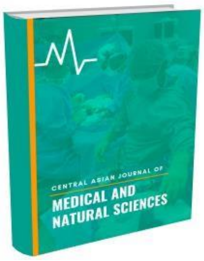

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Article

Experimental Evaluation of a New Method for Achieving Aerostasis in Lung Surgery

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Abstract: Postoperative air leakage-alveolo-pleural fistula, is one of the most frequent and insidious complications in thoracic surgery and the main limiting factor in early discharge of patients from the hospital. One of the directions of the search for means to reduce the risk of developing these complications is the development of new implants and methods of their application. In this regard, at the present time, it is necessary to continue the development of new biocompatible coatings and methods of their application. The article considers an experimental evaluation of a new method for ensuring tightness of sutures in lung surgery to reduce the risk of such manifestations as aerostasis failure. The essence of the technique consists in intraparenchymatous injection of a gel substance into the area of lung tissue damage. The biological reactions of tissues and the timing of gel resorption in lung tissue have been studied. This range of research is of fundamental importance for the new techniques created, while the main task is precisely to study the safety of intraparenchymatous use of a gel substance. In this aspect, the effectiveness and duration of aerostasis were evaluated in ex vivo and in vivo experiments. The conducted studies have established that 3.3% Hemoben gel injected into the lung parenchyma at a dose of 1 ml per 1 g does not have an irritating and toxic effect, and according to spectrophotometric studies, it is completely removed from the lung tissue within 7-10 days. At the same time, the proposed technique is characterized by the effectiveness and safety of application, and the results obtained make it possible to apply this method in clinical practice.

Keywords: aerostasis in lung surgery, hemoben gel, prolonged air leakage, drainage of the pleural cavity, problems of thoracic surgery

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1. Introduction

Prolonged air leakage (PAI) after lung surgery remains one of the urgent problems of thoracic surgery. The various proposed methods of prevention and treatment of PAI have both their advantages and disadvantages [1].

Drainage of the pleural cavity in the event of PAI leads to an extension of the length of stay of patients in the hospital and their subsequent long-term outpatient follow-up. Constant monitoring of negative pressure in the system and maintenance of drains. The use of crosslinking devices even with double stitching in experimental and clinical studies has shown the impossibility of ensuring complete germitization of the bronchial stump and lung tissue. Air leakage occurs from the line of stapler seams [2], [3]. In this regard, some authors propose to additionally strengthen the seam line with various synthetic or biological materials [4].

Technologies are being sought for the creation of bio-artificial materials and organs, which are a system of materials of artificial or biological origin, including cells of tissue organs, or stimulating the regeneration of the corresponding cells in the implantation zone. Resorbable materials with high biocompatibility are most in demand [5], [6]. The implants being developed in surgery, from filaments, meshes to the most complex organ replacement devices, are aimed at creating biologically compatible materials for surgery. They can be conditionally divided into groups depending on the type of materials used: the body's own biological tissues, blood preparations and its fractions, animal tissue processing products, preparations based on natural artificial polymers.

To date, adhesive coatings have been widely used in surgical practice [7]. Their use is associated with the need to have special equipment in the operating room, and operating surgeons and staff must know the technique of mixing its components. The rapid polymerization of the prepared preparation and the occurrence of an adhesive process in the application area explain the restrained attitude of surgeons to the widespread introduction of such adhesive compositions in abdominal and thoracic surgery [8], [9], [10].

One of the directions of the search for funds for local aero- and hemostasis was the use of collagen and gelatin. Gelatin sponges are produced abroad under the names "Spongostan", "Gelfoam", etc. [11]. The experience of using such drugs has shown mixed effectiveness, especially in cases of blood clotting disorders, as well as the danger of renewed bleeding. In addition, biological films have an antigenic property, stimulate tissue reaction and lead to increased adhesion processes. With massive, profuse bleeding, it shifts and "washes away" from the wound surface. The drug does not adhere well to an uneven wound surface due to the rigidity of collagen fibers.

Thus, substances used in clinical practice for local strengthening of the damaged lung area are often characterized by insufficient effectiveness and unidirectional effects. Many of these coatings are made of biological materials (animal or plant origin), which causes their high antigenicity, as well as destruction during thermal sterilization.

In this regard, at the present time, it is necessary to continue the development of new biocompatible coatings and methods of their application. The ideological basis for this study was the possibility of developing a new method for ensuring the tightness of sutures in lung surgery, namely, reducing the risk of such manifestations as failure of aero- and hemostasis. It should be noted that the proposed method has no analogues, since the biological implant is not applied superficially on top of the damaged lung tissue, but is injected directly into the lung parenchyma in the area of damage. Accordingly, in order to be able to implement and confirm the effectiveness of the new technique, the entire range of preclinical studies, including experimental morphological studies, is required.

2. Materials and Methods

Taking into account the new method of using the implant to eliminate the failure of aero- and hemostasis, which had not been previously performed, the possibility of using the hemostatic drug Hemoben in the form of a gel for injection into lung tissue was initially studied. At this stage, a technique was developed for the formation of a gel substance from a sterile powder, the viscosity of which would allow the resulting substrate to be productively used for intraparenchymatous injection into lung tissue through an injection needle. This factor is important due to the fact that the resulting gel composition should be easily injected, while the time interval before the final stabilization of the gel should be sufficient to carry out a full-fledged piercing. The next stage of the study was the study of the biological reaction of tissues and the timing of gel resorption in lung tissue, depending on the method of administration and dosages - toxicological studies. This range of research is of fundamental importance for the new techniques created, while the main task is precisely to study the safety of intraparenchymatous use of a gel substance. In this aspect, the evaluation of the effectiveness and duration of aerostasis in ex vivo experiments served as the next stage, after which an in vivo experiment was also conducted to compare these parameters with other types of wound coatings for aerostasis.

Experimental studies were conducted in the laboratory laboratory of the State Institution "Republican Specialized Scientific and Practical Medical Center for Surgery named after Academician V.Vakhidov" in 2022-2023.

The experimental model included conducting experiments on sheep lung and mongrel white rats of both sexes weighing 250-280 g. Light sheep were obtained from a slaughterhouse (the average weight of sheep is 20-30 kg), while the absence of visible pathology and defects was a prerequisite. For In vivo experiments, the conditions of detention, intake of water and feed, animal care, as well as euthanasia were carried out in accordance with the requirements of the European Convention for the Protection of Vertebrates Used for Experimental and Other Scientific Purposes (Strasbourg, 1986).

The studies were carried out in two series of experiments (Table 1):

1) Ex vivo - to study the effectiveness of wound coatings to achieve aerostasis on isolated sheep lungs;
2) In vivo - to study the reaction of biological tissues and the features of lung wound healing in an experiment on laboratory rats.

Table 1. The number and type of studies in the experiment

Type of research	Biological glue	A new way	Total
Ex vivo	5	5	10
In vivo	40	40	80
Total:	45	45	90

Euthanasia was performed in accordance with the provisions of ISO 10993-2 under general anesthesia. The corpse of the experimental animal was subjected to section. During the experiment, a macroscopic assessment of changes in the abdominal cavity during autopsy of animals after euthanasia was analyzed.

To prepare morphological preparations, liver tissue, including the wound, was excised and fixed in a 10% solution of neutral formalin. After the fixation period expired, the biopsy was poured into paraffin. Paraffin blocks were made. Serial sections with a thickness of 3-4 microns were made. Histological preparations were stained with hematoxylin and eosin.

2.1. Ex vivo studies with lung wound modeling

The ex vivo model presents a study on the lung of a sheep (n = 10) obtained from a slaughterhouse (the average weight of sheep is 20-30 kg). Lungs without visible pathology and defects were selected for the experiment. To conduct research, the organocomplex - trachea, lungs were freed from the heart, pericardium, esophagus and larynx. The trachea was crossed 15 cm above the carina. The experiment used lungs that retained their original moisture and elasticity. The dry surface of the lung led to compaction of tissues, worse aeration of the alveoli and greater pressure on inspiration to straighten the lungs. In this regard, the experiments were carried out within 6 hours after the organ was isolated.

To perform the studies, the lungs were placed in a transparent container of appropriate size, into which a saline solution was poured at a temperature of 20-25 degrees. The breathing process of the isolated lung was carried out by connecting an artificial lung ventilation device (RO-6) through an intubation tube of a suitable diameter equipped with an inflated cuff to ensure tightness of the connection.

Before the start of the research, lung ventilation was performed to achieve complete expansion of the pulmonary parenchyma within 5-10 minutes. The volume of ventilation was up to 500 ml per inhalation, and the maximum pressure rise was up to 30 cm of water. In the experiment, lungs were used without violating the integrity of the visceral pleura.

2.2. In vivo research methodology

To evaluate the effectiveness of aerostasis, the reaction of tissues to the interstitial administration of Hemoben gel and the time of its resorption, studies were conducted on white mongrel male rats weighing 250-280 g. Under general anesthesia with sevoflurane vapors, the rat was placed on a manipulation table in a supine position with its limbs spread and fixed. After treatment of the injection site with a 70% alcohol solution, a puncture of the right pleural cavity was performed with damage to lung tissue, which was determined by air entering the syringe. Hemoben gel was injected through a needle in a 3.3% concentration in an amount of 0.1 ml. Then the needle was removed. The puncture area was treated with a betadine solution.

3. Results and Discussion

3.1. Ex vivo and In vivo studies

For ex vivo studies, fresh sheep lung-heart organ complexes obtained within no more than 6 hours after slaughter were used. In the control group, the effectiveness of aerostasis was assessed by surface application of biological glue. To obtain a gel from Hemoben powder, a series of experiments was initially carried out by dissolving it in various volumes of saline solution. When diluted in 10 ml of solution, the gel substance was subjected to rapid thickening, which did not allow it to be used for injection by means of an injection needle. A similar pattern was observed when diluted in 15, 20, 25 ml of saline solution, in these cases the gel became dense within 1.5-3 minutes. An adequate volume for diluting the powder was the proportion of 1.0 g of Hemoben per 30 ml of saline solution, the resulting concentration of 3.3% retained the properties of the gel composition for 5 to 7 minutes, which allowed both the gel to be injected through an injection needle and infiltrate the lung parenchyma along the entire perimeter of the tissue damage zone. Accordingly, in the experimental group, Hemoben powder was dissolved in saline solution to a concentration of 3.3% and within 1 minute gel was injected along the perimeter of the lung defect with a single injection of 0.3-0.5 ml (Figure 1, 2, 3). The number of injections depended on the area of damage and in our studies their number reached 8 with a total injection of up to 2.5-4 ml of gel solution.

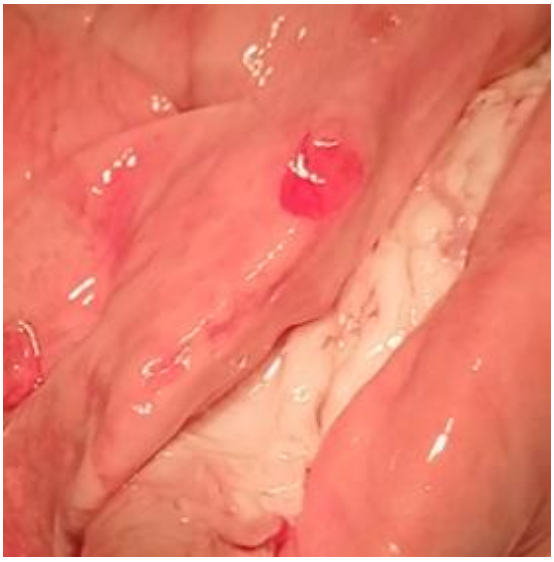

Figure 1. Formation of a lung tissue defect in an ex vivo experiment

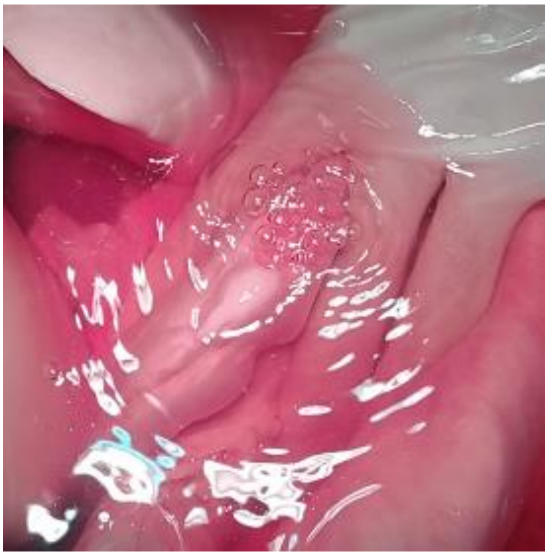

Figure 2. The appearance of air bubbles during artificial ventilation with immersion of the lung in a reservoir with saline solution

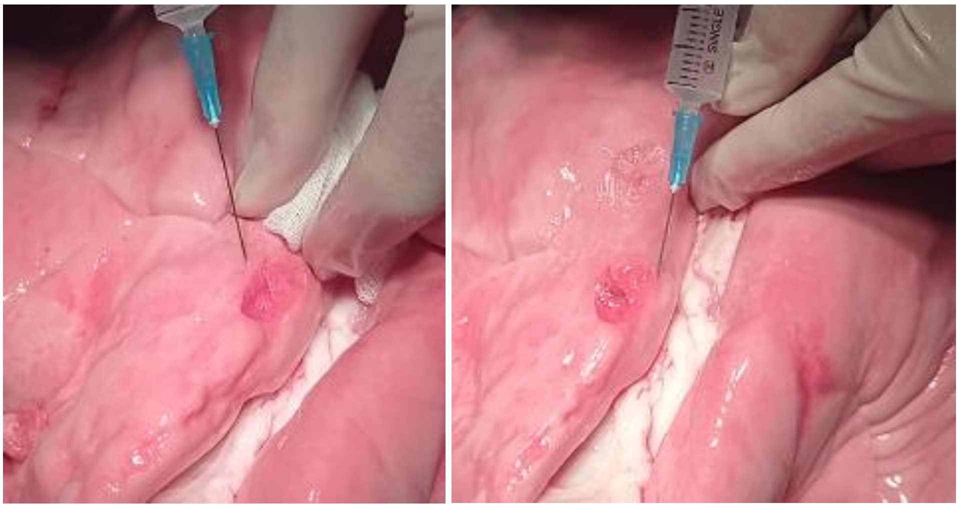

Figure 3. The process of puncturing a lung tissue defect with Hemoben gel using a syringe

Comparative studies of the effectiveness of aerostasis using surface application of biological glue and injection of Hemoben gel along the perimeter of the damaged lung tissue have established that during the application of glue, the surface of the lung must be thoroughly dried, after applying the glue, polymerization should be waited with the formation of a film on the wound surface of the lung for 3-5 minutes. To accelerate the polymerization process, it is possible to use a hot air insufflator, which accelerates the process of film formation on the surface of the lung wound. At the same time, injection of Hemoben gel does not require drying of the wound surface, pricking occurs quickly enough, while it can be observed how the gel leads to the formation of a homogeneous wound surface with the closure of the lumen of the alveoli and small bronchi. The whole process of aerostasis takes no more than 2 minutes.

In the near future, after the introduction or application of glue to the lung wound, aerostasis was achieved in all cases. In the first 5 minutes of observation, there was a high adhesive adhesion to the wound surface, which reached 150-200 kPa. However, there was a poor lung excursion at the glue fixation site, which led to contraction and deformation of the lung, the degree of which depended on the area of adhesive application. In the experimental group of animals, the aerostasis was complete in all cases. Unlike glue, the lung excursion process was not disrupted, since the wound surface was filled with an elastic coating in the form of a thick gel, preventing the entry of air and alveoli and small bronchioles.

20 minutes after the start of the experiment, aerostasis was preserved in the control series of experiments, however, a pattern of peeling of the edges of the film from the surface of the lung began to be observed, especially in places where the integrity of the visceral pleura was not violated. In the experimental series, the aerostasis was maintained under all ventilation modes.

45-60 minutes after the experiment, the edges of the adhesive plate continued to detach from the surface of the lung in the control group of animals. The degree of adhesion of the plate to the wound began to decrease and amounted to 60-80 kPa. Under normal ventilation conditions, the aerostasis was preserved, however, at peak values of air injection, small air bubbles began to appear through the detached edges of the adhesive plate. The deformation of the lungs persists and the excursion of the lungs is difficult. In the experimental group of animals, aerostasis was maintained under normal ventilation conditions (Figure 4).

Figure 4. Absence of air intake from the wound surface of the lung when artificial ventilation is connected with immersion of the lung in a reservoir with saline solution (45-60 minutes)

Thus, the injection of Hemoben gel in case of damage to lung tissue and air entry through the alveoli and small bronchi will achieve rapid and effective aerostasis, does not limit the excursion of the lung and has a long-lasting effect, which increases aerostasis as the gel swells.

To evaluate the effectiveness of biological glue, in vivo studies are required with a more distant period for evaluating the reaction of biological tissues to glue, since biological glue does not tend to biological degradation and cleavage. For this purpose, studies were conducted on white mongrel male rats weighing 250-280 g. Under general anesthesia with sevoflurane vapors, the rat was placed on a manipulation table in a supine position with its limbs spread and fixed. After treatment of the injection site with a 70% alcohol solution, a puncture of the right pleural cavity was performed with damage to lung tissue, which was determined by air entering the syringe. Hemoben gel was injected through a needle in a 3.3% concentration in an amount of 0.1 ml. Then the needle was removed. The puncture area was treated with a betadine solution.

1 hour after injection of Hemoben gel into lung tissue, a slight expansion of the drug distribution zone was noted without signs of infection or compression of the lung. The lungs are straightened, the airiness is preserved. During palpation, an elastic seal is determined in the area of gel injection.

1 day after the operation, the lungs are straightened, airy. The accumulation of fluid in the pleural cavities is not determined. The site of Hemoben gel injection is visually determined, which has clear boundaries and has slightly decreased in area (Figure 5). Tissue elasticity is determined by palpation.

Figure 5. 1 day after the introduction of Hemoben gel into the lung tissue

2 days after the introduction of Hemoben gel into the lung tissue along the posterolateral line. The place of gel injection is defined as a dark spot slightly rising above the surface of the lung with clear boundaries. In comparison with the area at the time of gel administration, it decreased by about 2-3 times. The lightness of the lung is preserved. There were no signs of infection and deformation of the pulmonary parenchyma.

On the 3rd day after the introduction of Hemoben gel into the lung tissue, the pleural cavities are free, the lungs are straightened, airy. Upon visual inspection, it is not possible to determine the place of administration of Hemoben gel. Control examinations were performed in 4 more animals during these observation periods. The drug is aimed at histological examination.

On the 4th day after the introduction of Hemoben gel into the lung tissue, the pleural cavities are free, the lungs are straightened. There were no signs of infection or adhesions.

When isolating and examining the lung tissue, the place of gel injection was not revealed. A similar pattern was observed 5 days after the introduction of Hemoben gel.

In the control group of animals, the glue was fixed to the surface of the lung wound only after its maximum drainage. Otherwise, the glue actually rolled down the visceral surface and adhesion was not observed. After fixing the adhesive to the wound surface, the formed glass plate remained without visible changes on the surface of the lung for 7 days after application. However, at the time of 14 days, the development of dense scarring of the lung with the chest wall with the formation of a foreign body was noted, and by 30 days, lung deforming and the process of rejection of the adhesive plate from the surface of the lung were observed.

Comparative studies conducted in experimental animals to study the effectiveness of aerostasis using highly adhesive wound coatings (medical glue) and a new method using interstitial administration of hemostatic agent Hemoben were performed at various times after surgery. It has been established that a highly adhesive coating – medical cyanacrylate glue allows to achieve effective aerostasis on the wound surface of the lungs, however, due to the fact that the glue practically does not undergo biological degradation, gradual rejection from the surface of the lung occurs and, when infection is attached, can become a source of abscess formation and rejection. Such a complication may not be so significant if it is applied to small lung surfaces. Another disadvantage of using glue is the need for careful drying of the wound surface, otherwise the glue simply drains and does not adhere to the wound surface. The third is the need to wait for several minutes when the glue is completely polymerized. If two lung surfaces are glued together, this simplifies the procedure, since the risk of glue sticking to the surgeon's hands or a napkin is eliminated. In the long term, after applying the glue, rejection occurs starting from 7 days and the glue can completely move away from the wound surface by 12 days. At the same time, a pronounced inflammatory reaction develops with the involvement of surrounding tissues and the formation of coarse scars and infiltrates.

A new method was used in the experimental group of animals – the introduction of Hemoben gel into the parenchyma of the damaged lung surface to a depth of 2-3 mm. In this case, the effect occurs quite quickly due to further swelling of the gel by absorbing water from the surrounding tissues. The method can also be applied on a wet or bleeding surface of a lung wound. There is no risk of sticking to the surgeon's fingers. The method can be repeated if necessary. The most important thing is that the gel, due to its elasticity, does not interfere with the excursion of the lungs and when the pressure in the airways increases, there is no violation of aerostasis. Hemobene in tissues biodegrades within 5-7 days without a pronounced inflammatory reaction by resorption.

3.2. The results of histological studies of lung biopsies

The animals, parts of the in vivo experiment were divided into two main groups, divided into 4 subgroups:

- Group I "A" – 1 hour after the introduction of Hemoben gel into the lung parenchyma;
- Group II "A" – 1 hour after applying glue to the wound surface;
- Group I "B" -1 day after gel administration;
- Group II "B" – 1 day after applying the glue;
- Group I "B" – 3 days after gel administration;
- Group II "B" – 3 days after applying the glue;
- Group I "G" – 5 days after gel administration;
- Group II "G" – 5 days after applying the glue.

In the study of histopreparations of the first "A" group, filling of the destroyed alveoli with Hemoben gel is noted, in some areas an increased concentration of gel is determined, with sections of the liquid fraction of the substance, edema of the interalveolar septa is noted from signs of reaction to acute damage, infiltration by shaped elements is absent. Both areas of atelectasis and areas of distelectasis are also determined. It should be noted that there are no hemorrhage sites in the studied group of drugs (Figure 6, 7).

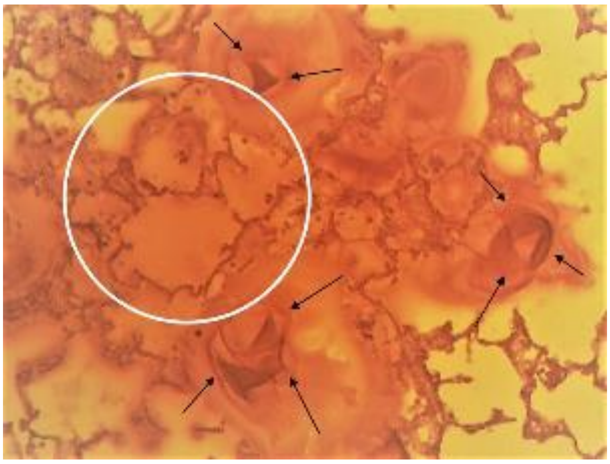

Figure 6. Histopreparation of rat lung, group I "A". Damaged alveoli filled with gel. With areas of gel concentration (↑), as well as areas containing a liquid fraction of the gel (highlighted in white). Stained with hematoxylin and eosin. Magnification×40.

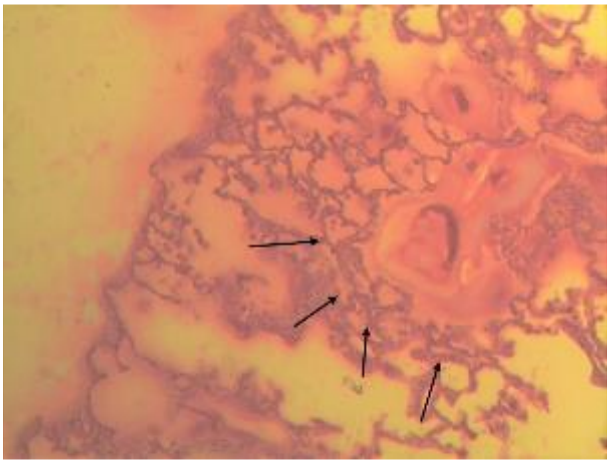

Figure 7. Histopreparation of the lung of a rat of group I "A". Against the background of gel-filled alveoli, there are areas with distelectases (↑) directly adjacent to the damaged alveoli. Stained with hematoxylin and eosin. Magnification×40.

In some preparations, the accumulation of gel is noted precisely in the areas of the defect of the partitions. It can be assumed that when the integrity of the alveolar septum is violated, the polarity of the wall changes at the sites of ruptures, with the appearance of a negative charge on the surface of pneumocytes, whereas the gel carries positively charged particles, which is why the gel accumulates at the sites of the defect of the septa.

In the study of the second group "A" with glue applied to the damaged surface of the lung, after one hour, the presence of edema is histologically noted, with uneven areas of atelectasis and hemorrhages, the presence of glue not only on the surface of the alveolar septa, but also in some areas it impregnates the walls, is determined in the thickness of the alveolar septa, followed by crystallization, in as a result, the elasticity of the partitions is lost, they become brittle and with a slight increase in pressure in the lumen of the alveoli, the walls collapse into small fragments. Also, in the first hours after an acute injury, with the application of glue to the surface of the wound, there is a fullness of blood vessels and hemorrhages in the thickness of the alveolar septa.

On the 1st day after administration of hemostatic gel Hemoben in group I "B", morphological manifestations of a typical edematous syndrome are observed in the damage zones. The interalveolar septa were unevenly thickened due to infiltration by lymphocytes, neutrophils and histiocytes. Polymorphocellular infiltrates with a predominance of granulocytes were adjacent to some vessels and small bronchi. The airiness of lung tissue over the entire area of the cut was uneven. Areas of complete infiltrative compaction alternated with incomplete atelectasis and normal alveoli. Areas of alveolar emphysema were extremely rare and without ruptures of the interalveolar septa.

The gel of homogeneous concentration (determined by the intensity of staining) is contained in the lumen of the alveoli, in the lumen of the bronchioles, as well as capillaries and venules. The edges of the wound surface, acute lung injury, thicken due to the appearance of fibrin and lymphohistiocytic infiltration.

In histopreparations of group II "B", diffuse thickening of the interalveolar septa is noted, not only due to glue impregnation and hemorrhages, but also as a result of polymorphocellular infiltration (lymphocytes, neutrophils, histiocytes). It should be noted that in this group (on the 3rd day after applying the glue), the beginning of the formation of micro-abscesses in the thickness of the infiltrated walls of the alveoli is noted. During these periods of the study, the processes of "melting" and malation of the interalveolar septa are noted.

Perivascular edema is detected around the blood vessels, and in some cases pronounced diffuse or focal infiltration by lymphocytes and macrophages with the formation of nodules and infiltrates. There is an increase in the thickness of the muscular plate of the bronchial mucosa and perivascular edema mainly around the venous vessels, in which there is stagnation of the shaped blood elements. Infiltration of peribronchial connective tissue, lymphocytes, macrophages increases, plasma cells appear.

Aggregates from erythrocytes, focal edema of the subendothelial space, and structural changes in endothelial cells appear in the expanded capillaries of the walls of the alveoli. In the I-th "B" group, on the 3rd day of the experiment after the introduction of Hemoben gel into the lungs, microscopically there was a progression of infiltration processes, which was manifested by thickening of the interalveolar septa, the appearance of macrophages, lymphocytes with an admixture of neutrophils, in the lumen of the alveoli. In some bronchi, the exfoliated epithelium and faintly distinguishable pink strands (fibrin filaments) were visualized. Peribronchial edema and peribronchial infiltration are noted. Fullness of bronchial vessels. A similar picture was visualized by blood vessels, perivascular edema adventitia, infiltration, a thickened layer of infiltration with fibrin directly at the edge of the lesion.

On the third day after applying glue to the lung wound, group II "B" notes that Part of the bronchi is in a dormant state, in others the lumen is expanded, the walls of the alveoli are thickened. The distances between the smooth muscle cells of the bronchial mucosa increase, signs of sclerosis are revealed in the peribronchial connective tissue around the bronchial blood vessels, perivascular edema and pronounced infiltration by lymphocytes and macrophages by the type of granulomatous formations are observed.

In the peribronchial connective tissue, bundles consisting of collagen fibers increase in size, and their number increases in the wall of the alveoli, especially around the blood capillaries. The shape and size of the alveoli vary. There is swelling of alveocytes and a moderate number of macrophages in the lumen of the alveoli. The bronchial wall is thickened.

On the fifth day after the introduction of the gel into the area of acute lung injury of group I "G" microscopically occurred, the infiltration zones are small, the number of cells of various types decreases. Perivascular edema is less significant. In the respiratory department, most of the alveoli retain the usual structural plan, sharply thickened walls of the alveoli, turning into dense connective tissue formations (Figure 8).

On the fifth day, a shell of connective-woven fibers is formed, the gel preparation is actually completely dissolved in liquid media, moderate hypertrophy in alveocytes is observed, focal infiltration of the alveolar wall (Figure 9). The histological picture in group II "G" preparations is characterized by the presence of signs of inflammation, formation of granulation tissue on the surface, perivascular and peribronchial infiltration and edema, areas of hemorrhage, desquamated epithelium in the bronchial lumen (Figure 10, 11).

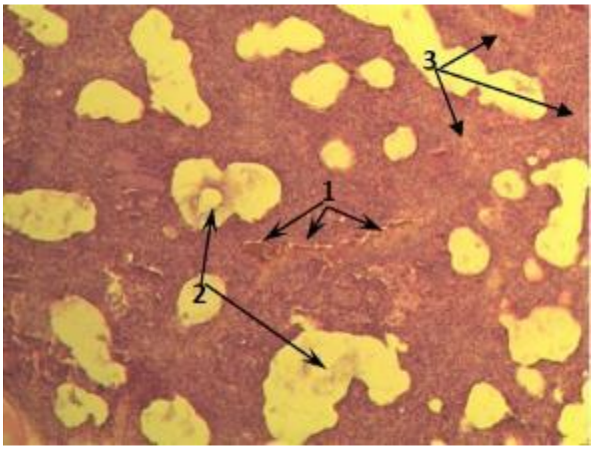

Figure 8. A full-blooded vessel (1), remnants of Hemobene gel in the lumen of the cavities of the alveoli with thickened partitions in which the sclerosing process begins (3). Rat lung 5 days after modeling acute damage, gr. I "G". Stained with hematoxylin and eosin. Magnification×40.

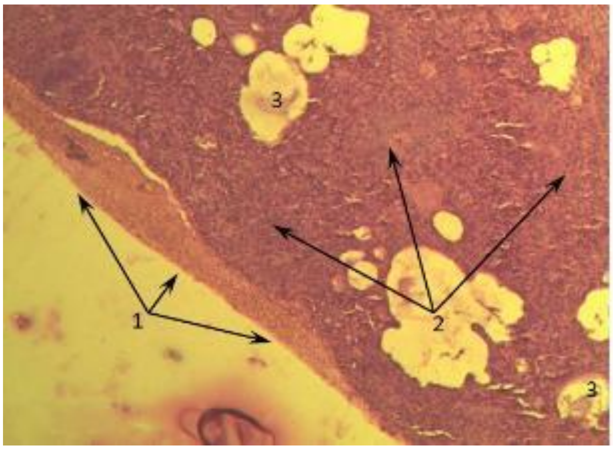

Figure 9. Formation of the connective tissue membrane on the wound surface (1), the beginning of the processes of fibrosis of thickened septa (2), gel residues in the cavities (3). Rat lung 5 days after modeling acute injury, gr. I "G". Stained with hematoxylin and eosin. Magnification×40.

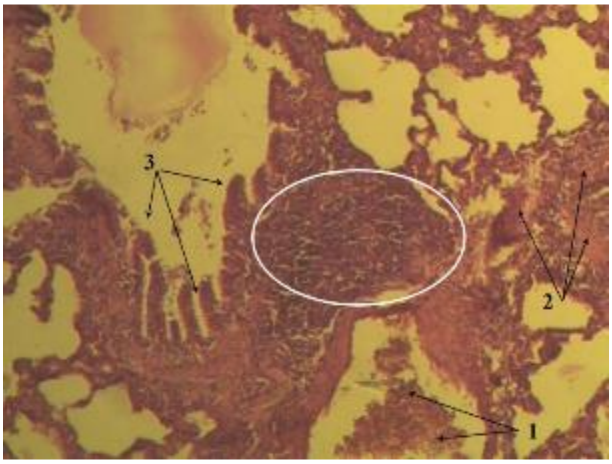

Figure 10. Peribronchial abscess (highlighted in white), blood clot in the lumen of a vessel with a hypertrophied wall (1), elastic and collagen fibers in the wall of the alveoli (2), hypertrophy of the bronchial mucosa (3). Lung micro-preparation of group II "G". GE. Magnification×40.

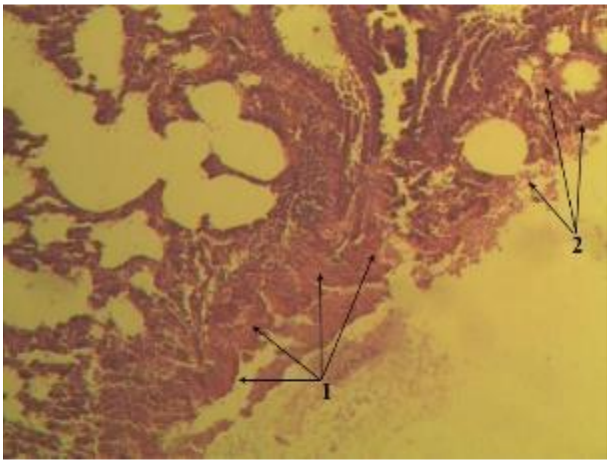

Figure 11. Granulation tissue (1) on the surface of the lesion on the 5th day of glue application with signs of inflammation and malarial processes (2). Lung micro-preparation of the II "G" group. GE. Magnification×40.

Vascular fullness and foci of emphysematous dilation and atelectasis of the lung tissue are noted. The shape and size of the alveoli varies, most of the alveoli wall is thickened, it contains elastic fibers, the number and size of which are different. Collagen and the basic substance are formed, with the development of granulation tissue at the site of the defect.

Histological examination of the group using glue confirmed the presence of pulmonary edema with uneven areas of atelectasis and hemorrhages. At the same time, in rats, signs of inflammation in the first phase of the wound process were more pronounced than in animals to which the gel was injected, and manifested themselves in the form of distelectases, and expanded areas were present along with areas of alveolar collapse.

There were large areas with the walls of the alveoli destroyed into small fragments. With signs of malarial infection at a later stage of healing. The walls of the alveoli thicken, and numerous shaped blood elements are present in their blood capillaries. Pericapillary and perivascular edema are detected. Extensive infiltration zones are found in the peribronchial connective tissue and the walls of the alveoli. The number of macrophages and alveolocytes is increased. Numerous abscesses appear in the septal septa.

The analysis of histological preparations showed that in the lungs of experimental animals, when Hemoben gel is administered, a complex of morphofunctional transformations occurs, affecting the air-conducting structures, the respiratory department, as well as the interstitial lung. Due to capillarostasis and infiltration, the interalveolar septa gradually thickened during the entire observation period, and the lumen of the alveoli narrowed with the formation of multiple atelectasis zones.

4. Conclusion

According to the results of experimental studies, it was found that the introduction of Hemoben gel into the parenchyma of the damaged lung surface provides a rapid aerostatic effect due to local primary compression on the introduction of the substrate and further swelling of the gel due to the absorption of water from surrounding tissues, while due to elasticity the implant does not interfere with lung excursion, and persistent aerostasis persists even with maximum pressure increase in the airways.

Morphological studies have established that the introduction of 3.3% Hemoben gel into the lung parenchyma is limited to the zone of alveoli and small bronchioles, thereby does not disrupt local pulmonary ventilation and does not cause a cellular reaction in the form of the formation of giant cells of a foreign body, while the implant is resorbed from 3-5 days without the development of a pronounced inflammatory tissue reaction.

Starting from 2 days after the introduction of the gel into the lung parenchyma, the formation of a surface film is noted directly in the area of damaged tissue, which is dominated by randomly arranged connective tissue fibers with leukocyte infiltration, while the elasticity of the walls of adjacent alveoli is not disturbed, as evidenced by the presence of both areas of preserved airiness and areas of increased airiness, i.e. emphysematous the alveoli. The formation of this surface film with intraparenchymal gel administration changes the elasticity of the lungs in the area of damage to 3.0 ± 0.3 g/cm^2 (normally 1.0 ± 0.2 g/cm^2), whereas when forming a film from biological glue, this indicator reaches 10.0 ± 0.8 g/cm2 (GOST 6806-73).

Toxicological studies have revealed that 3.3% Hemoben gel injected into the lung parenchyma at a dose of 1 ml per 1 g does not have an irritating and toxic effect, and according to spectrophotometric studies, it is completely eliminated from lung tissue within 7-10 days. Thus, the proposed technique is characterized by the effectiveness and safety of its use, and the results obtained make it possible to apply this method in clinical practice.

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