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The use of gas-liquid artificial lung ventilation in acute inhalation chlorine poisoning (experimental study)

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Introduction. Currently, chlorine is widely used in industry and agriculture. There are thousands of industrial facilities located on the territory of the Russian Federation that have chlorine reserves in quantities that, in the event of an emergency, can lead to massive damage to people. Chlorine poisoning has stages of development of the toxic process with the development of toxic pulmonary edema (TPE). Respiratory therapy for TPE consists in the use of artificial lung ventilation (ALV) with positive pressure at the end of exhalation and an oxygen content in the inhaled mixture (FiO_2) of at least 40%. Currently, scientists are actively developing methods of liquid artificial lung ventilation (LALV) using perfluorocarbon (PFC) liquids as an alternative to gas artificial lung ventilation (ALV), in particular, in the treatment of toxic pulmonary edema. This article shows the possibility of sequential cyclic use of liquid and gas (intermittent gas-liquid) artificial ventilation in combination with hypothermia in a model of acute inhalation chlorine damage in rats.

The study aims to evaluate the prospects of using intermittent gas-liquid artificial lung ventilation combined with hypothermia for the treatment of severe inhaled chlorine lesions.

Materials and methods. The authors have conducted a study on male Wister rats aged 4 months and weighing 192.1±2.3 g. Toxic pulmonary edema was initiated by 15-minute inhalation of chlorine at an estimated dose of 35 mg/l. The animals were anesthetized and then randomized into two groups, control and experimental (6 individuals each) based on inclusion criteria: decreased oxygen saturation (SpO_2)<80 and increased heart rate (HR)>240 beats/min. The scientists performed artificial lung ventilation throughout the study in the control group. The animals of the experimental group were subjected to hypothermic liquid ventilation for an hour, after which they were switched to gas ventilation, and when SpO_2 and heart rate dropped below acceptable values, the cycle was repeated. At the same time, the authors continued to ventilate with gas until the end of the experiment. Scientists used perfluorodecalin as a PFU liquid. They recorded heart rate, SpO_2, rectal temperature, overall survival, and life expectancy.

Results. After inhalation, the researchers observed severe chlorine damage in all animals. 10 minutes after the start of ventilation in the animals of the control group, the authors observed an increase in saturation to 90% and a decrease in heart rate to 220–240 beats per minute, followed by 20–25 minutes. They also observed a rapid decrease in SpO_2 to extremely low values and an increase in heart rate, which indicated inefficiency of ventilation and caused the development of adverse outcomes. In turn, in the experimental group, during the first 5 minutes after the start of liquid artificial lung ventilation (LALV), the researchers recorded a sharp decrease in heart rate to 104±3.5 beats/min. and an increase in SpO_2 to 94±2.4%. After switching to gas artificial lung ventilation (AVL), the time for lowering the controlled parameters below the permissible values was 45±7.9 minutes. 5 minutes after the start of the second liquid artificial ventilation session, all animals showed an increase in SpO_2 and a decrease in heart rate, while the values of these indicators did not differ from the values recorded during the first session.

After the 2nd transfer to a gas ventilator, there was a short-term improvement in the studied indicators, followed by a deterioration that ended in an unfavorable outcome.

When studying survival, the authors found that the average duration of survival in the experimental group was 4.57 times longer than in the control group, and amounted to 190.0±6.3 and 41.6±3.0 minutes, respectively (p<0.001).

When assessing the amount of edematous fluid released during liquid artificial lung ventilation, the researchers found that during the experiment, that during the experiment, an average of 5.9±1.8 ml/kg was aspirated in animals of the experimental group. The average body temperature of the animals in the control group was 36.2±0.3°C. In turn, the animals of the experimental group showed a sharp decrease in temperature during the first 30 minutes of liquid artificial ventilation, by an average of 6.1±1.2°C. After that, the temperature stabilized and was in the range of 30–31°C until the death of the animals.

A pathoanatomic examination revealed that in the animals of the control group, a large amount of edematous fluid and foam was found in the respiratory tract and lungs, while in the experimental group, edematous fluid prevailed in the upper respiratory tract, and perfluorodecalin in the lower.

At the same time, the mass coefficients of the lungs of the control and experimental groups were 1.89±0.08% and 2.70±0.03%, respectively.

Limitations. There are quantitative restrictions on the presence of animals in the sample, as well as qualitative restrictions in experiments with animals with pulmonary edema after inhalation chlorine poisoning.

Conclusion. *Inhalation seeding with chlorine in a 200-liter chamber with an estimated dose of 35 mg/l for 15 minutes leads to the lightning-fast development of toxic pulmonary edema in small laboratory animals (bypassing the stage of primary clinical manifestations and the latent period). The use of liquid artificial ventilation with PFDs makes it possible to evacuate edematous fluid from the lungs in case of toxic edema caused by severe inhalation chlorine poisoning, and thereby preserve gas exchange in the lungs. The use of intermittent hypothermic gas-liquid ventilation makes it possible to maintain gas exchange in the lungs in the case when conventional mechanical ventilation is ineffective and thus significantly (p<0.001) increase the survival time of laboratory animals by 4.57 times. The results obtained indicate the prospects for further development of respiratory support methods based on hypothermic ventilation as a treatment for severe forms of acute respiratory distress syndrome, in the case when traditional ventilation is no longer effective.*

Ethics. Studies involving laboratory animals were conducted in compliance with the following regulations: the Helsinki Declaration of 2000. "On humane treatment of animals", Order of the USSR Ministry of Health No. 755 dated 08/12/1977 "Rules for carrying out work using experimental animals", Order of the Ministry of Health and Social Development of Russia No. 199n dated 04/01/2016 "On approval of the rules of laboratory practice". The research protocol was approved by the Ethics Committee of the Izmerov Research Institute of Occupational Health. Protocol No. 4 dated May 25, 2022.

Keywords: *perfluorocarbon; perfluorodecalin; inhaled chlorine poisoning; acute respiratory distress syndrome; toxic pulmonary edema; hypothermia; artificial lung ventilation; liquid artificial lung ventilation*

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Isabekov N.R. — research concept and design, data collection and processing, text writing;
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Krikunov O.V. — conducting inhalation priming, data collection and processing;
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Introduction. Chlorine poisoning has been widely known since the First World War, when it was first used as a chemical warfare agent. Currently, chlorine is widely used in industry and agriculture. There are thousands of industrial facilities on the territory of the Russian Federation that have chlorine reserves in quantities that, in the event of an accident, can lead to mass injury to people. In addition, the above-mentioned objects can be classified as potential targets for sabotage and terrorist activities.

Chlorine is a yellow-green gas with an unpleasant odor, which is classified as a class II toxic substance. Upon contact with the mucous membranes, chlorine interacts with water to form hydrochloric and hypochlorous acids, thereby causing an acid burn at the point of contact. Chlorine poisoning has stages of development of the toxic process of pulmonary edema. In the clinical picture, researchers identify the following periods (stages): reflex, latent, pronounced clinical manifestations and recovery. The reflex stage is coughing, tickling in the nasopharynx, lacrimation and salivation, and a feeling of heaviness in the chest. Later, shortness of breath appears in the exhalation-inhalation type with the participation of auxiliary muscles and tachycardia [1–3]. In the latent stage (imaginary well-being), which lasts an average of 4–6 hours, signs of acute respiratory failure (ARF) persist, but the patient's general condition improves somewhat. Depending on the severity of the lesion, the duration of this stage can vary significantly, as it may be absent in extremely severe lesions [1–3]. The stage of pronounced clinical manifestations is characterized by a worsening of the general condition: increased headaches, general malaise, loss of consciousness, as well as decompensation from the respiratory system: cough, chest pain, shortness of breath and cyanosis. The progression of ARF occurs due to impaired ventilation of the lungs and damage to the membrane of the alveolar capillaries, which is manifested by a sharp decrease in the partial pressure of oxygen and an increase in the partial pressure of carbon dioxide in the arterial blood. Pink foam begins to appear from the patient's mouth, small bubbly wet wheezes are heard during auscultation, and focal darkening can be seen on the X-ray [1–3]. With timely initiation of treatment, pathological changes reverse their development. Recovery can occur within a few weeks. It is worth noting that the stage of recovery is characterized by complications such as secondary pulmonary edema, pneumonia, and pulmonary emphysema [1–3].

In cases of decompensation from the respiratory system, specialists perform artificial ventilation with a positive pressure at the end of exhalation of more than 5 cm H_2O and a high oxygen content of at least 40% in the inhaled mixture. The main areas of improvement of respiratory therapy for toxic pulmonary edema (TPE) are optimization of parameters, as well as the development of new methods and modes of artificial lung ventilation (ALV). Currently, scientists are actively developing methods of liquid artificial lung ventilation (LALV) using perfluorocarbon (PFC) liquids as an alternative to gas ventilation in the treatment of toxic pulmonary edema [4, 5].

Over the past twenty years, scientists have conducted a large number of experimental studies on the use of liquid artificial lung ventilation methods for the treatment of acute lung injury — acute respiratory distress syndrome (ARDS) [4–8]. Thus, using a model of combined ARDS in cats caused by intravenous administration of oleic acid and lung lavage with hypertonic NaCl solution, it was shown that the use of bronchoalveolar lavage (BAL) with oxygenated PFC liquid can significantly improve gas exchange after severe lung injury by removing edematous fluid [9]. In turn, Volker M.T. and co-authors [10] described a case of the clinical use of a single perflubron (PFB) instillation in a patient with ARDS who is on an artificial lung ventilation and extracorporeal membrane oxygenation (ECMO) for vital indications. It was shown that the use of PFB in the patient significantly increased the amount of protein secretions removed from the respiratory tract over the next 6 days, and also contributed to the patient's weaning from the ECMO device 11 days after instillation.

In our studies, it was demonstrated that the combination of liquid artificial lung ventilation with hypothermia during the development of the alveolar stage of toxic pulmonary edema led to compensation for respiratory and hemodynamic disorders, and the subsequent transition to gas ventilation was accompanied by a long-term stabilization of the animal's condition. In this regard, it was suggested that the sequential cyclic use of liquid and gas artificial ventilation (hereinafter referred to as intermittent gas-liquid artificial ventilation [4]) in combination with hypothermia will significantly increase the effectiveness of respiratory therapy in the treatment of severe chlorine inhalation lesions accompanied by TPE, in comparison with conventional mechanical ventilation.

The study aims to evaluate the prospects of using intermittent gas-liquid artificial lung ventilation combined with hypothermia for the treatment of severe inhaled chlorine lesions.

Materials and methods. The authors conducted a study on male Wistar rats aged 4 months and weighing 192.1±2.3 g. Before the study, the animals were quarantined for 14 days. The statistical processing recommendation[1] was used to determine the number of animals in the sample and to distribute them into groups.

The researchers placed the animals in a 200-liter A. Kurlandsky (type B) chamber equipped with a fan, in which static chlorine seeding was performed. The authors obtained chlorine gas for the seed by the reacting potassium permanganate (CDA, GOST 20-490-75) with hydrochloric acid (HC, GOST 3118-77) in accordance with the chemical reaction[2] equation:

$$2KMnO_4 + 16HCl \rightarrow 5Cl_2 + 2KCl + 2MnCl_2 + 8H_2O$$

[1] Recommendations on statistical processing of the results of experimental toxicological studies. Council for the Coordination of Scientific Research and the introduction into practice of scientific achievements of the Ministry of Health of the USSR 1965: 15–33.
[2] Olenin S.S., Fadeev G.N. *Inorganic chemistry.* Moscow, "HIGHER SCHOOL"; 1979.

The scientists estimated the concentration of chlorine in the chamber based on the theoretical yield of the reaction and without taking into account possible sorption losses and, according to the calculation, was 35 mg/l. The reaction took place in a chemical beaker made of heat-resistant glass with a volume of 250 ml of a standard form, installed in the chamber when hydrochloric acid was added to the calculated amount of potassium permanganate. Hydrochloric acid for the reaction was added in excess of one serving. The resulting chlorine was mixed throughout the entire volume of the priming chamber by a fan. Inhalation priming was carried out for 15 minutes.

After priming, the rats were given general anesthesia with intramuscular administration of zoletil and medetomidine at doses of 1.0 and 0.5 mg/kg, respectively. After that, the animals were intubated using a 16G intravenous catheter (CK-FLON, India). The animals were randomized into 2 control and experimental groups (6 individuals each) based on inclusion and exclusion criteria. The inclusion criteria were used: decrease in oxygen saturation (SpO_2)<80 and increase in heart rate (HR)>240 beats/min. If the animals did not meet the specified criteria, they were excluded from the sample.

The authors measured SpO_2, the heart rate of both groups of animals every 5 minutes after priming using a portable pulse oximeter (Zoomed LLC, model UT100, Russia) and rectal temperature (TianJin electronic thermometer, model DC-1, China). After intubation, the animals of the control group were transferred to a gas ventilator using the Ugo Basile 7125-30 device (Italy) in volume control mode (VCM) with a respiratory volume (RV) of 10 ml/kg, respiratory rate (RR) of 75 breaths/min and oxygen content in the respiratory mixture (FiO2) of 21%, which was carried out until their death. In turn, the animals of the experimental group were operated with the Ugo Basile 7125-30 apparatus (Italy), which, due to its design features (piston type), can use both gas and liquid as a working medium. The connection diagram of the device in the live mode is shown in ***figure 1***.

To perform liquid artificial lung ventilation (LALV), the researchers connected a special line from two tanks with pre-oxygenated PFCs liquid to the inhalation valve of the device, the first with a temperature of 4°C, the second — 32°C. In addition, they connected a control unit to the device, which allowed them to adjust the ratio of the duration of the inhalation and exhalation phases (I : E). To extract the perfluorocarbon, the scientists connected a medical suction device (FAZZINI F-30) configured to discharge 15 kPA to the exhalation valve.

The authors performed liquid artificial lung ventilation with the following parameters: volume control mode (VCM), respiratory volume (RV) — 20 ml/kg, respiratory rate (RR) — 4–5 breaths/min, I : E — 3 : 1 and FiO_2 — 80%. The scientists performed liquid artificial lung ventilation for the first 5 minutes with a solution of PFD from the first container, then for 50 minutes from the second container. The total duration of LALV was 60 minutes. After that, the authors transferred the animals to gas-ALV with the regime used in the control group. When SpO_2 decreased below 70%, the animals were repeatedly transferred for 60 minutes to a liquid artificial lung ventilation device with previously used parameters, and then to gas-ALV.

Perfluorodecalin (PFD; HaloPolymer JSC) was used as a PFCs liquid [11]. Prior to mechanical ventilation, perfluorodecalin was enriched with oxygen using a Mark 5 Nuvo Lite oxygenator (Nidek, Japan) to 80 volume %, which was determined using a Microx 4 oxygen analyzer (PreSens, Germany). The temperature of the PFCs liquid was measured using a TP-300 thermometer (Cuiisw, China).

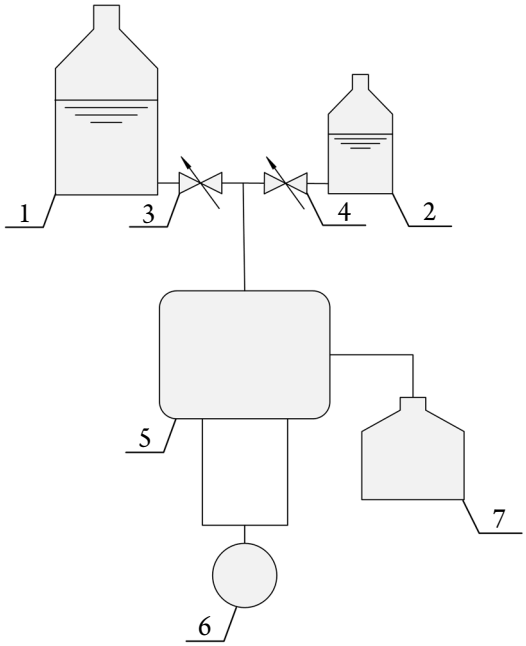

Fig. 1. Connection diagram of the Ugo Basile 7125-30 device in LALV mode
Notes: 1 — a container with a PFU liquid with a temperature of 32°C, 2 — a container with a PFU liquid with a temperature of 4°C, 3, 4 — ball valves, 5 — Ugo Basile 7125-30 device, 6 — animal, 7 — aspirator. (Solid lines indicate hydraulic connections).

The researchers collected the spent perfluorodecalin in a special container and after phase separation, they determined the volume of edematous fluid evacuated from the lungs. After death, all animals were autopsied to determine pathoanatomic changes in the lungs and lung mass coefficients were determined.

The authors carried out statistical processing of the data obtained by methods of variational statistics using the Microsoft Excel program. To analyze the date, they used descriptive statistics: they calculated the mean values *(M)* and the standard errors of the mean value *(m)*. The data were checked for the normality of the distribution using the Shapiro–Wilk criterion. The experts analyzed the intergroup differences using parametric methods using the Student's criterion. The differences were considered significant at $p<0.05$. For data belonging to a non-normal distribution, the authors applied the nonparametric Mann–Whitney method.

Results. After extraction from the seed chamber, severe chlorine inhalation was observed in all animals, as evidenced by salivation and lacrimation, redness of the mucous membranes of the eyes, coughing, rare and deep breathing, as well as a decrease in SpO_2<80% and an increase in heart rate >240 beats per minute.

In the control group, all animals showed an increase in SpO_2 to 90% and a decrease in heart rate to 220–240 beats/min after switching to a gas-ALV during the first 10 minutes. Subsequently, decompensation was observed in animals 20–25 minutes after sowing, which led to the death of animals and manifested by a rapid decrease in SpO_2 to extremely low values and an increase in heart rate ***(Fig. 2, 3)***.

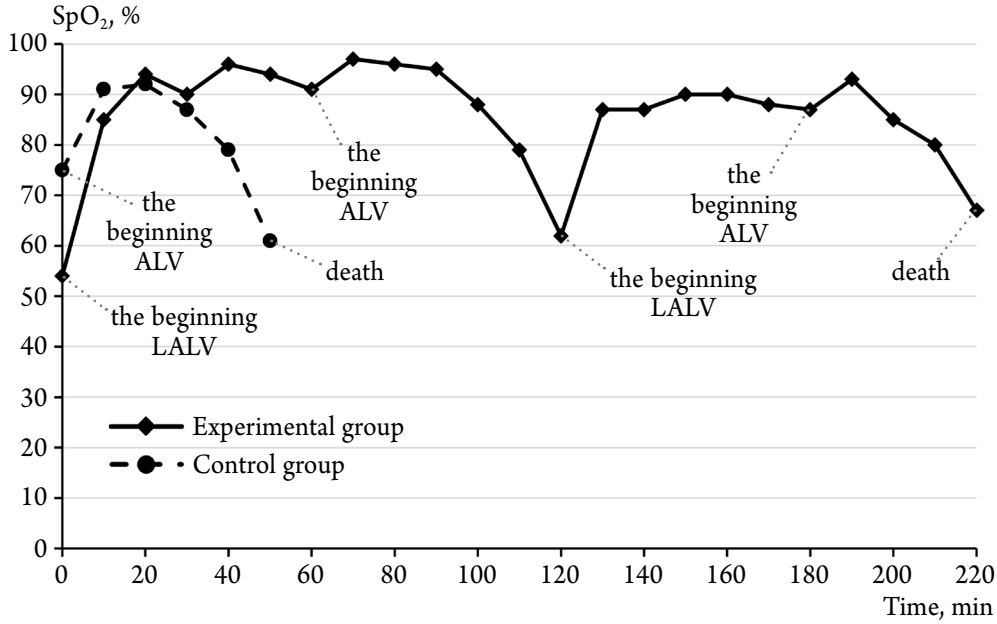

Fig. 2. Changes in oxygen saturation in animals of the control and experimental groups

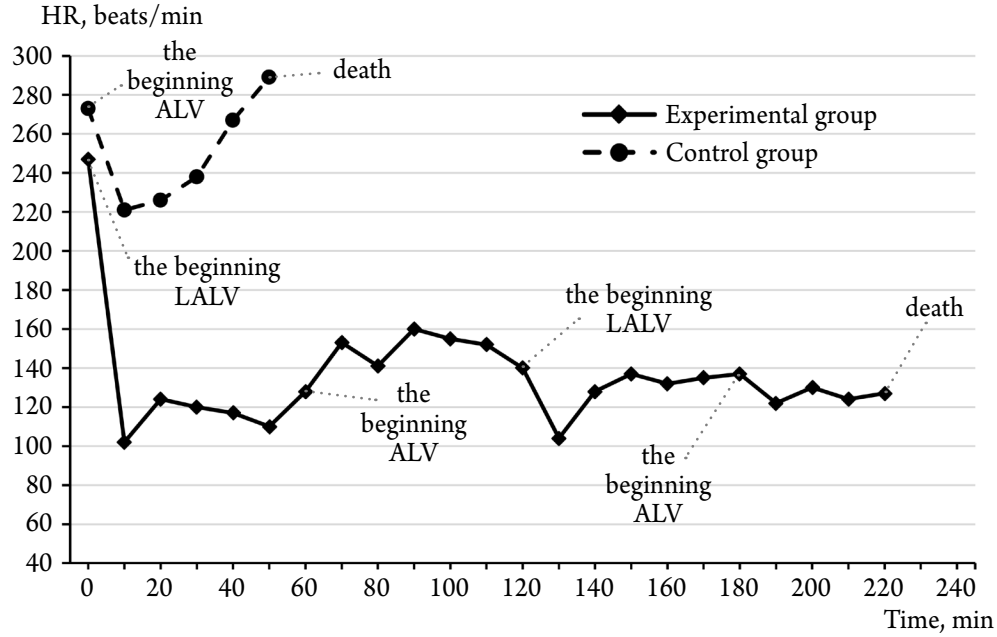

Fig. 3. Changes in heart rate in animals of the control and experimental groups

In turn, in the experimental group, during the first 5 minutes after the start of LALV, scientists recorded a sharp decrease in heart rate to 104±3.5 beats per minute and an increase in SpO_2 to 94±2.4%. Subsequently, oxygen saturation did not fall below 90% during the entire ventilation. After transferring the animals to gas artificial ventilation for 5 minutes, the authors noted a slight increase in SpO_2 and heart rate. However, there were no significant changes in the next 15–20 minutes. 25–30 minutes after switching to gas artificial ventilation, the researchers observed a gradual decrease in SpO_2 to 70%, indicating the need for a second session of LALV. At the same time, the total time of the first cycle of gas artificial lung ventilation in animals was 45±7.9 minutes.

Five minutes after the start of the second session of LAVL, all animals showed an increase in SpO_2 and a decrease in heart rate. It should be noted that during the second session, SpO_2 practically did not differ from the values recorded during the first LAVL session. After the second 60-minute LAVL session, the animals were re-transferred to a gas artificial lung ventilation (AVL). After that, most animals showed a sharp decrease in SpO_2 and an increase in heart rate within 5–15 minutes, resulting in the development of an unfavourable outcome. At the same time, the duration of the second session of gas ventilation averaged 10±8.4 minutes. ***(Fig. 2, 3)***.

When assessing the amount of edematous fluid released during liquid artificial lung ventilation (LALV), the authors found that during the experiment, an average of 5.9=1.8 ml/kg was aspirated in the animals of the experimental group.

During the experiment, there were no significant temperature changes in the animals of the control group. The average temperature in the animals of this group was 36.2±0.3°C ***(Fig. 4)***. In turn, the animals of the experimental

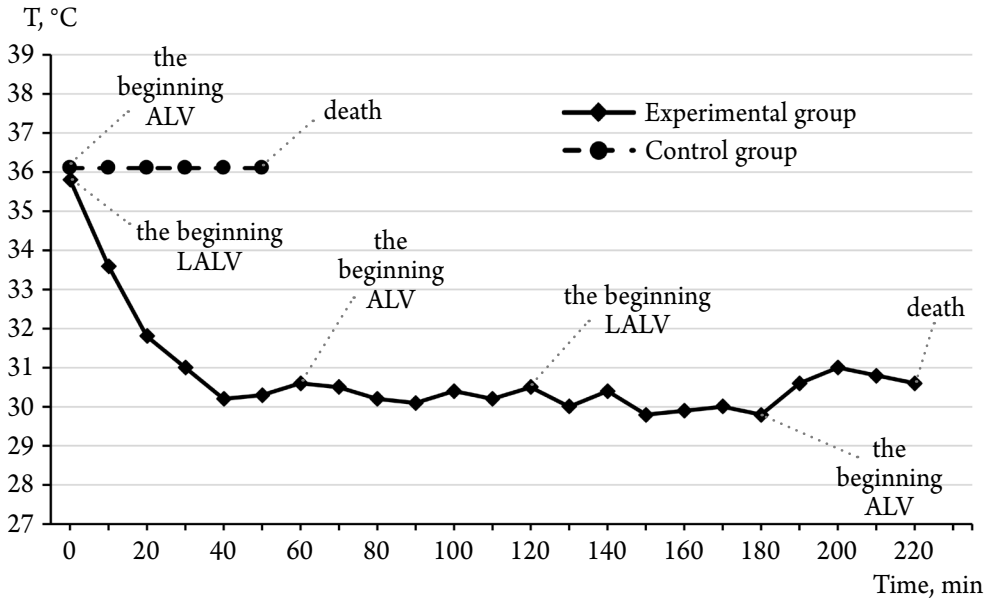

Fig. 4. Changes in rectal temperature in animals of the control and experimental groups

group had a sharp decrease in temperature during the first 30 minutes of LALV, by an average of 6.1±1.2°C. After that, the temperature stabilized and remained within 30–31°C until the second session.

When studying survival, experts found that all animals in the experimental group lived for more than 180 minutes, while none of the animals in the control group exceeded the 50-minute mark ***(Fig. 5)***. At the same time, the average survival time in the experimental group was 4.57 times longer than in the control group, and amounted to 190.0±6.3 and 41.6±3.0 minutes. respectively (p<0.001).

As a result of the pathological examination, it was found that in the animals of the control group, a large amount of edematous fluid and foam was found in the respiratory tract and lungs, while in the experimental group edematous fluid prevailed in the upper respiratory tract. In the lungs of the animals of the experimental group, PFC-fluid prevailed over edematous. As a result of liquid artificial lung ventilation (LALV) in animals of the experimental group, their lungs acquired a characteristic "crimson" colour. The authors also observed significant differences in the study of lung mass coefficients. So, in the control group it was 1.89±0.08%, while in the experimental group it was 2.70±0.03%

Discussion. Inhalation of chlorine at the dose used was accompanied by more severe disorders of the respiratory and cardiovascular systems, in comparison with the previously used intravenous administration of 0.1 M hydrochloric acid solution [11–13]. This was due to both the lack of premedication in animals with inhaled chlorine and the inability to use an artificial lung ventilation device at the initial stage of the development of toxic pulmonary edema (TPE). After priming, all animals showed signs of extremely severe inhaled chlorine poisoning, which manifested itself not only in the previously listed clinical signs, but also in extremely low saturation and pronounced tachycardia. At the same time, the implementation of gas artificial lung ventilation in animals of the control group contributed to the temporary compensation of the studied indicators. However, after

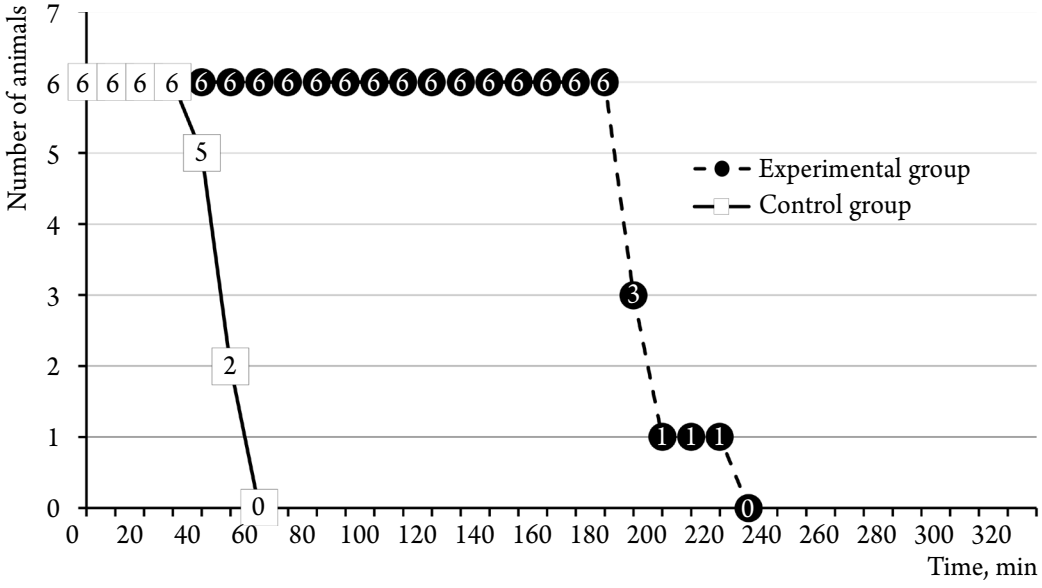

Fig. 5. Kaplan–Meyer survival curves in control and experimental animals

15–20 minutes there was a sharp decrease in vital signs, indicating the ineffectiveness of the gas ventilation. In turn, the animals of the experimental group showed stable indicators of the respiratory and cardiovascular systems, comparable to the background values, during two sessions of liquid artificial lung ventilation on the background of hypothermia. It should also be noted that after LALV and the transition to gas ventilation, all animals of the experimental group initially showed an increase in saturation, the duration of which in the first case was longer than in the second. Based on the data obtained, it can be said that the use of intermittent gas-liquid ventilation in combination with hypothermia in severe chlorine damage contributes to the restoration and long-term maintenance of acceptable SpO_2 values, which, in turn, is accompanied by a significant decrease in heart rate and, as a result, a decrease in the load on the heart and a decrease in the cardiogenic effect on the development of pathological processes in the lungs [11, 12], as well as a decrease in the production of edematous fluid and its excretion.

The data presented above generally corresponds to the previously obtained research results on the use of hypothermic liquid artificial lung ventilation in toxic pulmonary edema caused by instillation of hydrochloric acid solution. However, it is noteworthy that with a single use of LALV, there was a longer stabilization of the studied parameters (SpO_2 and heart rate) after switching to ALV, which in turn may indicate a less pronounced lung lesion created in this mode. At the same time, despite the more severe lung damage caused by chlorine inhalation compared with endotracheal hydrochloric acid administration, the survival time in animals subjected to hypothermic intermittent gas-liquid lung ventilation and hypothermic artificial ventilation did not differ significantly. Nevertheless, during intermittent gas-liquid ventilation, SpO_2 retention was observed at an acceptable level for a longer time compared with a single application of liquid artificial lung ventilation [13].

Taking into account all of the above, we can say that the method of hypothermic intermittent gas-liquid artificial lung ventilation, after appropriate refinement, can be successfully applied in the treatment of acute respiratory viral infections caused by chlorine poisoning, as well as in severe primary acute respiratory distress syndrome (ARDS) caused by other causes.

Conclusion:

1. Inhalation of chlorine into a 200-liter chamber with an estimated concentration of 35 mg/l for 15 minutes leads to the rapid development of toxic pulmonary edema in small laboratory animals (bypassing the stage of primary clinical manifestations and the latent period).

2. The use of LALV using perfluorodecalin (PFD) allows the evacuation of edematous fluid from the lungs in case of toxic edema caused by severe inhaled chlorine poisoning, and thereby preserve gas exchange in the lungs.

3. The use of hypothermic intermittent gas-liquid ventilation makes it possible to maintain gas exchange in the lungs in the case when conventional mechanical ventilation is ineffective and thus significantly ($p<0.001$) increase the survival time of laboratory animals by 4.57 times. The results obtained indicate the prospects for further development of respiratory support methods based on hypothermic LAVL as a treatment for severe forms of acute respiratory distress syndrome (ARDS), in the case when traditional ventilation is no longer effective.

1. *Medical toxicology. National leadership.* Luzhnikov E.A. Moscow: GEOTAR-Media; 2014 (in Russian).
2. Akimov A.G., Khalimov Yu.Sh., Shilov V.V. Acute industrial poisoning with chlorine and ammonia: clinic, diagnosis, treatment. Modern ideas. *Ehkologiya cheloveka.* 2012; 6: 25–36 https://doi.org/10.17816/humeco17463 (in Russian).
3. *Intensive care: national guidelines: in 2 volumes.* Ed. by I.B. Zabolotskikh, D.N. Protsenko. 2nd ed., reprint. and add. Moscow: GEOTAR-Media, 2022; Vol. 1 (in Russian).
4. Bonitenko E.U., Belyakova N.A., Barinov V.A., Krasnov K.A., Gladchuk A.S., Burov A.A. et al. Perfluorocarbons in the treatment of severe bronchopulmonary pathology. part I: classification of methods (analytical review). *Medline.ru.* 2023; 24: 1368–1397 (in Russian).
5. Hill S.E. Perfluorocarbons: knowledge gained from clinical trials. *Shock.* 2019; 52(1): 60–64. https://doi.org/10.1097/SHK.0000000000001045
6. Nocentini G., Maclaren G., Bartlett R., De Luca D., Perdichizzi S., Stoppa F., et al. Perfluorocarbons in Research and Clinical Practice: A Narrative Review. *ASAIO J.* 2023; 69(12): 1039–1048. https://doi.org/10.1097/MAT.0000000000002017
7. Wei F., Hu Y., Jiang M., Ye L., Yang L. Effect of perfluorocarbon partial liquid ventilation-induced hypothermia on dogs with acute lung injury. *Ann. Palliat. Med.* 2020; 9(4): 2141–2151. https://doi.org/10.21037/apm-20-1275
8. Rambaud J., Lidouren F., Sage M., Kohlhauer M., Nadeau M., Fortin-Pellerin E. et al. Hypothermic total liquid ventilation after experimental aspiration-associated acute respiratory distress syndrome. *Ann. Intensive Care.* 2018; 8(1): 57. https://doi.org/10.1186/s13613-018-0404-8
9. Richman P.S., Wolfson M.R., Shaffer T.H. Lung lavage with oxygenated perfluorochemical liquid in acute lung injury. *Crit. Care Med.* 1993; 21(5): 768–774.
10. Voelker M.T., Laudi S., Henkelmann J., Bercker S. Extracorporeal membrane oxygenation and perfluorocarbon in a therapy refractory case of acute respiratory distress syndrome. *Ann. Thorac Surg.* 2022; 113(5): e355–e358. https://doi.org/10.1016/j.athoracsur.2021.07.045
11. Isabekov N.R., Tonshin A.A., Bonitenko E.U. Substantiation of the possibility of using bronchoalveolar lavage with perfluorocarbon fluids for the treatment of the alveolar stage of toxic pulmonary edema. *Med. truda i prom. ekol.* 2024; 64(2): 105–110. (In Russian) https://doi.org/10.31089/1026-9428-2024-64-2-105-110
12. Isabekov N.R., Tonshin A.A., Bonitenko E.U. Hypothermia induced by bronchoalveolar lavage with perfluorocarbon liquids as a method for the treatment of the alveolar stage of toxic pulmonary edema. Experimental assessment. *Med. truda i prom. ekol.* 2024; 64(5): 293–302. https://doi.org/10.31089/1026-9428-2024-64-5-293-302
13. Isabekov N.R., Tonshin A.A., Bonitenko E.U. Justification of the possibility of using liquid artificial lung ventilation for the treatment of acute respiratory distress syndrome of toxic genesis. *Med. truda i prom. ekol.* 2024; 64(8): 506–517. https://doi.org/10.31089/1026-9428-2024-64-8-506-517

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