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Original Research Article

Effectiveness of the new polyfunctional infusion solution of blood substitutes on the activity of lipid peroxidation and antioxidant protection of heart in acute fatal blood loss

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ABSTRACT

Background: One of the important directions of modern medicine is improving treatment of extreme conditions, the mortality rate of which is still very high, which is often associated with insufficient effectiveness of modern blood substitutes. Purpose of the study was to investigate the efficacy of a new multifunctional blood substitute in acute fatal blood loss on the activity of lipid peroxidation (LPO) and antioxidant system (AOS) of the heart, which showed its high antioxidant efficiency.
Methods: Experiment was carried out on 60 rats weighing 180-200 g, clinical death was caused under etaminal anesthesia by acute blood loss from the carotid artery. After bleeding rats were given injection of infusions. Animals were divided into following groups: group I – before blood loss (intact), group II - clinical death, group III (control) – acute fatal blood loss after infusion of saline solution, group IV (comparison) - after acute lethal blood loss with infusion of reo-sorbilact, and group V (main, experimented) - after acute lethal blood loss with the new infusion of multifunctional blood substitute.
Results: The level of MDA in clinical death (in group II) had increased by almost 2.0 times, as well as diene ketones, indicators of antioxidant activity decreased. The enzyme activity of GR in heart was 1.2 times lower, GPO - 1.5 times, SOD-2.0 times, catalase-4.4 times. In group III where animals after clinical death were revived with saline solution, AD increased to 45.6±0.4 mm Hg after 1 hour, and CBV increased to 44.8±0.4 ml/kg, the values of these parameters in the intact animals of the first group were 40.2% and 76.6%, respectively. After infusion of saline glomerular filtration rate was 0.61±0.02 ml/min, and diuresis of 0.21±0.02 ml/min compared with the values of these parameters in the intact animals was 46.9% and 65.6%, respectively. Life expectancy of animals after infusion of physiological saline was 12.3±1.2 hours, 30% of the animals survived. After infusion of reosorbilact in group IV, the survival rate was 40%, and after the infusion of a new multifunctional blood substitute in group IV -70%, which is 30% higher
Conclusions: The infusion of a new multifunctional blood substitute during acute fatal blood loss leads to a more effective delay of LPO processes and restoration of AOS in heart, in comparison with the use of reosorbilact. The use of a new multifunctional blood substitute during acute lethal hemorrhage in rats, compared with infusion of reosorbilact, leads to a more pronounced recovery of hemodynamic parameters, biochemical parameters of blood and ABS.

Keywords: AOS, Acute fatal blood loss, LPO, New multifunctional infusion blood-substituting solution

INTRODUCTION

One of the important directions of modern medicine is improving treatment of extreme conditions, the mortality rate of which is still very high, which is often associated with insufficient effectiveness of modern blood substitutes.[1,2]

The increasing efficiency of fluid therapy in critical conditions, in particular, in case of acute fatal blood loss, could be the use of a new drug created in the Scientific-Research Institute of Hematology and Blood Transfusion, Ministry of Health, Uzbekistan, which has antioxidant, diuretic, detoxifying activity and hemorheological actions to ensure the body's energy needs, and is able to inhibit lipid peroxidation (LPO) and repair the antioxidant system (AOS) of the body, restore kidney function and metabolic processes at the cellular and tissue level.[3,4]

The aim of the study was to investigate the efficacy of a new multifunctional blood substitute in acute fatal blood loss on the activity of lipid peroxidation and antioxidant system of the heart.

METHODS

In 60 rats, weighing 180-200 g, clinical death was caused under etaminal anesthesia by acute blood loss from the carotid artery within 3-5 minutes, by lowering blood pressure to 0 mm Hg. Recovery was carried out immediately by the introduction in the tail vein of rats following substitutes depending on the group: saline (0.9% sodium chloride) (group III), reosorbilact (group IV) and a new multifunctional blood substitute (group V) at the rate of 40 ml/kg of body weight.[5,6]

Animals were divided into following groups: group I-before blood loss (intact), group II - clinical death, group III (control) – acute fatal blood loss after infusion of saline solution, group IV (comparison) – after acute lethal blood loss with infusion of reosorbilact, and group V (main, experimented) – after acute lethal blood loss with the new infusion of multifunctional blood substitute.

In the initial state and 1 hour after infusion of blood substitutes, hemodynamic parameters were determined; acid-base status of blood, blood pressure (BP) was carried out by a conventional method, the circulating blood volume – by dilution of Evans blue and glomerular filtration rate.[7]

Acid-base status of the blood (ABS) (pH of blood) was studied on the device OP-215 (Radelkis, Hungary).[8,9]

Glomerular filtration rate was calculated with the formula:

GFR= ITU×V/PSE

V-volume of urine excretions, ITU-Evans Blue dye concentration in urine, PSE is the concentration of Evans Blue dye in blood plasma.[10]

To determine the intensity of LPO processes and activity of AOS, heart was homogenized in the freezer and the homogenate was determined by the content of MDA, diene ketones, glutathione reductase (GR), glutathione peroxidase (GPO), superoxide dismutase activity (SOD) and catalase during clinical death and 15 min, 1 h, 12 h, 24 h, 36 h, 48 h, 72 h after recovery and infusion of saline solution in group III, after infusion of reosorbilact in group IV and in group V - the infusion of new multifunctional blood substitute.[9]

To obtain a homogenate, sample of rat heart was homogenized using ho-mogenizer T10 4-fold volume of chilled medium allocation (0.1 M tris-HCl-buffer (pH 7, 8) containing 1 mM Ethylenediaminetetraacetic acid (EDTA), 1% b-mercaptoethanol) and centrifuged at 10’000 g for 15 min.[11]

The activity of glutathione peroxidase and glutathione reductase was determined spectrophotometrically at 340 nm. For the enzyme unit (E) was taken the amount of enzyme required to convert 1 mcmole substrate in 1 min at 25°C. Enzyme activity was expressed in U per gram of crude mass of heart, and the specific activity. The activity of GR was determined in the environment containing 50 mm potassium phosphate buffer (pH 7.4), 1 mm EDTA, 0.16 mm NADPH, and 0.8 mm oxidized glutathione (GSSG). Measuring the activity of MPO was performed in 50 mm potassium-phosphate buffer (pH 7.4) containing 1 mM EDTA, 0.12 mM NADPH, 0.85 mM GSH, 0.37 mM H2O2, 1 U/ml GR.[12]

The activity of superoxide dismutase (SOD) was assessed by the ability of homogenates of myocardial tissue to inhibit spontaneous oxidation of adrenaline in alkaline environment (pH=10.2) and expressed in mmol/min/mg protein.[7,8] As the standard a purified preparation of SOD (ICN Biomedicals, USA) was used. Catalase activity of samples was determined spectrophotometrically and expressed in mmol/min/g protein.[12] The measurements were performed on a spectrophotometer UNICO 2800 (United products and instruments, Inc., USA).

The resulting digital data were subjected to statistical analysis using Stu-dent's criterion and a special software package on a personal computer with the help of the program "Microsoft Office Excel 2007" and "Biostatistics 4.03". The criterion for statistical significance was pp<0.05.

RESULTS

It is shown that in rats with the decrease in blood pressure to 0 mm Hg, the value of CBV was impossible to determine within 3-5 min. The animals were in a state of clinical death. In majority of animals respiration and

cardiac activity stopped. Duration of dying was 4.5±0.7 min. Biochemical parameters and electrolytic composition of the blood in such a short period was not changed, except for lowering the total protein level in 1.3 times (27.3%) (Table 1).

Table 1: Changes of some indicators in blood loss (blood pressure to 0 mmHg) and after infusion of blood substitutes in rats (M±m).

Indicators	Groups				
	I	II	III	IV	V
BP mm Hg	113.4±0.5	0	45.6±0.4*	50.5±0.4*^	69.9±0.6*^#
CBV ml/kg	58.5±0.2	0*	44.8±0.4*	46.2±0.3*^	50.6±0.3*^#
Glomerular filtration rate ml/min	1.30±0.20	0*	0.61±0.02	0.81±0.01^*	1.06±0.03^#
Diuresis ml/min	0.32±0.02	0*	0.21±0.02	0.23±0.02*^	0.3±0.02^#
Life expectancy of animals h	-	-	12.3±1.2	16.9±1.1	20.2±1.9
Survival rate %	-	-	30	40	70
pH. conv un.	7.42±0.02	7.34±0.03*	7.22±0.02*^	7.21±0.03*^	7.29±0.02*#&
Total protein g/l	68.5±2.2	53.8±5.4*	51.4±4.9*	51.6±5.8*	52.0±5.3*

* – significant difference ($p<0.05$) when comparing results with the baseline data (group I); ^ – the same ($p<0.05$) when comparing the results with those obtained by clinical death; # – the same ($p<0.05$) when comparing the results with those obtained in group III; & - the same ($p<0.05$) when comparing the results with those obtained in group IV

Table 2: The effect of acute fatal blood loss on the intensity of LPO processes in the heart during the recovery period after revival (M±m).

Stages of the experiment	MDA µmol/100g	Diene ketones. nmol/mg
Intact	3.15±0.09	1.52±0.05
Clinical death	6.21±0.08*	2.98±0.20*
Postresuscitation period	–	–
15 min	9.01±0.10*$	3.69±0.30*
	8.45±0.08*^$	3.64±0.20*
	7.31±0.09*^#	3.60±0.20*
1 hours	8.45±0.09*&$	3.89±0.10*&$
	8.25±0.10*&$	3.76±0.09*&$
	6.80±0.08*^#&$	3.01±0.08*#&$
12 hours	9.05±0.09*@$	4.04±0.10*&@$
	8.80±0.10*&@$	4.01±0.20*&$
	6.20±0.10*^#@	3.12±0.09*&^#
1 day (24 hours)	7.10±0.09*&@®$	3.66±0.10*&®$
	6.99±0.08*&@®$	3.25±0.10*&^@®
	4.18±0.09*^#@®&	2.01±0.09*^#&@®
36 hours	6.18±0.10*@&®©	3.05±0.10*@®©
	5.18±0.09*^&@®©$	2.85±0.10*$@®©
	3.65±0.08*^#&@®©$	1.85±0.09*^#$&@®
2 day (48 hours)	5.20±0.09*&@®©§$	2.89±0.04*@®©
	5.00±0.10*&@®©$	2.55±0.09*^@®©§
	3.25±0.09^#&@®©§$	1.65±0.10^#$&@®©
3 day (72 hours)	4.35±0.10*&@®©§$	2.30±0.10*@®©§ δ
	4.25±0.09*^@®©§ δ $	1.98±0.09*^&@$®©§δ
	3.18±0.10^#&@®©§$	1.53±0.08^#&$@®©§

$p<0.05$ in comparison with indicators of group I; $ – $p<0.05$ in comparison with the clinical indicators of death in group II; ^ – $p<0.05$ in comparison with indicators of group III; # – $p<0.05$ in comparison with indicators of group IV; # – $p<0.05$ in comparison with indicators of group IV; # – $p<0.05$ in comparison with indicators of group IV; & – $p<0.05$ in comparison with indicators of the relevant group in 15 min; @ – $p<0.05$ in comparison with indicators of the relevant group in 1 h; ® – $p<0.05$ in comparison with indicators of the relevant group in 12 h; © – $p<0.05$ in comparison with indicators of the relevant group in 24 h; § – $p<0.05$ in comparison with indicators of the relevant group in 36 h; δ – $p<0.05$ in comparison with indicators of the relevant group in 48 h

Table 3: The effect of acute fatal blood loss on the intensity of the processes of the aos in the heart during the recovery period after revival (M±m).

Stages of the experiment	Groups	GR nmol/mg	GPO µmol/kg
Intact	I	5.01±0.2	7.56±0.06
Clinical death	II	4.10±0.3*	4.99±0.26*
Postresuscitation period		-	-
15 min	III	3.80±0.1*	5.40±0.10*
	IV	3.90±0.2*	5.50±0.20*
	V	3.90±0.2*	6.00±0.40*$
1 hours	III	3.10±0.3*&$	3.56±0.30*&$
	IV	3.20±0.2*$	3.58±0.20*&$
	V	3.86±0.2*#	4.71±0.20*^#&
12 hours	III	2.76±0.2*&$	3.55±0.20*&$
	IV	2.98±0.3*&$	3.44±0.15*&$
	V	3.80±0.2*#	4.96±0.59*^#
1 day (24 hours)	III	2.82±0.3*$	3.98±0.20*&$
	IV	3.10±0.3*$	4.02±0.20*&®$
	V	4.01±0.2*#	6.61±0.20*^#@®$
36 hours	III	2.89±0.2*&$	4.76±0.30*@®©
	IV	3.40±0.3*	4.98±0.20*@®©
	V	4.30±0.1*#@®	6.98±0.30^@®$
2 day (48 hours)	III	2.90±0.3*&	5.68±0.40*@®©
	IV	3.90±0.2*^	6.10±0.20*@®©§$
	V	5.10±0.2*#&@®©$	7.00±0.30^#@®$
3 day (72 hours)	III	3.15±0.2*&$	6.11±0.50*@®©§$
	IV	4.10±0.2*@®©	6.60±0.13*&@®©§$
	V	5.70±0.3*#&@®©§$	7.21±0.29&@®$

p<0.05 in comparison with indicators of group I; $ – p<0.05 in comparison with the clinical indicators of death in group II; ^ – p<0.05 in comparison with indicators of group III; # – p<0.05 in comparison with indicators of group IV; # – p<0.05 in comparison with indicators of group IV; # – p<0.05 in comparison with indicators of group IV; & – p<0.05 in comparison with indicators of the relevant group in 15 min; @ – p<0.05 in comparison with indicators of the relevant group in 1 h; ® – p<0.05 in comparison with indicators of the relevant group in 12 h; © – p<0.05 in comparison with indicators of the relevant group in 24 h; § – p<0.05 in comparison with indicators of the relevant group in 36 h; δ – p<0.05 in comparison with indicators of the relevant group in 48 h

As indicated in Table 2, the level of MDA in clinical death (in group II) had increased by almost 2.0 times, as well as diene ketones, indicators of antioxidant activity decreased. During clinical death in group II with respect to the values of intact animals, the enzyme activity of GR in heart was 1.2 times lower, GPO - 1.5 times, SOD – 2.0 times, catalase – 4.4 times. 15 min after resuscitation in group II the intensification of the processes of LPO is noted: the increased levels of MDA and diene ketones 2.9 and 2.4 times, respectively. Deep hypoxia induced by acute exsanguination of the organism, increases the amount of oxygen dissolved in the lipid matrix of the mitochondria of the myocardium and thus increases the probability of reaction of molecular oxygen with the recovered carriers of the respiratory chain, which leads to increased formation of free radicals with the further involvement of phospholipids membranes in the chain of free radical reactions on the background of the decreased activity of antioxidant enzymes and reduced inventory bioantioxidants.[5] The activity of antioxidant enzymes decreased: GR – 1.3 times, GPO – 1.4 times, the activity of SOD – 3.0, catalase – 2.4 times (Table 3, 4). At the same time, in comparison with relevant indicators in clinical death in the 15th minute after acute blood loss and infusion of saline SOD activity decreased by 1.5 times, the catalase increased by 1.9 times, also there was a tendency to a slight decrease in GR and insignificant increase in GPO.

In group III where animals after clinical death were revived with saline solution, AD increased to 45.6±0,4 mm Hg after 1 hour, and CBV increased to 44.8±0.4 ml/kg, the values of these parameters in the intact animals of the first group were 40.2% and 76.6%, respectively. After infusion of saline glomerular filtration rate was 0.61±0.02 ml/min, and diuresis of 0.21±0.02 ml/min compared with the values of these parameters in the intact animals was 46.9% and 65.6%, respectively. Life expectancy of animals after infusion of physiological saline was 12.3±1.2 h, 30% of the animals survived.

1 hour after the study, after infusion of saline, compared with intact animals the level of MDA was higher by 2.7 times, diene ketones – 2.6 times, as compared to values

of group II, MDA was higher by 1.4 times, diene ketones – 1.3 times. After the infusion of the saline solution after 1 hour, the activity of GR was lower by 1.6 times, GPO – 2.1, SOD – 2.8 times, catalase – by 2.3 times, and the relative values of this indicator in group II GR was lower by more than 1.3 times, GPO and SOD – 1.4 times, and catalase was higher by 1,9 times.

After 12 hours there was an increase of LPO processes in group III, in comparison with the values of intact animals in the group I, the level of MDA and diene ketones were higher by 2.9 times, as compared to values of group II, the levels of these indicators were higher by 1.5 times, respectively. The activity of antioxidant enzymes decreased after infusion of saline: GR – 1.8 times, GPO – 2.1 times, activity of SOD – 2.0 times, catalase – 2.0 times, respectively. After 12 hours, relative to values of group II after infusion of saline solution GR was lower by 1.5 times, GPO – 1.4 times, catalase is higher by 2.5 times, and significant changes in the activity of SOD were not found. After 24 hours in group III, there was a tendency to a slight recovery of the studied parameters, although in comparison with the values of indicators in the group I - the level of MDA was 2.3 times higher, diene ketones - 2.4 times, and compared with the II group the level of MDA was more than 1.1 times higher, and the level of diene ketones - 1,2 times. Indicators of AOS in group III decreased. So GR was 1.8 times lower, GPO - 1.9 times, the activity of SOD and catalase – 1.7 times, and as compared with the results obtained during clinical death, GR was almost 1.5 times lower, GPO - 1.3 times, the activity of catalase, in contrast, was 2.6 times higher and there was an increase tendency in the activity of SOD.

Table 4: The effect of acute fatal blood loss on the intensity of the aos processes in the heart during the recovery period after revival (M±m).

Stages of the experiment	Groups	SOD 103 units/h×kg	Catalase 104 units/h×kg
Intact	I	210.0±8.5	509.0±24.0
Clinical death	II	107.0±14.2*	114.6±21.0*
Postresuscitation period			
15 min	III	70.1±7.8*$	112.3±24.0*$
	IV	69.2±8.8*$	120.4±21.0*$
	V	72.3±9.0*$	225.0±20.1*$#
1 hours	III	75.6±7.2*$	221.3±20.4*$
	IV	78.2±8.1*$	234.0±21.0*$
	V	110.1±10.2*^#&$	285.0±21.0*$
12 hours	III	106.0±10.2*&@	291.0±23.0*&@$
	IV	137.0±8.4*^&@	301.2±29.6*$
	V	163.0±8.7*^#&@	395.4±31.5*#@&
1 day (24 hours)	III	123.2±6.6*&@®	297.5±21.0*&@$
	IV	143.2±5.2*^&@	311.3±40.0*$
	V	192.3±4.8^#&@®$	402.3±20.0*^&@$
36 hours	III	144.3±5.6*&@®©$	335.3±22.0*&@$
	IV	152.1±6.1*&@$	355.8±32.0*&@$
	V	201.2±8.1^#&@®$	431.0±21.0*^&
2 day (48 hours)	III	169.2±5.3*&@®©§$	402.2±31.0*&@®©
	IV	171.3±6.3*&@®©§$	411.2±22.0*&@©$
	V	211.2±5.4^#&@®©$	491.0±18.0^#&©§
3 day (72 hours)	III	189.3±9.5&@®©§$	461.2±32.0&@©§
	IV	190.0±10.2&®@©§$	476.0±57.0@®©$
	V	220.0±10.0^#&@®©$	511.0±19.0&@®©§$

p<0.05 in comparison with indicators of group I; $ – p<0.05 in comparison with the clinical indicators of death in group II; ^ – p<0.05 in comparison with indicators of group III; # – p<0.05 in comparison with indicators of group IV; # – p<0.05 in comparison with indicators of group IV; # – p<0.05 in comparison with indicators of group IV; & – p<0.05 in comparison with indicators of the relevant group in 15 min; @ – p<0.05 in comparison with indicators of the relevant group in 1 h; ® – p<0.05 in comparison with indicators of the relevant group in 12 h; © – p<0.05 in comparison with indicators of the relevant group in 24 h; § – p<0.05 in comparison with indicators of the relevant group in 36 h; δ – p<0.05 in comparison with indicators of the relevant group in 48 h

36 hours after the infusion of saline, the intensification of the processes of LPO declined and became moderate, though, compared to the intact group, it remained at a high level: the level of MDA was 2.0 times higher, diene

ketones – 2.0 times. 36 hours after infusion of saline, the improvement in AOS was also noted; compared with results taken after 24 hours, GR remained reduced, GPO - was 1.2 times higher, SOD - almost 1.2 times, catalase - more than 1.1 times, respectively. As compared to the values in the second group, GR was 1.4 times lower, SOD was 1.3 times higher, catalase- 2.9 times and there was a slight tendency to GPO decrease.

48 hours after lethal blood loss and infusion of saline, inactivation of LPO processes continued and AOS activity increased compared to 36 hours: MDA decreased by 1.2 times, diene ketones – slightly, GR did not change, GPO - 1.2 times, SOD and catalase – 1.2 times, respectively, and concerning values of indicators in the II group, after use of saline, MDA was lower for almost 1.2, diene ketones were marginally lower. On the 2nd day of the study after infusion of saline solution, compared with values of indicators in group I, and GR was 1.7 times lower, GPO – 1.3, SOD – 1.2, catalase – 1.3 times. On the 3rd day compared to the II group, the MDA content decreased 1.4 times, diene ketones – 1.3 times, and the activity of enzymes of AOS increased: GR – 1.3, and GPO - 1.2 times, SOD – 1.8, and catalase – 4.0 times. Compared with I group, the MDA level remained 1.4 times higher, diene ketones - 1.5 times. Indicators of the AOS – GR and GPO were lower than in the intact group: the GR was 1.6 times lower, GPO - 1.2 times, respectively; significant differences in the content of SOD and catalase were not observed.

In group III during postoperative period, the intensity of lipid peroxidation in the heart increased, reaching after 15 minutes and 12 hours its maximum. The activity of antioxidant enzymes in the heart also changed: GR, GPO reached the lowest values after 12 and 24 hours, SOD and catalase - in 15 minutes after clinical death. Animal survival rate was 20%.

In a comparative analysis of the use of a new blood substitute with reosorbilact the following changes were identified: So in group V there was a complete recovery of hemodynamic parameters 1 hour after clinical death, compared with infusion of reosorbilact: BP was higher for 38.4%, the CBV was 9.5% higher. However, the levels of AD and CBV, compared with intact animals were 38.4% and 13.5% lower, respectively. Also, 1 hour after the infusion of new multifunctional blood substitute in the group V the volume of diuresis recovered to the original size, which compared to the value of this indicator in groups III and IV was 42.9 and 30.4% higher, respectively, and glomerular filtration rate-73.8% and 30.9%, respectively.

In the group V, blood pH increased and made up 7.29±0.02, which is 0.08 units higher than in group IV. During the examination of LPO and intensity of antioxidant protection of the heart after 15 minutes of study, after infusion of reosorbilact and new blood substitute an increase of LPO was observed in both groups, but MDA was 15.6% lower during the infusion of a new solution, and there was a tendency to decreased levels of diene ketones, and a decrease of catalase activity was observed, although it was 86.9% higher than after infusion of reosorbilact. 1 hour after the infusion of the new blood substitute, LPO was decreased, MDA level was 21.3% lower, diene ketones – 24.9%, and the activity of antioxidant enzymes increased: GR was 20.6% higher, GPO - 31.6%, SOD – 40.8%, catalase – 21.8%, respectively, compared with infusion of reosorbilact.

12 hours after the infusion of a new blood substitute, the following changes were obtained: MDA level continued to decline and was 41.9% lower, diene ketones – 28.5%, the enzyme activity continued to rise: GR was 27.5% higher, GPO – 44,2%, SOD activity – 19.0%, catalase – 31.3% compared with the results after infusion of reosorbilact. These changes indicate a more pronounced antioxidant reaction of the new blood substitute. In the group V, 24 hours after the infusion of the new multifunctional blood substitute, the level of MDA was 67.2% lower, diene ketones – 61,7%, and the enzyme activity of GR was 29.4% higher, GPO - 64.4%, SOD - 34.3%, catalase – 29.2% compared to reosorbilact.

36 hours after the infusion of the new substitute, compared to infusion of reosorbilact, MDA level was 41.9% lower, diene ketones – 54.1%, the enzyme activity of GR was 26.5% higher, GPO - 40.2%, SOD activity - 32.3% higher, catalase - 21.1%. After the infusion of a new blood substitute in 48 hours, LPO and activity of AOS enzymes returned to normal values, which was not observed durinh the infusion of reosorbilact. After infusion of reosorbilact in a group IV, the survival rate was 40%, and after the infusion of a new multifunctional blood substitute in group IV -70%, which is 30% higher.

DISCUSSION

Acute blood loss led to a significant accumulation MDA and diene ketones in heart by the end of clinical death (Table 2) when blood circulation and oxygenation is completely stopped. The resulting severe hypoxia of the body inhibits the respiratory chain of heart mitochondria, which naturally leads to the restoration of NAD and NADH, release of ferritin, and Fe^{2+} from the membranes and getting them into the cytosol, as well as the incomplete recovery of dissolved in the lipid matrix of the cardiomyocytes membranes of molecular oxygen, which is associated with the formation of active forms of oxygen: superoxide anion radical, hydrogen peroxide and hydroxyl radicals.[3]

It is known that in conditions of hypoxia, the respiratory chain of cardiomyocytes, in particular, cytochrome oxidase, begins to generate reactive oxygen species, including hydroxyl radicals, which have a devastating effect on sarcoplasmic reticulum through rapid activation of lipid peroxidation and the destruction of SH-groups of proteins. In addition, increased formation of reactive

oxygen causes acute dysfunction of the endothelium and is accompanied by ultrastructural changes of vascular endothelium cells, exerts prothrombotic effects.[5] After the infusion of a new blood substitute in 72 hours, the activity of AOS enzymes such as GR, SOD, catalase was slightly higher than in group I of the intact animals, which was not observed during the infusion of reosorbilact.[6,8]

Thus, a new blood substitute has antioxidant properties. Characteristically, the intensity level of LPO started to decrease 1 hour after the infusion of a new blood substitute, and on the 2nd day reached normal values, which was not observed during the infusion of reosorbilact, after which, even after 3 days, the LPO did not reach the initial level.

The level of antioxidants in the cardiac muscle had the minimum value at 15 minutes after the revival of animals and was fully recovered on the 2 day, which was not observed during the infusion of reosorbilact. New blood substitute was more effective in the revival of animals in acute lethal blood loss.[6]

Life expectancy after infusion of a new multifunctional blood substitute was higher in comparison with the result of the infusion of reosorbilact for 3.3±0.1 hours. Thus, the results of the study showed that a new multifunctional blood substitute effectively restores hemodynamic, renal blood flow, has no adverse effects on biochemical parameters of blood serum, and increases the survival rate and life expectancy of animals in the experiment during the simulation of acute fatal blood loss. In general, the comparative study of the use of reosorbilact showed that the use of a new multifunctional blood substitute in acute fatal blood loss effectively slows down the processes of lipid peroxidation and restores the activity of antioxidant enzymes.[10,12]

CONCLUSION

The infusion of a new multifunctional blood substitute during acute fatal blood loss leads to a more effective delay of LPO processes and restoration of AOS in heart, in comparison with the use of reosorbilact. The use of a new multifunctional blood substitute during acute lethal hemorrhage in rats, compared with infusion of reosorbilact, leads to a more pronounced recovery of hemodynamic parameters, biochemical parameters of blood and ABS.

The infusion of a new multifunctional blood substitute during acute fatal blood loss leads to a more significant recovery of renal function compared with infusion of reosorbilact. The use of a new multifunctional blood substitute during acute fatal blood loss leads to a more significant increase in survival rate of animals in the comparative study of reosorbilact.

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