Nikolay R. Isabekov, Anton A. Tonshin, Evgenij Yu. Bonitenko

Justification of the possibility of using liquid artificial lung ventilation for the treatment of acute respiratory distress syndrome of toxic genesis

Izmerov Research Institute of Occupational Health, 31, Budyonnogo Ave, Moscow, 105275

Introduction. Pulmonotoxicants are chemicals that cause bronchospasm and damage to the alveolar capillary membrane. Lesions of the respiratory system with pulmonotoxicants in industrial accidents are especially relevant at the present time. Existing methods of treatment for the defeat of pulmonotoxicants and the development of acute respiratory distress syndrome (ARDS) are becoming ineffective, therefore, one of the tasks of modern medicine is to develop new methods of treating ARDS. One of these methods may be the creation of a "therapeutic window" by using perfluorocarbon (PFC) liquids. This article will present an experimental assessment of the use of liquid artificial lung ventilation (LALV) PFC liquids on the ARDS lung model.

The study aims to explore the possibility of using liquid artificial lung ventilation to create a therapeutic window in the treatment of acute respiratory distress syndrome of a chemical nature.

Materials and methods. The authors conducted a study on male Wistar rats aged 4 months, weighing 180–190 g. Toxic pulmonary edema was caused by endotracheal administration of 0.1 m HCl solution. The anesthetized patients were intubated using a cannula, after which the researchers intratracheally injected 0.1 M HCl solution at a dose of 2 ml/kg, a decrease in saturation below 80 was expected. Then the experts randomized the animals by weight into groups of 6 individuals each. They connected the animals of the control group to a ventilator. The animals of the experimental group were treated with PFC liquids for an hour, then transferred to a ventilator. Perfluorodecalin was used as a PFC liquid. The scientists recorded heart rate, blood oxygen saturation, rectal temperature, life expectancy and overall survival by group.

Results. In the control group, after instillation of 0.1 M HCl solution and connection to a ventilator during the first 25–30 minutes, there was a gradual decrease in SpO_2 to 74.0±5.6% (background — 95.0±3.5%) and an increase in heart rate to 182.0±8.6 beats/min., (background — 278.0±14.8 beats/min.) after which there was decompensation of the animal condition. In animals of the experimental group, after connecting to the LALV device, a sharp decrease in heart rate was recorded during the first 5 minutes to 61.0±8.5 beats/min. In turn, saturation did not change significantly throughout the LALV and was in the range from 95 to 100%. As a result of the experiments, it was noted that the average survival time in the experimental group was 256.0±34.5 minutes, which was significantly (p<0.001) more than 5 times higher than this indicator in the control animals — 45.3±4.3 minutes.

There were no significant changes in the study of rectal temperature in the animals of the control group. In turn, the animals of the experimental group showed a sharp decrease in rectal temperature during the first 30 minutes from the beginning of LALV, on average by 5.8±1.60°C.

As a result of the pathoanatomic autopsy, differences in lung mass coefficients were revealed in different groups. Thus, in the control group and the experimental groups, it was 1.67±0.06 and 2.4±0.045%, respectively.

Conclusion. *On the model of ARDS caused by endotracheal administration of 0.1M hydrochloric acid solution, it was shown that living with the use of PFC of low temperature liquids, unlike conventional mechanical ventilation, allows for a long time to maintain a stable condition of animals; evacuate a significant amount of edematous fluid from the lungs and thereby increase the duration of their survival. The data presented above indicate that the use of hypothermic LALV can be used to create a "therapeutic window" for ARDS, including its most severe form — the alveolar stage of toxic pulmonary edema.*

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

Keywords: *perfluorocarbon; perfluorodecalin; acute respiratory distress syndrome; toxic pulmonary edema; artificial lung ventilation (ALV); liquid artificial lung ventilation (LALV)*

For citation: Isabekov N.R., Tonshin A.A., Bonitenko E.Yu. 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://elibrary.ru/dvgnwe https://doi.org/10.31089/1026-9428-2024-64-8-506-517

For correspondence: *Nikolay R. Isabekov,* e-mail: isabekov.nikolai@yandex.ru

Contribution:

Isabekov N.R. — concept and design of research, data collection and processing, text writing;

Tonshin A.A. — concept and design of research, data collection and processing;

Bonitenko E.Yu. — concept and design of the study, editing.

Funding. The work was performed within the Framework of the state assignment, the topic code FGFE-2024-0003.

Conflict of interests. The authors declare no conflict of interests.

Received: 05.08.2024 / Accepted: 20.08.2024 / Published: 15.09.2024

Introduction. Currently, the chemical industry of the Russian Federation is experiencing a significant increase in the production of toxic chemicals. The emergence of new industrial enterprises leads to an increase in the risk of developing hazardous accidents at work with the release of highly toxic volatile chemicals into the atmosphere — pulmonotoxicants [1]. Pulmonotoxicants, entering the body by inhalation, affect the upper and lower respiratory tract, as well as the lungs, which in severe poisoning can lead to the development of acute respiratory distress syndrome and its terminal stage – toxic pulmonary edema (TPE). It should be noted that clinical manifestations under the action of pulmonotoxicants develop after a latent period, the duration of which directly depends on the severity of poisoning. In severe poisoning in the period of pronounced clinical manifestations, symptoms indicating the development of TPE come to the fore, in which two stages are distinguished: interstitial and alveolar. The latter is characterized by filling of the alveolar space and respiratory tract with edematous fluid.

The main methods in the treatment of TPE are drug and

respiratory therapy. Drug therapy includes high doses of diuretics, narcotic analgesics, glucocorticoids, as well as the use of defoamers. In turn, respiratory therapy is based on the use of artificial lung ventilation (ALV) with a positive end-exhalation pressure (PEEP) greater than 5 cm H_2O and an oxygen content in the inhaled mixture (FiO_2) of at least 40%. However, as a rule, the progression of TPE is accompanied by a rapid accumulation of edematous fluid in the alveoli, which in turn leads to the progression of respiratory failure even against the background of ongoing therapeutic measures and, as a result, the development of an unfavorable outcome [2] in connection with which, the development of new methods of treatment of the alveolar stage remains one of the priorities of modern medicine.

One of these methods may be the creation of a "therapeutic window" that would allow for more.

The therapeutic window is the time interval after the onset of the disease, during which specific therapy has maximum effectiveness and can either minimize the consequences or prevent them. Thus, in ischemic stroke, thrombolytic therapy in the first 3–4 hours from the onset of the disease reduces the number of deaths by 80% [3]. The use of moderate hypothermia (with a decrease in body core temperature in the range from 32 to 34°C) to create a "therapeutic window" is widely used in clinical practice for: spinal cord and brain injuries; cardiac surgery with cardioplegia, prevention of hypoxic-ischemic encephalopathy in the post-intensive care period [4, 5]. Taking into account all of the above, we assumed that a decrease in core temperature of the body and lungs, in particular, can significantly slow down the development of toxic pulmonary edema, thereby creating a "therapeutic window". As a method for creating local hypothermia of the lungs, the most promising is liquid artificial ventilation of the lungs using perfluorocarbon liquids, which allows you to quickly reduce the temperature of both the core of the body and the brain. This is due to the fact that perfluorocarbons have a significantly higher heat capacity compared to air, due to which the heat transfer process in the lungs proceeds more intensively [6, 7]. An additional argument for using LALV to create a "therapeutic window" is a higher (almost 2 times) density of perfluorocarbons compared to water and edematous fluid, which allows the latter to be displaced from the lungs as well as to straighten previously dormant alveoli [6, 7].

Numerous experimental studies have shown the high effectiveness of various types of LALV in the treatment of acute lung injury and ARDS of any ethology [8–12]. However, we have not found any works on the use of LALV to create therapeutic hypothermia in the treatment of ARDS, with the exception of studies published by Rambaud J. with co-authors [13] and Wei F. with co-authors [14].

Thus, Rambaud J. and co-authors [13] showed that the use of artificial lung ventilation devices to induce hypothermia in an experiment with ARDS in rabbits contributed to a decrease in the inflammatory reaction in the lungs and hemodynamic insufficiency compared with conventional ventilation in the absence of a negative effect on gas exchange and respiratory mechanics [13]. In turn, the induction of hypothermia by partial fluid ventilation in ARDS in dogs, conducted by Wei F. with co-authors [14], it was accompanied by an increase in the partial pressure of oxygen in arterial blood, as well as a decrease in the inflammatory reaction in the lungs compared with the use of traditional artificial lung ventilation. A decrease in the expression of proinflammatory interleukin-6 (IL-6), as well as an increase in the expression of anti-inflammatory interleukin-10 (IL-10) in both blood and bronchoalveolar fluid, indicated a decrease in the inflammatory response [14].

Another confirmation of our assumption may be the results of previous studies on the use of various variants of bronchoalveolar lavage (BAL) in TPE, including hypothermic, which demonstrated the possibility of PFC liquids to increase the survival time of laboratory animals [15, 16]. If the hypothesis of the possibility of using LALV with PFC with liquids to provide a "therapeutic window" is confirmed, conditions can be created and, first of all, temporary, for the use of other modern methods of treating ARDS and the alveolar stage of toxic pulmonary edema as its culmination.

The study aims to explore the possibility of using liquid artificial lung ventilation to create a therapeutic window in the treatment of acute respiratory distress syndrome of a chemical nature.

Materials and methods. The study was conducted on male Wistar rats aged 4 months, weighing 180–190 g. Before the study, the animals were quarantined for 14 days. To determine the number of animals in the sample and distribute them into groups, a statistical processing recommendation[1] was used. The animals were anesthetized with intravenous injection of zoletil and medetomidine at a dose of 1.0 and 0.5 mg/kg, respectively. After that, the rats were intubated using a 16G intravenous catheter (CK-FLON, India). ARDS was modeled by intratracheal administration of 0.1 M HCl solution at a dose of 2 ml/kg [15, 16].

After the introduction of the model substance, oxygen saturation (SpO_2) was expected to decrease below 80, then the animals were randomized by weight into 2 groups, a control and an experimental group of 6 individuals each. Scientists measured SpO_2 and heart rate (HR) in animals of both groups every 5 minutes from the beginning of acid instillation using a portable pulse oximeter (Zoomed LLC, UT100 model, Russia). Rectal temperature was measured throughout the experiment using an electronic thermometer (TianJin, DC-1 model, China). For conventional gas ventilation, the Ugo Basile 7125-30 device (Italy) was used in volume control mode (VCM) with a respiratory volume (RV) to10 ml/ kg and a respiratory rate (RR) of 75 breath/min, the ratio of inhalation: exhalation (I : E) — 1:1 and positive end-exhalation pressure (PEEP) 10 cm H_2O, which was provided due to specially selected resistance of the respiratory circuit. The animals of the control group underwent gas ventilation in the above-mentioned mode until the moment of death. In turn, the experimental animals were connected to the LALV apparatus, which was used as 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 LALV mode is shown in ***Figure 1***. A supply line from two containers with pre–oxygenated perfluorodecalin (PFD) was connected to the inhalation valve of the apparatus for supplying the working medium, the first with a temperature of 4°C, the second — 32°C. A control unit for the ratio of the duration of the inhalation and exhalation phases was connected to the device, and a medical suction (FAZZINI

[1] Recommendations for 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 from 15–33.

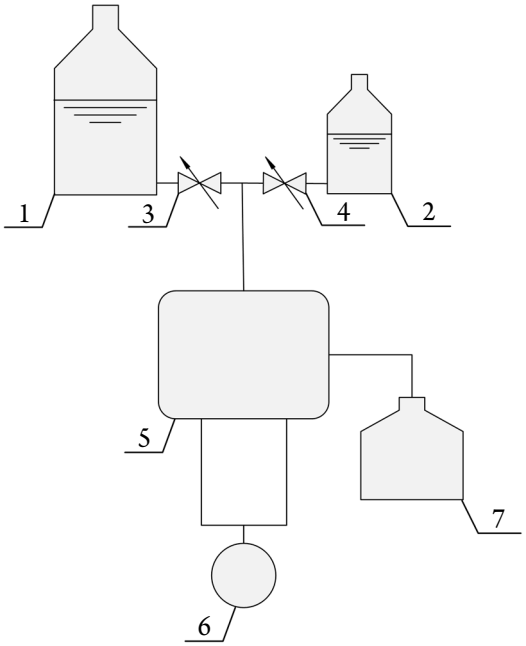

Fig. 1. Connection diagram of the Ugo Basile 7125-30 device in LALV mode
Notes: 1 — a container with a PFU liquid with a temperature of 32°C, 2 — a container with a PFU liquid with a temperature of 4°C, 3.4 — ball valves, 5 — Ugo Basile 7125-30 device, 6 — animal, 7 — aspirator. (Solid lines indicate hydraulic connections).

F–30) configured for a discharge of 15 kPA was connected to the exhalation valve to extract the working medium. LALV was performed with the following parameters: volume control mode (VCV), respiratory volume (RV) to — 20 ml/kg, respiratory rate (RR) — 4–5 breaths /min., I : E — 3 : 1. The first 5 minutes the animals of the experimental group were ventilated with a solution of PFD from the first container and then from the second. The total duration of the ventilator was 60 minutes. After that, the animals were transferred to a gas ventilator until the moment of death with a regime similar to that used in the control group. After death, the animals underwent necropsy. In animals of the experimental group, after injection, spent perfluorodecalin was collected in a flask to determine the volume of edematous fluid evacuated from the lungs.

The authors have carried out the statistical processing of the obtained data by methods of variational statistics using the Microsoft Excel program. Descriptive statistics were used to analyze the data: the average values *(M)* and standard errors of the mean *(m)* were calculated. The data were checked for the normality of the distribution using the Shapiro–Wilk criterion. The authors analyzed the intergroup differences by parametric methods using the Student's criterion. The differences were considered significant at $p<0.05$. The scientists used the nonparametric Mann–Whitney method for data related to a distribution other than normal.

Results. In the control group, after instillation of 0.1M HCl solution and connection to a ventilator during the first 25–30 minutes, there was a gradual decrease in SpO_2 to 74.0±5.6% (background — 95.0±3.5%) and an increase in heart rate to 182.0±8.6 beats/min., (background — 278.0±14.8 beats/min.) after which there was decompensation of the animal condition, which was manifested by a sharp decrease in SpO_2 to extremely low values — 57.0±10.5% and an increase in heart rate to 220.0 13.4, which indicated the development of the alveolar stage of TPE ***(Fig. 2, 3)***. In animals of the experimental group, after connecting to the LALV device, a sharp decrease in heart rate was recorded during the first 5 minutes to 61.0±8.5 beats/min. In turn, saturation did not change significantly throughout the entire LALV was in the range from 95 to 100%. After transferring the animals of the experimental group to an artificial lung ventilation device, no significant changes in heart rate and SpO_2 were recorded during the first 50–60 minutes. Subsequently, in these animals, we observed a gradual decrease in SpO_2 and an increase in heart rate until the moment of death ***(Fig. 2, 3)***.

A visual examination of the respiratory fluid collected during the LALV process revealed a phase separation into PFD and edematous fluid. As a result, 7.5±2.1 ml/kg of edematous fluid was aspirated in each animal of the experimental group during the experiment.

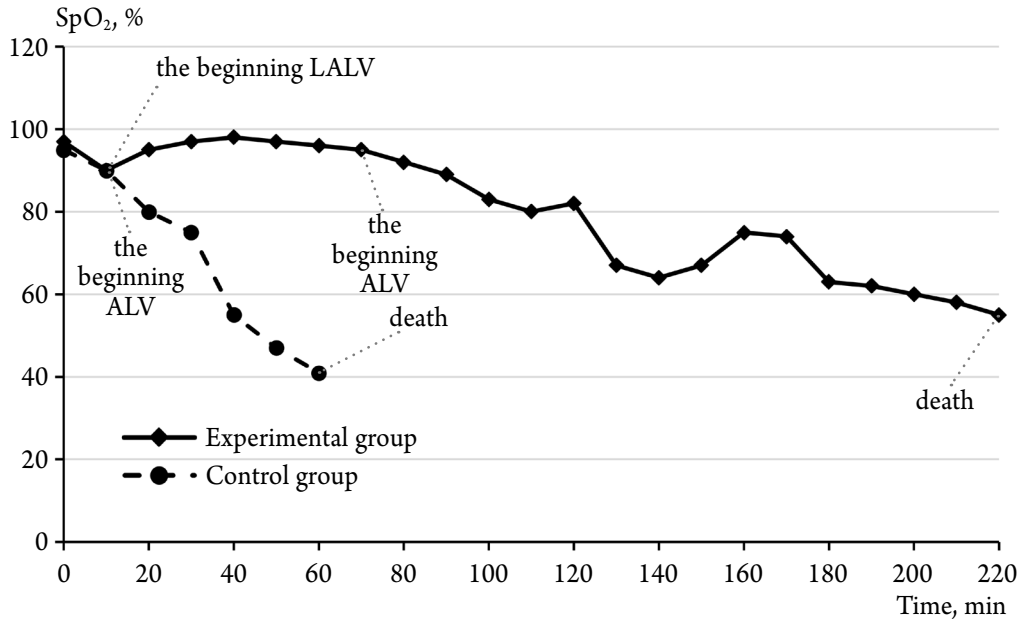

Fig. 2. Changes in oxygen saturation in animals of the control and experimental groups

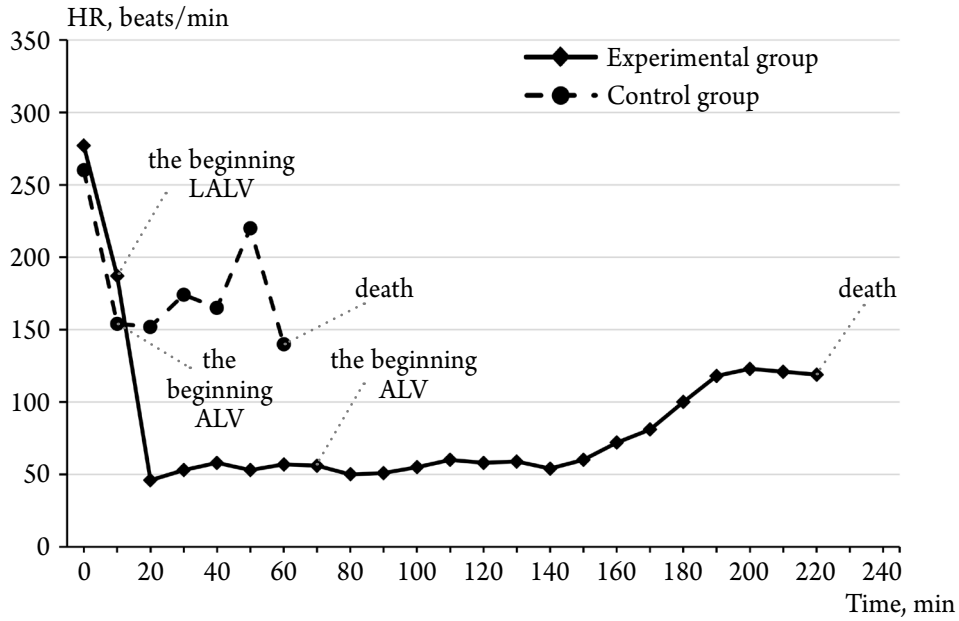

Fig. 3. Changes in the heart rate of the control and experimental groups

When studying rectal temperature in animals of the control group, the scientists did not find significant changes, the average temperature during the experiment was 36.0=0.6°C ***(Fig. 4)***. In turn, the animals of the experimental group showed a sharp decrease in rectal temperature during the first 30 minutes. from the beginning of the LALV, on average by 5.8±1.6°C, which was also accompanied by a decrease in heart rate. Subsequently, during the next 90–120 minutes, no significant temperature changes were recorded ***(Fig 4)***. After 120 minutes. from the beginning of the experiment, the temperature began to rise gradually, which was also accompanied by an increase in heart rate and a decrease in saturation.

When studying the timing of death, we found that all animals of the experimental group lived for more than 200 minutes, while none of the control group exceeded the 70-minute mark ***(Fig. 5)***. At the same time, the average survival time in the experimental group was 256.0±34.5 minutes, which is reliable ($p<0.001$) more than it was 5 times higher than this indicator in control animals — 45.3±4.3 minutes.

As a result of the pathological examination, significant differences were revealed in the animals of the control and experimental groups. Thus, in control animals, a large amount of transudate was found in the trachea and bronchi, while in experimental animals — mainly in the middle sections of the lungs, while a small amount of perfluorodecalin was detected in the lower ones. Due to the presence of PFD in the lungs of animals of the experimental group, they had a characteristic "crimson" color for LALV. We also observed significant differences in the study of lung mass coefficients: in the control and experimental groups, they amounted to 1.67±0.06 and 2.4±0.045%, respectively.

Discussion. As can be seen from the presented data, the researchers observed decompensation in animals of the control group 20–30 minutes after the start of lung ventilation, due to a decrease in oxygenation, which manifested itself with

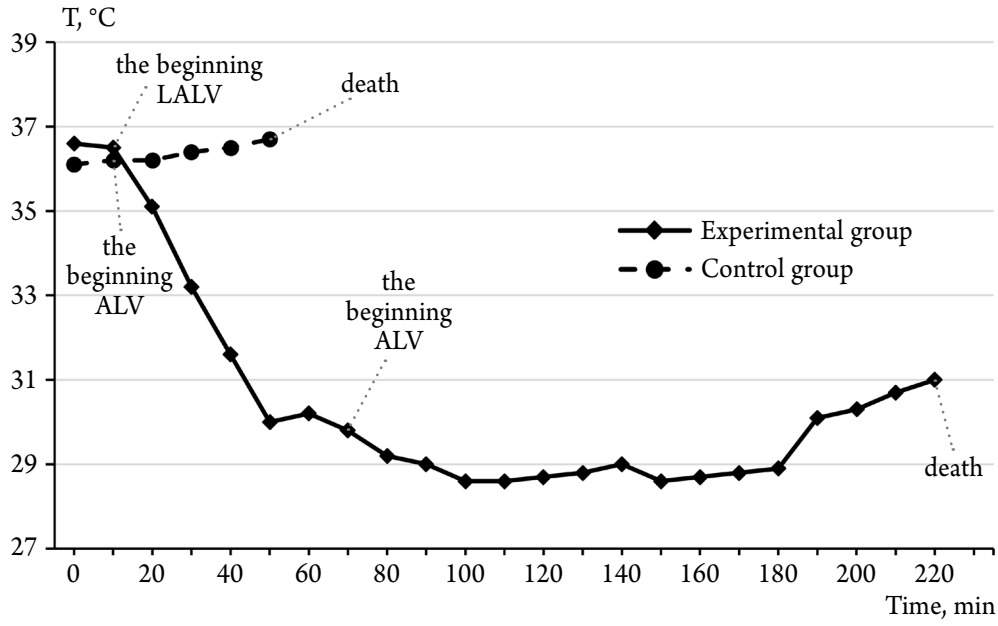

Fig. 4. Changes in rectal temperature in the animal of the control and experimental groups

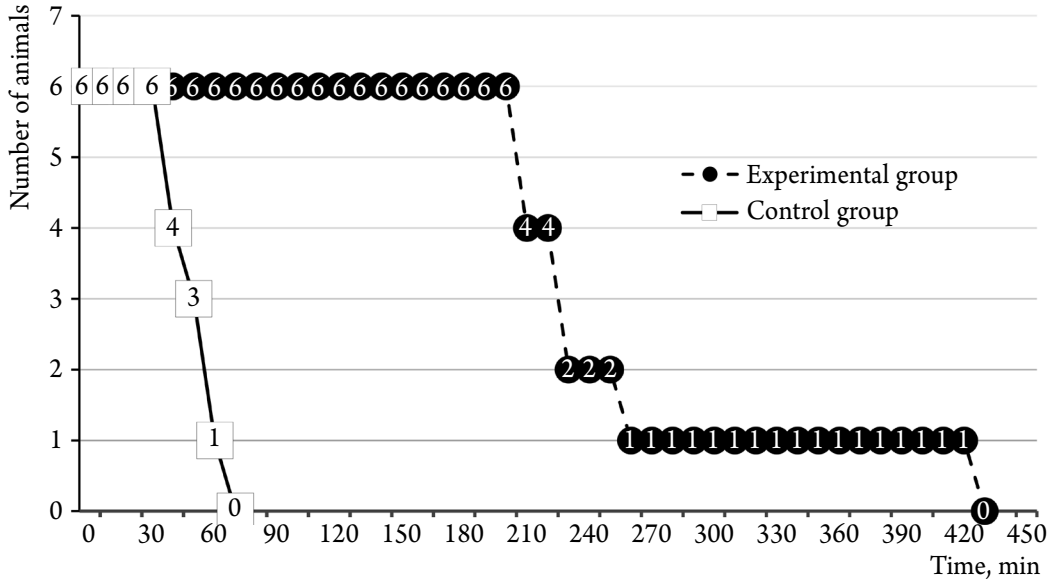

Fig. 5. Kaplan–Meyer survival curves in control and experimental animals

violations of systemic hemodynamics, which indicated the progression of acute respiratory failure.

In turn, decompensation was not observed in animals of the experimental group during LALV, and after switching to gas ventilation, there was a long-term stabilization of both heart rate and saturation, which indicates the influence of hypothermic liquid ventilation on significant pathogenesis links in the development of ARDS in general and the alveolar stage of TPE in particular.

A sharp decrease in saturation and an increase in heart rate observed in animals of the experimental group after 60–70 minutes. after the transfer from liquid ventilation to gas ventilation, combined with an increase in rectal temperature, indicated the progression of acute respiratory failure caused by a breakdown of the compensatory capabilities of the body. Based on the data obtained, it can be said that the use of LALV with PFC at low temperatures, with the development of ARDS and in the subsequent alveolar stage of TPE leads to the development of deep hypothermia [17], and also provides good evacuation of the resulting edematous fluid from the lungs, thereby increasing the survival time of laboratory animals.

Previous studies on the use of normo- [15] and hypothermic BAL [16] in the alveolar stage of TPE showed high efficiency of PFCs of liquids, which was manifested not only by an increase in the average duration of animal survival, but also by the extraction of large volumes of edematous fluid from the lungs. However, the positive effects of BAL are short-term in nature, as a result of which they cannot significantly affect the course and outcome of toxic pulmonary edema. In turn, the use of both normal and hypothermic livers with TPE, having positive properties of BAL, demonstrates a number of advantages over the latter, as evidenced by an increase in the average survival time of animals by 5 times compared with normal and 2.8 times with hypothermic BAL with PFC liquid, respectively. LALV also increases the removal of edematous fluid from the lungs by more than 3.4 times in toleration compared to BAL with PFC liquid [15, 16]. The creation of hypothermia at the expense of LAVL in order to influence the experimentally created ARDS was demonstrated in the article Rambaud J. with co-authors [13]. However, unlike the present study, the duration of the created session was significantly less pronounced, and therefore we did not identify qualitative and quantitative differences between the use of gas and liquid ventilation. In turn, we have shown that with the development of the terminal stage of ARDS, alveolar pulmonary edema, the use of artificial lung ventilation is ineffective and does not prevent the rapid death of animals.

However, unlike the present study, the lung lesion created was significantly less pronounced, and therefore there were no qualitative and quantitative differences between the use of gas and liquid ventilation. In turn, we have shown that with the development of the terminal stage of ARDS, alveolar pulmonary edema, the use of a ventilator is not effective and does not prevent the rapid death of animals.

It should be noted that the combination of hypothermic liquid and gas ventilation has demonstrated its effectiveness throughout the experiment, which opens up the possibility for further study of their combinations.

Conclusion:

1. On the model of ARDS caused by endotracheal administration of 0.1M hydrochloric acid solution, it was shown that LALV using PFC liquids of low temperature liquids, unlike conventional mechanical ventilation, allows for a long time to maintain a stable condition of animals; evacuate a significant amount of edematous fluid from the lungs and thereby increase the duration of their survival.

2. The data presented above indicate that the use of hypothermic LALV can be used to create a "therapeutic window" for ARDS, including in its most severe form — the alveolar stage of toxic pulmonary edema.

References

1. Federal service for supervision of consumer rights protection and human well-being. State report. *On the state of sanitary and epidemiological welfare of the population in the Russian Federation in 2021–2022:* 145–164.
2. Basharin V.A., Chepur S.V., Tolkach P.G. et al. *Toxicology of pulmonotoxicants: textbook*. Levsha Publishing House. St. Petersburg, 2021.
3. Marino P.L. *Intensive therapy.* 2nd ed. 2022: 393–398.
4. Grigoriev E.V., Shukevich D.L., Plotnikov G.P., Tikhonov N.S., Therapeutic hypothermia: possibilities and prospects. *Klinicheskaya meditsina.* 2014: 9; 9–16.
5. Arrich J., Schütz N., Oppenauer J., Vendt J., Holzer M., Havel C. et al. Hypothermia for neuroprotection in adults after cardiac arrest. *Cochrane Database Syst Rev.* 2023; 5(5): CD004128. https://doi.org/10.1002/14651858.CD004128.pub5
6. Dirkes S. Liquid ventilation: new frontiers in the treatment of ARDS. *Crit. Care Nurse.* 1996; 16(3): 53–58.
7. Rambaud J., Lidouren F., Sage M., Kohlhauer M., Nadeau M., Fortin-Pellerin É., 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
8. Barinov V.A., Bonitenko E.U., Belyakova N.A., Rodchenkova P.V., Tonshin A.A., Panfilov A.V. et al. The use of perfluorocarbon fluids in the treatment of respiratory distress syndrome. *Medline.ru.* 2022; 23: 515–555.
9. Foust R. 3rd, Tran N.N., Cox C., Miller T.F. Jr., Greenspan J.S., Wolfson M.R., et al. Liquid assisted ventilation: an alternative ventilatory strategy for acute meconium aspiration injury. *Pediatr. Pulmonol.* 1996; 21(5): 316–322. https://clck.ru/3CkbAP
10. Hirschl R.B., Parent A., Tooley R., Shaffer T., Wolfson M., Bartlett R.H. Lung management with perfluorocarbon liquid ventilation improves pulmonary function and gas exchange during extracorporeal membrane oxygenation (ECMO). Artificial Cells Blood Substit Immobil. *Biotechnol.* 1994; 22(4): 1389–1396. https://doi.org/10.3109/10731199409138842
11. Costantino M.L. The use of liquid perfluorocarbons for neonatal lung ventilation. *Int. J. Artif. Organs.* 1996; 19(5): 284–290.
12. 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.
13. Rambaud J., Lidouren F., Sage M, Kohlhauer M., Nadeau M., Fortin-Pellerin É., Micheau P., Zilberstein L., Mongardon N., Ricard J.D., Terada M., Bruneval P., Berdeaux A., Ghaleb B., Walti H., Tissier R. Hypothermic total liquid ventilation after experimental aspiration-associated acute respiratory distress syndrome. *Ann Intensive Care.* 2018 May 2; 8(1): 57. https://doi.org/10.1186/s13613-018-0404-8
14. Wei F., Wen S., Wu H., Ma L., Huang Y., Yang L. Partial liquid ventilation–induced mild hypothermia improves the lung function and alleviates the inflammatory response during acute respiratory distress syndrome in canines. *Biomed. Pharmacother.* 2019; 118: 109344. https://doi.org/10.1016/j.biophah.2019.109344
15. Isabekov N.R., Tonshin A.A., Bonitenko E.Yu. 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. https://doi.org/10.31089/1026-9428-2024-64-2-105-110 (in Russian).
16. Isabekov N.R., Tonshin A.A., Bonitenko E.Yu. 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
17. Hutin A., Lidouren F., Kohlhauer M., Lotteau L., Seemann A., Mongardon N., Renaud B., Isabey D., Carli P., Vivien B., Ricard J.D., Hauet T., Kerber R.E., Berdeaux A., Ghaleb B., Tissier R. Total liquid ventilation offers ultra-fast and whole-body cooling in large animals in physiological conditions and during cardiac arrest. *Resuscitation.* 2015; 93: 69–73. https://doi.org/10.1016/j.resuscitation.2015.05.020

About the authors:

Nikolay R. Isabekov Researcher, Laboratory for the Development of the Method of Gas-Liquid Artificial Ventilation of the Lungs, Izmerov Research Institute of Occupational Health.
E-mail: isabekov.nikolai@yandex.ru
https://orcid.org/0009-0002-0321-2829

Anton A. Tonshin Head of the Laboratory of Toxicology, Izmerov Research Institute of Occupational Health, Dr. of Sci. (Biol.).
E-mail: atonshin@yandex.ru

Evgenij Yu. Bonitenko Chief Researcher, Laboratory for the Development of a Method of Gas-Liquid Artificial Lung Ventilation, Izmerov Research Institute of Occupational Health. Dr. Sci. (Med.), Professor.
E-mail: eu_bonitenko@mail.ru
https://orcid.org/0000-0002-3627-7031