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Respiratory Function and Blood Gases Transport State at Experimental Hypoxia: Ozone Therapy Correction

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Abstract

In condition of reproduction of hemorrhagic shock according to Wigger's experimental model, the efficacy of systemic use of ozonotherapy together with infusion therapy of hypovolemic condition. It has been shown that the infusion of ozonized saline strengthens adaptable reactions of respiratory and gas transport systems. Ozone increases the level of serotonin in the blood, decreases the frequency of respiration and increases volume of respiration and oxygen consumption.

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Introduction.

Non-fully oxidized products of carbohydrate metabolism, proteolysis, lypolysis and toxic lypoperoxidation substances play an important role in emergency poststress pathology progress. They cause microcirculation disorders, biological membranes damage, endogenic intoxication elevation, which formed irreversible homeostasis changes, leading to multiorgan insufficiency[1,2].

At last time we scoped elevation growth of specialists interesting to early detoxication by natural oxidants systems modeling[3,4]. Small arsenal of oxidant (sodium hypochloride, hydrogen peroxide, hyperbaric oxygenation and ozone) limits to possibilities of early oxidative therapy of posthypoxic disorders. It was stated, that ozone therapy has a maximal methodic advantage over other variants of rehabilitation[5]. The aim of this work is comparison of respiration and blood gases transport state with lypoperoxidation and serotonin level at systemic ozone therapy of posthypoxic pathology.

Materials and methods.

We created experimental hypovolemic hypotension at 86 adult mongrels (5-6 years old, body weight 13.8±1.3 kg) by free hemorrhage from femoral artery. The dogs were maintained and handled according to the recommendations of the National and international animal ethics guidelines. Animals were housed in individual clear plastic cages at standard room temperature under a 12-hour light/dark cycle. They were allowed free access to food and water.

Arterial pressure was reduced to 5.3 kPa (40 mm Hg) and stated on this level during 60 min (Wiggers method(10)). Total hemorrhage volume was 32 ml/kg. Dogs were divided at two equal groups. Animals of control group were infused by sodium chloride (32 ml/kg) in 60 min after hemorrhage. Dogs of main group were infused by ozonized sodium chloride (32 ml/kg; ozone dose 3000 μg/l). Check points were before and in 15 and 60 min after infusion. Respiratory pattern was registered at spirograph SG-2M. Acid-base balance and blood gases level was estimated at microanalyser Radelkis. Serotonin level was detected by Shuder and Sulaman method (1965).

The data were expressed as mean ± standard error of measurement. The data collected were analyzed using Statistical Package for Social Science (SPSS) software version 11. For the data that was not normally distributed, Mann-Whitney test was used for the statistical analysis. Fisher Exact test and Chi square test were used to analyze the results where appropriate. The p value of <0.05 is considered as statistically significant.

Result and discussion.

In one hour after hypotension we found meaningful increase of respiratory volume (at 24% from preliminary level) and elevation of minute respiratory volume (at 43%) by intensification of breath (growth of respiratory rate at 85%). At this time oxygen consumption and use was enlarged at 33 and 55%, respectively. In addition, elevation of all estimated breath motion

components (expiration volume and specific respiratory volume) was stated (table 1).

Table1. Respiratory function parameters at hemorrhagic shock during sodium chloride infusions

Parameters	Basal level	After 60 min of hypotension	After sodium chloride (NaCl) solution infusion			
			15 min		60 min	
			NaCl	O_3 + NaCl	NaCl	O_3 + NaCl
Respiratory rate, min^{-1}	20.0±1.5	37.0±2.6*	31.0±3.7*	27.0± 2.1*. **	36.0± 4.0*	30.0±3.0*
Respiratory minute volume, ml	24.0±1.5	18.2±1.2*	18.0±1.3*	25.0±3.5	17.0±1.0	25.0± 2.3*.***
Expiration volume, ml/min	485.0±42.0	694.0±73.0*	609.0±97.0	914.0± 127.0	593.0± 149.0	915.0± 162.0*
Specific respiratory volume, ml/min/kg	6.0±0.5	4.0±0.5*	3.3±0.3	5.0± 0.7***	3.3±0.3	3.5±0.7
Oxygen use coefficient, %	14.2±2.0	6.4±1.2	10.9±1.9**	9.2±1.5	7.1±1.2	5.0±0.8

Legend: Data were expressed as mean of observations ± SD. «*» - p<0.05 to basal level; «**» - p<0.05 to 60 min hypotension; «***» - p<0.05 between main and control groups

It seemed this tendency in connection of decreasing of lung blood flow must cause to changes of blood gases transport, but we do not revealed hypoxia signs at the height of hemorrhagic shock. For example, pO2 level, plasma-soluted and hemoglobin-bound oxygen are saved at preliminary level.

We surmise holding of high blood oxygenation in this condition taken place as a result of respiratory system activation without decreasing ventilation and perfusion relation. At respiratory system activation we do not determined marked reduction of lung barrier function as reaction to organs and tissues hypoperfusion. It was indirectly indicated by constant serotonin level during this stage of experiment. In connection with it disorders of peripheral blood circulation lead to tissue hypoxia progress. It was reflected in decreasing of oxygen tension, saturation and total concentration in venous blood and was associated with growth of tissue oxygen utilization degree (at 2.7 times) and arteriovenous difference to oxygen (at 265%).

Oxyhemoglobin level in venous blood was decreased at 54% to preliminary value, because its dissociation degree was elevated in consequence of blood acidification. In this period we observed marked metabolic acidosis with increase of buffer bases deficiency at 3.9 times in arterial and venous blood. Reduction of pCO2 level in arterial blood may be caused by respiration intensification and alveolar interchange of gases elevation.

In control group animals after 60 min hypotension and sodium chloride infusions (control point – 15 min after procedures) we registered decreasing of respiration frequency (at 16% to

posthypotension level) and lowering of air flow speed (at 12% to posthypotension level) for constant respiratory volume (table 1). This tendency indicated on changes of lung ventilation pattern at blood restoration volume: adequate minute ventilation and blood oxygenation were supplied with blood bypass vessels in pulmonary circulation. It was demonstrated in high level of venous blood return (central venous pressure was elevated at 29% to posthypotension level). It may be associated with growth of functional blood bypass in lungs, prevalent to true bypass. That is why discharge of venous blood caused to oxygen utilization in lungs at this experiment (oxygen utilization coefficient was increased at 1.7 times). This variant of compensation is not adequate for organism at all, because during 60 min after experimental treatment we registered tachypnea with decrease of respiratory depth, reduction of air flow speed and oxygen utilization coefficient in animals of this group. Arterial blood oxygenation was kept on constant level, but carbon dioxide elimination from blood was reduced in comparison with untreated hemorrhagic shock. It may be explained by constant breath depth and blood bearish carbon dioxide level from peripheral to central vessels. In blood we observed acidosis and buffer bases deficiency. Use of ozonized sodium chloride solution leads to change of respiratory reaction to hypotension (table 2). First of all, we stated marked elevation of breath depth and expiration volume (at 1.5 times to control group level) with decrease of respiration frequency. This compensation variant was more adequate at modeled hypotension, because oxygen consumption and use are increased simultaneously. It supplied elevated oxygen needs of peripheral tissues. That is why utilization of arterial blood oxygen elevated at 1.4 times relative to the control group. It is important to say, that arterial blood oxygenation was increased in 15 and 60 min after infusion of ozonized sodium chloride solution (at 37 and 10% to control level).

At use of ozonized sodium chloride solution elevation of blood pO2 level may be caused by vasodilation and optimization of blood circulation in lungs. In addition, in 15 min after systemic ozone therapy venous blood return and central venous pressure were lower, than at control group (at 74%), but cardiac output was equally at control and main group. So, lung artery pressure and venous blood discharge were lower too.

We supposed true bypass prevalence to functional may be realized by dilation vessels in lesser circulation and optimization of pulmonary blood flow at all. It was indirectly corroborated by changes of parameters, illustrated reserve possibilities of cardiovascular system (cardiac index, heart rate, pO2 level and arteriovenous difference to oxygen). These parameters dynamics indicated to mechanisms of supplying of elevated need in oxygen, which take place at ozone use. They are gain of oxygen consumption by lungs, growth of arteriovenous difference to oxygen (at 1.4 and 1.5 times to control group in 15 and 60 min respectively), more optimal functional state of cardiovascular and respiratory systems (systolic output was provided with increased oxygen consumption with minimal energy cost).

At total volume insufficiency compensation reactions of cardiovascular and respiratory systems at ozone use may be realized by changes of its metabolisms, associated with oxidant action. It was confirmed by dynamics of serotonin synthesis and release. V.P. Hrapovitsky et al. (1984) data about ozone action on these processes fully corroborated with our results on serotonin level dynamics in arterial blood[6]. It was stated brief ozone action on blood proteins, serotonin-produced and serotonin-contained cell induced activation of synthesis and release of this ligand. It was fixed, that after infusion of ozonized sodium chloride solution serotonin level in arterial

blood was meaningfully elevated. It may be a factor in respiration stimulation as result of receptors activation in zone, located between vena cava and auriculars, or substance direct effect on vessels muscular elements[7].

Table 2 – Blood gas transport parameters at hemorrhagic shock during sodium chloride infusions

Parameters	Basal level	After 60 min of hypotension	After sodium chloride (NaCl) solution infusion			
			15 min		60 min	
			NaCl	O_3 + NaCl	NaCl	O_3 + NaCl
pO2, kPa	13.0±0.4 6.8±0.2	13.0±0.9 3.7±0.2*	12.3±0.5 3.5±0.4	17.0± 0.5**.*** 6.0±0.4***	15.2±1.1 5.3±0.2	16.6±0.6 4.4±0.3***
SaO2, %	93.0±1.2 72.0±2.4	95.0±0.8 33.0±2.5*	96.0±0.9 67.0±3.5**	96.0±0.7 59.0±3.4**	96.0±2.2 69.0±1.9	97.0±1.1 47.0±4.9***
Concentration of bonded O2, ml/100 ml	18.2±0.7 14.0±0.5	17.9±0.3 6.7±0.1	15.6±0.4* 12.2±0.8**	15.5±0.4* 9.9±0.9**	15.6±0.4 10.7±0.5	15.8±0.6 8.2±1.0***
Concentration of soluted O2, ml/100 ml	0.3±0.001 0.14±0.008	0.29±0.002 0.1±0.008	0.3±0.002 0.15±0.01	0.4±0.01*** 0.1±0.01	0.3±0.02 0.1±0.01	0.4±0.01*** 0.1±0.01
TotalO2 concentration, ml/100 ml	18.5±0.4 14.2±0.5	18.2±0.3 6.8±0.1*	16.0±0.5 12.2±0.8**	15.8±0.5 10.4±0.7**	15.9±0.5 10.8±0.5	16.2±0.7 8.3±0.4***
Arteriovenous coefficient	43.0	114.0*	38.0	54.0	51.0	79.0
Oxygen utilization coefficient, %	23.0	62.0*	24.0	34.0	32.0	49.0

Legend: first value – in arterial blood, second value – in venous blood. Data were expressed as mean of observations ± SD. «*» - p<0.05 to basal level; «**» - p<0.05 to 60 min hypotension; «***» - p<0.05 between main and control groups

It was observed optimization of oxygen provision of peripheral tissues after ozone action does not connected with marked correction of acid-base balance. During 60 min after infusion we registered strongly pronounced acidosis and buffer bases deficiency in consequence of restoration of peripheral blood circulation and elimination of non-fully oxidated reactions products from vessels.

In addition, restoration of lungs blood circulation was associated with optimization of blood oxygenation. Increasing of peripheral blood flow speed and safety of its bypass mechanisms lead to lowering oxygen return at peripheral capillaries. That is why oxygen utilization coefficient was decreased at 1.6-2.6 times as compared with control in 60 min after infusion of ozonized sodium chloride solution. In connection with it lung barrier function realized in blood serotonin metabolization was slacken. In 15 min after revolumization serotonin level in arterial blood was decreased (90% to preliminary; $p<0.01$), but in 60 min its level was lower to previous value at 19% (81% to preliminary; $p<0.01$). We supposed it was associated with inactivating role of monoaminooxidase[7-9].

Conclusion.

Our results allow demonstrating, that systemic ozone therapy in correction of experimental hypotension is more effective to organism metabolic adaptation, than sodium chloride solution infusion. It is important, that investigated oxidant has a direct effect on blood component at the moment of infusion, because ozone has high reaction activity and dissociates after contact with metabolites immediately. On the other hand, ozone-initiated response reactions were observed in 60 min after infusion. In connection with it treating role of ozone includes «catalytic» effect on enzyme-associated processes, catabolism and synthesis of biologically active substances, lypoperoxidation in tissues and blood.

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