} \pm m$) and the duration of the post-burn period					
	MDA, nmol/g	DK, μmol/g	total glutathione, mM	SOD, units per tonne	GP, units/h	GP, units per hectare
1st day						
1 (control)	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 (burn)	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 (burn + NaCl)	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 (LS)	2,01±0,19	0,23±0,03	1,7±1,2	1,17±0,11	1,96±0,17	2,12±0,18
5 (burn + LS)	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%)	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 (burn + HAES-LX 5%)	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_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.01 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.01 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.01 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05
3rd day						
1 (control)	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 (burn)	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 (burn + NaCl)	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 (LS)	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 (burn + LS)	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%)	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 (burn + HAES-LX 5%)	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_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.01 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05
7th day						
1 (control)	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 (burn)	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 (burn + NaCl)	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 (LS)	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 (burn + LS)	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%)	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 (burn + HAES-LX 5%)	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_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} >0.05 P_{2-7} <0.05 P_{5-7} >0.05

Other Scientific Purposes (Strasbourg, 1986), the guidelines of the SFC of the Ministry of Health of Ukraine "Preclinical Studies of Medicines" (2001) and the rules and conditions for the humane treatment of experimental animals approved by the Bioethics Commission of Odesa National Medical University (Protocol No. 17–C of 12.11.2021).

Thermal skin burns of the 2nd – 3rd degree were modelled according to a well–known method by pressing hot copper plates to the pre–depilated lateral surfaces of the rat body for 10 s [9].

Experiments and laboratory measurements were performed in the following groups of animals: group 1 – intact rats (n=48); group 2 – rats with skin burns (n=68); group 3 – rats with skin burns injected with 0.9% saline (n=66); group 4 – intact rats injected with drug solution (n=42); group 5 – rats with skin burns injected with drug solution (n=42); group 6 – intact rats injected with HAES–LX 5% solution (n=42); group 7 – rats with skin burns injected with HAES–LX 5% solution (n=42).

During the first 7 days of the post–burn period, 0.9% saline NaCl, as well as solutions of LS (10 ml/kg) and HAES–LX 5% (10 ml/kg) were injected into the inferior vena cava once daily. Shaving, vein catheterisation and skin burns

Table 2. **The effect of hyperosmolar colloidal solutions on the severity of changes in lipoperoxidation and antioxidant defence in the rat kidney parenchyma 14, 21 and 30 days after thermal damage to the thyroid gland**

Groups of rats	The content of the test substances (x̅ ± m) and the duration of the post-burn period					
	MDA, nmol/g	DK, μmol/g	total glutathione, mM	SOD, units per tonne	GP, units/h	GP, units per hectare
14th day						
1 (control)	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 (burn)	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 (burn + NaCl)	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 (LS)	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 (burn + LS)	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%)	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 (burn + HAES-LX 5%)	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_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05
21st day						
1 (control)	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 (burn)	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 (burn + NaCl)	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 (LS)	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 (burn + LS)	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%)	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 (burn + HAES-LX 5%)	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_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05
30th day						
1 (control)	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 (burn)	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 (burn + NaCl)	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 (LS)	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 (burn + LS)	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%)	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 (burn + HAES-LX 5%)	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_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} <0.05 P_{5-7} >0.05

were performed under intravenous anaesthesia with propofol (60 mg/kg).

At 1, 3, 7, 14, 21 and 30 days after thermal skin burns, rats were euthanised and their kidneys were removed and homogenates were prepared. In kidney homogenates, the concentration of malondialdehyde (MDA) and diene conjugates (DC), as well as the activity of glutathione, superoxide dismutase (SOD), glutathione peroxidase (GP) and glutathione reductase (GR) were determined by conventional methods [12].

To determine renal function, water for injection was injected intraperitoneally into the control group rats and after 2 h, water loading was performed – a model of induced water diuresis, under which functional studies were performed. The concentration of total protein and creatinine was determined in rat urine samples 1, 3, 7, 14, 21 and 30 days after thermal burn.

The results were statistically calculated using the Bonferroni parametric multiple test. The minimum statistical significance was determined at $p<0.05$.

Results

On the 1st day after thermal skin injury, the concentration of MDA in the kidney tissue was 1.9 times higher ($p<0.001$)

Table 3. **Effect of hyperosmolar colloidal solutions on the severity of changes in renal function in rats under conditions of induced water diuresis 1, 3 and 7 days after thermal damage to the thyroid gland**

Groups of rats	Values of the studied indicators ($\bar{x} \pm m$) and the duration of the post-burn period			
	protein concentration in urine, mg/l	protein excretion, mg/h	urine creatinine concentration, mmol/l	creatinine excretion, μ mol/l
1st day				
1 (control)	23,7±1,4	0,04±0,01	1,16±0,05	2,11±0,09
2 (burn)	284,7±13,8	0,23±0,02	2,65±0,12	1,69±0,08
3 (burn + NaCl)	269,2±14,1	0,21±0,02	2,38±0,11	1,72±0,09
4 (LS)	22,1±1,8	0,05±0,01	1,21±0,07	2,14±0,11
5 (burn + LS)	246,3±17,2	0,22±0,02	2,33±0,14	1,71±0,09
6 (HAES-LX 5%)	24,3±1,9	0,04±0,01	1,13±0,06	2,16±0,09
7 (burn + HAES-LX 5%)	269,2±14,1	0,21±0,02	2,38±0,11	1,77±0,09
	P_{1-2} <0.001 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.01 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05
3rd day				
1 (control)	22,4±1,5	0,05±0,01	1,15±0,05	2,08±0,09
2 (burn)	327,2±16,1	0,27±0,03	2,77±0,16	1,61±0,08
3 (burn + NaCl)	313,9±14,9	0,24±0,03	2,78±0,18	1,64±0,08
4 (LS)	22,6±1,7	0,05±0,01	1,18±0,06	2,11±0,11
5 (burn + LS)	276,3±23,8	0,21±0,02	2,36±0,19	1,76±0,09
6 (HAES-LX 5%)	23,7±1,8	0,04±0,01	1,14±0,07	2,07±0,09
7 (burn + HAES-LX 5%)	258,7±18,9	0,23±0,03	2,28±0,21	1,79±0,09
	P_{1-2} <0.001 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.01 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05
7th day				
1 (control)	23,2±1,4	0,04±0,01	1,17±0,06	2,07±0,08
2 (burn)	367,7±18,7	0,29±0,03	2,84±0,16	1,56±0,07
3 (burn + NaCl)	354,3±17,9	0,27±0,03	2,61±0,16	1,61±0,08
4 (LS)	24,7±2,1	0,05±0,02	1,22±0,08	2,04±0,09
5 (burn + LS)	218,6±13,6	0,21±0,03	2,36±0,17	1,78±0,11
6 (HAES-LX 5%)	23,6±1,9	0,04±0,02	1,16±0,09	2,04±0,11
7 (burn + HAES-LX 5%)	223,7±14,7	0,19±0,03	2,29±0,18	1,74±0,11
	P_{1-2} <0.001 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05

Table 4. **Effect of hyperosmolar colloidal solutions on the severity of changes in renal function in rats under conditions of induced water diuresis 14, 21 and 30 days after thermal damage to the thyroid gland**

Groups of rats	The value of the studied indicators ($\bar{x} \pm m$) and the duration of the post-burn period			
	protein concentration in urine, mg/l	protein excretion, mg/h	urine creatinine concentration, mmol/l	creatinine excretion, μ mol/l
14th day				
1 (control)	22,9±1,6	0,04±0,01	1,16±0,06	2,12±0,08
2 (burn)	379,8±20,2	0,32±0,03	2,87±0,18	1,54±0,07
3 (burn + NaCl)	367,7±18,7	0,29±0,03	2,72±0,17	1,59±0,07
4 (LS)	22,3±1,8	0,05±0,02	1,19±0,08	2,17±0,12
5 (burn + LS)	211,4±16,8	0,19±0,03	2,27±0,17	1,71±0,09
6 (HAES-LX 5%)	23,3±1,9	0,04±0,02	1,22±0,08	2,22±0,13
7 (burn + HAES-LX 5%)	206,2±17,1	0,23±0,03	2,21±0,18	1,76±0,11
	P_{1-2} <0.001 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05
21st day				
1 (control)	21,9±1,3	0,05±0,01	1,18±0,06	2,11±0,09
2 (burn)	312,4±16,3	0,22±0,03	2,36±0,13	1,66±0,08
3 (burn + NaCl)	291,2±14,1	0,21±0,02	2,18±0,11	1,75±0,08
4 (LS)	21,1±1,7	0,06±0,02	1,23±0,09	2,14±0,09
5 (burn + LS)	137,6±11,2	0,14±0,03	1,53±0,13	1,89±0,13
6 (HAES-LX 5%)	22,8±1,8	0,04±0,02	1,14±0,07	2,09±0,11
7 (burn + HAES-LX 5%)	149,1±13,2	0,16±0,03	1,47±0,11	1,83±0,14
	P_{1-2} <0.001 P_{2-5} <0.01 P_{2-7} <0.01 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.01 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05
30th day				
1 (control)	23,9±1,6	0,06±0,01	1,15±0,04	2,06±0,08
2 (burn)	241,1±12,9	0,17±0,02	1,92±0,11	1,79±0,08
3 (burn + NaCl)	219,8±11,7	0,15±0,02	1,78±0,11	1,88±0,08
4 (LS)	23,2±1,8	0,05±0,02	1,13±0,06	2,11±0,09
5 (burn + LS)	102,3±9,8	0,11±0,02	1,28±0,09	1,98±0,11
6 (HAES-LX 5%)	22,4±1,7	0,04±0,01	1,22±0,04	2,14±0,09
7 (burn + HAES-LX 5%)	111,6±10,2	0,09±0,02	1,24±0,09	1,94±0,11
	P_{1-2} <0.001 P_{2-5} <0.01 P_{2-7} <0.01 P_{5-7} >0.05	P_{1-2} <0.001 P_{2-5} <0.05 /P_{2-7} <0.01 P_{5-7} >0.05	P_{1-2} <0.05 P_{2-5} <0.05 P_{2-7} <0.05 P_{5-7} >0.05	P_{1-2} >0.05 P_{2-5} >0.05 P_{2-7} >0.05 P_{5-7} >0.05

than the corresponding control value, and the concentration of DP in the kidney tissue was 2.6 times higher (p<0.001) than the corresponding control value (*Table 1*). The activity of glutathione in the renal parenchyma was 1.7 times lower (p<0.01), the activity of SOD – 1.6 times (p<0.01), the activity of GP – 1.8 times (p<0.05), and GC – 1.7 times (p<0.01) than the corresponding control values.

After administration of 0.9% saline solution of NaCl to rats with skin burns, the values of all studied parameters of lipoperoxidation and antioxidant protection in the renal parenchyma were comparable to those in the case of skin burns without pharmacological correction (p>0.05).

After administration of a hyperosmolar colloidal solution of drugs to rats with skin burns, all studied indicators of lipoperoxidation and antioxidant protection in the renal parenchyma differed from the corresponding indicators of rats with skin burns without pharmacological correction in the range from 2.8% (SOD indicators) to 9.0% (DC indica-

tors), which also did not have a statistically significant difference (p>0.05).

After administration of hyperosmolar colloidal solution HAES–LX 5% to rats with skin burns, the values of all studied parameters of lipoperoxidation and antioxidant protection in the renal parenchyma were also comparable to those in skin burns without pharmacological correction (p>0.05).

Comparable data were obtained on day 3 of the experiment. The concentration of MDA and DC in the kidney tissue, as well as the activity of the studied antioxidant enzymes, were identical to those of intact rats (p>0.05).

The values of the studied parameters of rats with skin burns injected with a hyperosmolar colloidal solution of drugs were significantly different from the corresponding parameters of rats with skin burns without pharmacological correction (p<0.05).

Similar differences in the absolute values of the studied parameters were recorded in rats with skin burns injected with hyperosmolar colloidal solution HAES–LX 5% (p<0.05).

The recorded protective effect of the applied hyperosmolar colloidal solutions of LS and HAES–LX 5%, which was manifested by the restoration of the concentrations of underoxidized substances MDA and DC and the activity of antioxidant enzymes, lasted until the end of the experiment (*Table 2*).

In 1 day after thermal skin burn, the concentration of protein in the urine of rats was 12 times higher (p<0.001) than the corresponding normal value, the concentration of creatinine was 2.3 times higher (p<0.01) than the corresponding normal value (*Table 3*). Protein excretion by the kidneys during this interval of the experiment exceeded the corresponding control value by 5.75 times (p<0.001), creatinine excretion was 19.9% less (p<0.05) than the corresponding value in intact rats.

After administration of 0.9% saline NaCl solution to rats with skin burns, the values of all studied parameters of renal excretory activity were comparable to those in the case of skin burns without pharmacological correction (p>0.05).

After administration of a hyperosmolar colloidal solution of the drug to rats with skin burns, all studied parameters of renal excretory activity differed from the corresponding parameters in the case of skin burns without pharmacological correction in the range from 1.2% (creatinine excretion) to 13.5% (urinary protein concentration), which also did not have a statistically significant difference (p>0.05).

After administration of hyperosmolar colloidal solution HAES–LX 5% to rats with skin burns, the values of all studied parameters of renal excretory activity were also comparable to the corresponding values in the case of skin burns without pharmacological correction (p>0.05). Under such conditions, all studied parameters of renal excretory activity in rats with burns after administration of solutions of LS and HAES–LX 5% did not differ significantly from the corresponding parameters of rats with thyroid burn without pharmacological correction (p>0.05) and had significant differences with the corresponding control parameters (p<0.05).

Similar data on changes in renal function were recorded on day 3 of the experiment.

On day 7 of the experiment, the absolute values of urinary protein concentration and its excretion in rats with skin burns injected with a hyperosmolar colloidal solution of the drug significantly differed from the corresponding values in rats with skin burns without pharmacological correction (p<0.05). Creatinine concentration and its excretion remained unchanged under these conditions (p>0.05).

A similar direction of restorative effects on urinary protein concentration and its excretion in rats with skin burns was recorded in response to the administration of hyperosmolar colloidal solution HAES–LX 5%.

The restorative effects of both hyperosmolar colloidal solutions, similar in severity, lasted until the end of the experiment (*Table 4*). Starting from the 21st day of the experiment, the concentration of creatinine in the urine significantly decreased under the influence of a hyperosmolar colloidal solution of the drug (p<0.05), and this effect continued until the end of the experiment.

Discussion

We have obtained several sets of results that are of undoubted fundamental importance. Therefore, we consider it appropriate to focus on the methodological features of this part of our work. We are talking about the direct damage to thyroid tissue initiated by thermal exposure, which has been proven morphologically [8, 13] and functionally [9, 12]. That is why, after applying thermal damage to the skin of rats, we interpreted the subsequent actual results as those obtained as a result of thermal damage to the thyroid tissue.

We have proved the involvement of the kidneys in mediating a number of pathological processes initiated by the effect of an excessive thermal factor on the body. Our conclusion is based on the proven acceleration of lipoperoxidation and the corresponding inhibition of the activity of the antioxidant defence system in rat kidney tissue under model conditions. Taking into account the known fundamental data, the result of the above–mentioned conjugated processes is necrosis and subsequent cell death, which is exactly what happens to nephrocytes in burn conditions [4].

This part of the data logically "fits" into the fundamental concept of the formation of pathological dysregulation of organs and systems under conditions of pathological processes, in particular, in thermal damage to the thyroid gland [14]. Similar results, for example, were obtained when the spleen and thymus are involved in mediating thermal damage to the body [15, 16], when cirrhotic liver parenchyma damage

is formed with a systemic response to this pathological process [17], as well as in the context of pathological dysfunction of the nervous system in the case of chronic convulsive syndrome [18] and chronic cerebral ischaemia [19]. On the other hand, we consider it fundamental to note that the "renal" array of data obtained proves the need to correct the functional state of the kidneys as part of a comprehensive pathogenetically based scheme of pharmacological correction of thyroid disorders initiated by excessive thermal exposure, since in this aspect we are talking about adherence to the generally accepted view of the pathogenetic focus of any treatment of a specific pathological condition [6].

In addition to the peroxidative mechanism of pathogenic changes in the kidneys of animals during the post–burn period, renal dysfunction under these conditions has been proven, which is confirmed by impaired filtration (formation of proteinuria and a decrease in glomerular filtration rate by creatinine) renal function. Taking into account the impaired excretory function of the kidneys [10], experimental evidence of the formation of pathological dysregulation of organs and systems in thermal damage to the thyroid gland is needed, which we consider an important fundamental conclusion in the analysis of the results.

Some of the purely pathophysiological studies were not an end in themselves in our work. Another important block of the results obtained is the proven effectiveness of pathogenetic correction of the functional breakdown of renal activity in conditions of thermal burn of the thyroid gland by using hyperosmolar colloidal solutions of LS and HAES–LX 5%. Their protective effectiveness under model conditions is proved by inhibition of lipoperoxidation processes and restoration of the activity of the antioxidant defence system in the kidney parenchyma, as well as restoration of their functional activity. We note the absence of a thermoprotective effect of 0.9% NaCl saline in the skin burn model, which also gave us an additional impetus to search for new components of the complex correction of thyroid disorders initiated by skin burn. When discussing this part of the results, there are many possibilities for branching out, but first we note that the obtained restorative functional effects of hyperosmolar colloidal solutions are identical to their corresponding thermoprotective effects [11], which proves the non–randomness and systematic nature of the results obtained and their importance for fundamental science.

In this aspect, our data on the thermoprotective effects of the applied hyperosmolar colloidal solutions are in some way consistent with their proven positive effects in thermal damage to the spleen and thymus [20, 21]. There was an improvement in the functional parameters of the liver with the use of hyperosmolar colloidal solutions of LS and HAES–LX 5% during the stage of burn shock [22]. Morphological studies of the liver parenchyma proved its recovery in the early stages of burn disease in response to the infusion of hyperosmolar colloidal solutions [23]. From the analysis of the data obtained, it is clear that they indirectly coincide with the conclusions about the adaptogenic (cytoprotective and angioprotective), reparative and prophylactic (preventing primary and secondary alteration processes) properties of hyperosmolar colloidal solutions of LS and HAES–LX 5% in burn disease [24, 25].

From a comparative point of view, none of the hyperosmolar colloidal solutions used in the study has advantages in normalising renal functional activity. From the point of view of the duration of the protective effect, it is important to start their antioxidant effect from the 3rd day of the post–burn period, as well as to restore the functional activity of the kidneys from the 7th day of the experiment. The restoration of intrarenal transport processes gave grounds to judge the more pronounced effectiveness of the hyperosmolar colloidal solution of the drug, since, in contrast, the effectiveness of the hyperosmolar colloidal solution HAES–LX 5% was not sufficient to restore glomerular filtration processes by creatinine.

In summary, it is worth noting the pathogenetic validity of the scheme of pharmacological correction of thermal damage to the thyroid gland with the introduction of hyperosmolar colloidal solutions with a multionic composition of drugs and HAES–LX 5%, since this scheme not only prevents the death of nephrocytes by the peroxidative mechanism in the dynamics of the post–burn process, but also is able to restore their functional activity.

Conclusions

1. Within 30 days of the post–burn period, there are pronounced impairments of renal function, which are manifested by changes in their filtration, excretory and detoxification functions, as well as acceleration of lipoperoxidation processes and inhibition of antioxidant defence activity in their parenchyma. The impairment of renal functional activity reaches its maximum on days 3–14 of the study.

2. It was proved that 0.9% saline NaCl solution has no thermoprotective effect in the skin burn model. The use of hyperosmolar colloidal solutions of LS and HAES–LX 5% is effective in preventing the free radical mechanism of nephrocyte damage and activating the enzymatic link of antioxidant defence.

3. Hyperosmolar colloidal solutions of LS and HAES–LX 5% in conditions of thermal damage to the thyroid gland contributed to the restoration of specific renal function.

4. The optimum protective activity of the applied hyperosmolar colloidal solutions of LS and HAES–LX 5% falls on the 7th–14th day of the experiment and lasts until its completion.

5. We consider the scheme of pharmacological correction of thermal damage to the thyroid gland with the intro-

duction of hyperosmolar colloidal solutions with multionic composition of drugs and HAES–LX 5% to be pathogenetically sound and capable not only of restoring the functional activity of nephrocytes but also of preventing their damage in the dynamics of the post–burn process.

Funding. This work is a fragment of the research work of the Department of Histology, Cytology, Embryology and Pathological Morphology with the course of Forensic Medicine of Odesa National Medical University of the Ministry of Health of Ukraine on the topic "Features of micro–/ultramicroscopic structure and histochemistry of the properties of body tissues during the development of compensatory and adaptive reactions" (state registration number 0121U108204).

Authors' contribution. Tiron O. I. – design, collection and processing of material; Khomenko I. P., Lurin I. A. – definition of the purpose, concept of the study; Tertyshnyi S. V. – preparation of the article for publication; Stepanov G. F. – writing the text; Vastianov R. S. – formulation of conclusions.

Conflict of interest. The authors have declared that they have no conflict of interest.

Consent to publication. The authors have read and approved the final version of the manuscript and agreed to its publication.

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Received 25.03.2024