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Geprotsel, biocompatible implant: comparative estimation of its application results for providing airstasis and hemostasis in the lung surgery

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ABSTRACT

Introduction. In surgery, the prevention of postoperative complications has always been and remains relevant. One of the most important components that contribute to reducing the number of complications, in addition to effective drainage, restoration of muscle tone and adequate breathing, is reliable aerostasis and hemostasis. When performing operations on the lungs against the background of the presence in patients of factors affecting the incidence of failure in aero- and hemostasis (COPD, emphysema), the risk of developing these complications can reach 11.8% after lobectomy, after wedge-shaped resections up to 9.1% and after decortication up to 33.3%, which is 14.7% for all operations in general (violation of aerostasis - 5.9% and hemostasis - 8.8%.

Aim. The aim of study was to investigate the effectiveness of the proposed domestic implant "Geprocel" in the treatment and prevention of disorders of aero- and hemostasis during pulmonary operations.

Methods. The study included 69 patients operated in the department of surgery of the Lung and Mediastinum of the "Republican Specialized Scientific and Practical Medical Center of Surgery named after Academician V. Vakhidov" State Institution for the period from 2015 to June 2018. Hemostatic implant in the form of a fine powder was developed at RSRCS named after acad. V. Vakhidov". Geprotsel consists of the following components: the sodium salt of carboxymethyl cellulose, oxidized cellulose and nanocellulose associated with calcium ions (Patent No. IAP 20160273), in accordance with requirements of ISO 10993-1-2011.

Results. The use of the Heprotsel biological implant reduced the need for additional single lung tissue flashing to ensure adequate aero- and hemostasis from 38.2% to 11.4% and multiple reinforcement with sutures from 29.4% to 5.7% ($\chi 2 = 7.706$; Df = 2; P = 0.021).

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INTRODUCTION

The issues of postoperative complications still remain actual for the surgery. As it is known, the main predetermining moment in the prophylaxis of respiratory disorders and prevention of infectious complications at the thoracic surgeries is a quick and a complete spread of lung in the postoperative period. A reliable airstasis and hemostasis besides effective drainage, recovery of muscular tonus and adequate respiration are very important promoting factors [1-2].

The absence of persistent airstasis leads to: an incomplete spread of lung, a pneumothorax with a formation of residual cavities, the development of empyema and bronchial fistulas. Theses complications together with the infection become a main cause of progressing respiratory and cardiac failures leading to the lethal outcomes [3-4].

Unconvincing intraoperative air- and hemostasis and complications force sometimes to increase the scope of surgery; seal failure of the pleural cavity in the early postoperative period in some cases serves as indication for the rethoracotomy and the extension of surgery scope due to the remained lung lobes [5].

The problems connected with air- and hemostasis are one the most often occurred in the lung surgery. A variety of methods for solving them have been offered, but the majority of them are characterized by the prime cost of the used material. So, the development of domestic materials for their use at different surgical interventions, particularly in the lung surgery is an actual issue of health care. In our previous researches, we

proved the efficiency of proposed biodegradable polycomposite implant with oxidized cellulose – "Geprotsel" with air- and hemostatic aim at lung surgeries. Subject to the positive results of experimental investigations the next stage for the biological implant efficiency were clinical trials.

Polymer implants are increasingly used in medicine. Cellulose derivates are non-toxic, have good biocompatibility and provide tremendous opportunities for medical application. Oxidized cellulose is a very interesting material for biomedical research, due to its degradation in human body, hemostatic and antibacterial properties [6]. Collagen-based hemostatic agents have relatively low hemostatic activity in a wet environment, in systemic coagulopathies and thromboblastemia, infection risk. Collagen tends to lose the hemostatic capacity after autoclaving, which limits the application [7]. Oxidized cellulose is widely used in surgery for the treatment of skin lesions, long-term chronic wounds, liver, kidney resection, etc. Oxidized cellulose is insoluble in water, has a fibrous structure and high mechanical strength [8-10].

Therefore, the objective of the clinical study was to evaluate the effectiveness of Geprocel, a new domestic implant, in the treatment and prevention of disorders of aero- and hemostasis failures at lung surgeries.

MATERIAL AND METHODS

Hemostatic implant in the form of a fine powder was developed at RSRCS named after acad. V. Vakhidov". Geprotsel consists of the following components: the sodium salt of carboxymethyl cellulose, oxidized cellulose and nanocellulose associated with calcium ions (Patent No. IAP 20160273), in accordance with requirements of ISO 10993-1-2011.

A total of 69 patients operated at the department of lungs and mediastinum surgery of the Republican Specialized Research Centre of Surgery between 20015 and June, 2018 were included into this part of investigation.

All those patients had the risk development connected with air- and hemostasis both in intra-operative and in the postoperative periods. There were 35 patients in the main group (2017-2018) after resection phase or the lung parenchyma injury at the discharge from commissures. "Geprotsel" film has been applied over the defect of lung tissue for providing air- and hemostasis. 34 patients (2015-2017) were included into the group of comparison (comparable by age, sex, pathology, type of surgery and other objective criteria of contrastive analysis homogeneity).

Surgical procedure

The upper-midline laparotomy was performed under inhalation anesthesia (5% isoflurane). During the surgery, anesthesia was maintained by inhalation of 2- 2.5% isoflurane. The flat liver wounds of approximately 1 cm in diameter and 0.1 cm in depth were formed. Thus active parenchymal bleeding was stimulated (Figure 1). After suction, the hemostatic powder Heprocel was applied on the bleeding liver surface in Heprocel group. The control was treated only with standard gauze.

Ethical approval

The review board and ethics committee of RSCS named after acad. V.Vakhidov approved the study protocol and informed consents were taken from all the participants.

Statistical analysis

The obtained results were subjected to the statistical processing with the using the standard package of Microsoft Excel 2010 software by the method of variation statistics with the estimation of indexes' values (M±m).

RESULTS

The groups for comparison were representative by all main indices. In all cases during the intervention we noted the occurrence of injured part of pulmonary tissue parenchyma the form of which is depended on the resection type (organ lobe or its part) and also on the injury level during the discharge from commissures (echinococcectomy, decortications). Hemostasis in the area of pulmonary tissue injury (after acute resection at lobectomy or hardware wedge-shaped resection) was primary estimated after performing the main stage of surgery. In the comparison group we used standard methods for hemostasis achievement (tamponade, diathermo-coagulation, thermal effect).

At the absence of the effect we conducted a sewing of bleeding area. In the main group "Geprotsel" film was initially used for this aim – it was glue on the injured area with a fixation and a combined estimation of air- and hemostasis efficiency. Then we estimated hermeticity by conducting the test for airstasis. In the comparison group at the occurrence of air intake from organ parenchyma we also performed a fixation by additional sewing.

After performing the main stage of the surgery in 13 (37.1%) cases of the main group and in 12 (35,3%) cases of the comparison group there was noted non- intensive capillary bleeding from the injured part of pulmonary tissue. In the comparison group after using standard hemostatic procedures and estimation of airstasis efficiency in 13 (38.2%) cases we conducted the sewing of parenchyma defect and in 6 (17.6%) and in 4 (11.8%) patients the problem with air- and hemostasis was kept respectively. That is why they were undergone a recurrent sewing (10 – 29.4% cases). Hemorrhagic discharge through the drainage was determined in 3(8,8%) patients in the postoperative period and they were required additional hemostatic procedures. In other 2 (5.9%) patients we observed airstasis failure after surgery. We achieved positive clinical effect in the problem cases with both hemostasis and airstasis, but it influenced on the duration of pleural cavity drainage and then in 2 (5.9%) cases led to the development of the acute pleural empyema (Table 1).

Table 1. The frequency of intraoperative hemostasis and airstasis failures after anatomical or atypical resection of lung and additional sewing

Index	Main group		Comparison group	
	abs.	%	abs.	%
Intra-operative failures after resection	18	51.4%	17	50.0%
Hemostasis failure	13	37.1%	12	35.3%
Airstasis failure	5	14.3%	5	14.7%
Additional sutures on the lung tissue	4	11.4%	13	38.2%
Hemostasis failure	1	2.9%	6	17.6%
Airstasis failure	1	2.9%	4	11.8%
Total	2	5.7%	10	29.4%
Recurrent sewing of the lung tissue	2	5.7%	10	29.4%
Hemostasis failure (after surgery)	0	0.0%	3	8.8%
Airstasis failure (after surgery)	0	0.0%	2	5.9%
Total	0	0.0%	5	14.7%

Additional sutures on the lung tissue were required only in 4 (11.4%) cases in the main group after which they were kept only in 2 patients and then they were eliminated by recurrent fixation of sutures. There were no such complications in the postoperative period. It should be mentioned that after using the "Geprotsel" film we achieved an absolute air-and hemostasis in majority of cases and only in 4 (11.4%) patients we performed a recurrent sewing of the area with bleeding or affected airstasis. The problem with hemostasis or airstasis with the help of proposed biologic method, by our view, was connected with uneven surface of the injured area after lobectomy (2 cases), hardware sewing for wedge-shaped resection of peripheral benign tumor (neurofibroma - 1 case) and decortications (1 case). The applied film in those cases was not able to provide a complete hermiticity due to the tuberous surface of the defect – this area was additionally sewed and absolute hemostasis was achieved. The positive side of those cases is the fact that a biological material used for producing the "Geprotsel" film was used for getting another form of the implant – in the form of powder with analogous high adhesive properties providing an effective air- and hemostasis at application on small (up to 2-3 cm) uneven defect of pulmonary tissue parenchyma.

After singular application of fixing sutures on the pulmonary tissue the problems with airstasis were kept in 4 (11.8%) patients of the comparison group and only in1 (2.9%) patient of the main group. The problems with hemostasis were kept in 17.6% (6) and 2.9% (1) cases respectively (criterion χ^2=8.522; Df=3; P=0.047). In spite of the fact that additional fixing sutures had solved those problems, we noted airstasis failure in 2 (5.9%) cases and hemostasis failure in 3 (8.8%) patients of the comparison group in the postoperative period and in the whole it led to the development of these complications in 5 (14.7%) cases. The use of the "Geprotsel" film allowed to level completely the development risk of these complications in the postoperative period (criterion χ^2=9.107; Df=3; P=0.036). Subject to all intra- and postoperative failures of air- and hemostasis we reduced these complications indices in the main group from 44.1% (15 – comparison group; hemostasis - 9 (26.5%); airstasis - 6 (17.6%)) to 5.7% (2 – main group; 1 (2.9%) air-and hemostasis failures) (criterion χ^2=14.727; Df=3; P=0.003).

The necessity of achieving absolute air-and hemostasis was effected on the both duration of this stage and of surgery in the whole. The use of the "Geprotsel" film after surgery's main stage for leveling the complications development allowed to reduce the period for achieving air- and hemostasis from 32.8±2.5 minutes in the comparison group up to 12.5±1.2 minutes in the main group (T-criterion – 7.32; P<0.001). General duration of the surgery was reduced from 135.6±6.1 minutes т (comparison group) up to 107.2±4.7 minutes (T-criterion – 3.69; P<0.001) (Figure 1).

The complications development connected with air- and hemostasis failure in the postoperative period influenced on the duration of pleural cavity drainage. After 2-3 days the drain was removed in 97.1% (34 patients) in the main group and in 88.2% (31 patients) in the comparison group. After 4 days in 1 patient with airstasis failure of the main group the drain was also removed after its relief.

In 4 (11.8%) patients of the comparison group it was required a long term drainage with the drain removal after 5 days in 1 (2.9%) case, after 6-10 days in 2 (5.9%) cases and in 1 (2,9%) case the patient was discharged due to the development of acute empyema with further removal of the drain only at the achieving the complication regress after 33 days (Table 2).

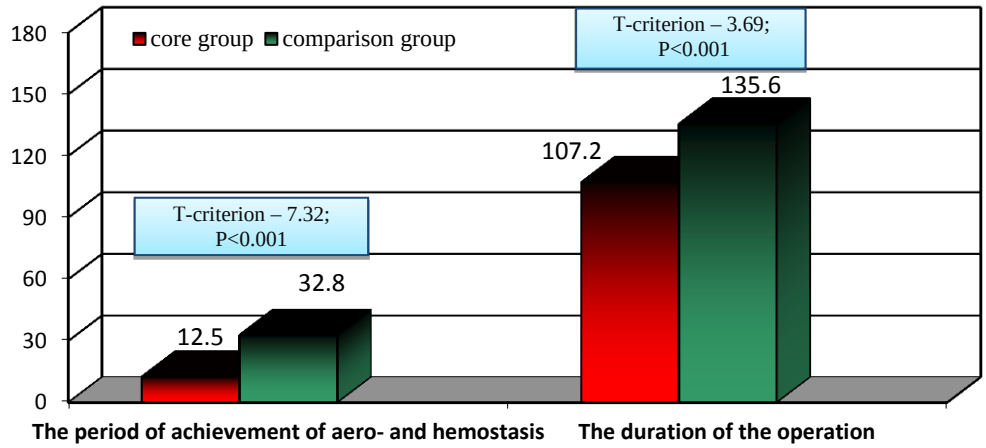

Figure 1. Average duration (minutes) of air- and hemostasis achieving period and the whole operative intervention

Table 2. The period of drain removal

Complication	Main group		Comparison group		Total	
	abs.	%	abs.	%	abs.	%
After 2 days	33	94.3%	29	85.3%	62	89.9%
After 3 days	1	2.9%	1	2.9%	2	2.9%
After 4-5 days	1	2.9%	1	2.9%	2	2.9%
After 6-10 days	0	0.0%	2	5.9%	2	2.9%
Discharged with drain	0	0.0%	1	2.9%	1	1.4%
Total	35	100%	34	100%	69	100%

At the mean data comparison of the pleural cavity drainage duration we noted a significant reduce of this index from 3.38±0.31 days in the comparison group up to 2.09±0.06 days in the main group (T-criterion – 4.09; P<0.001). The duration of the postoperative period on the background of intra-operative use of biological implant for air- and hemostasis reduced from 9.8±0.4 days up to 8.2±0.2 days (T-criterion – 3.58; P<0.01). The whole hospital stay was also significantly reduced from 12.1±0.4 days up to 10.7±0.2 days (T-criterion – 3.13; P<0.01). Summarizing the course of the postoperative period the following can be mentioned: intra-operative use of the domestic biological implant at the lung surgeries allowed to completely level the risk of air- and hemostasis failures in the postoperative period. In 3 (8.8%) cases of the comparison group we registered hemostasis failure and 2 (5.9%) cases of airstasis failure. The necessity in the additional fixing of sutures lines or defect zone of lung parenchyma after lobectomy in 1 case and in 1 case of decortications led to the significant deformation of adjacent organ tissue and in its turn it led to the development of the syndrome of the lung low volume - 5.9% (Table 3).

This complication was noted only in 1 (2.9%) case of the main group. In other 2 (5.9%) cases of the comparison group on the background of long term drainage with airstasis failure and in 1 patient with low volume of the lung the acute pleural empyema was developed which was solved conservatively. The general frequency of complications in both groups reduced from 14.7% (5 patients in the comparison group) up to 2.9% (1 patient in the main group) (significance of differences by χ^2: 8.737; Df=5; P=0.043). There rate of complications frequency affected on the hospital stay duration. In proper time, 7-9 days after the surgery 88.6% (31 patients) of the main group and 67.6% (23 patients) of the comparison group were discharged. A prolonged hospital stay was required to 4 (11.4%) and 11 (32.4%) patients respectively (Table 4). Hereby, the implementation of domestic biological implant into the clinical practice at performing lung surgeries allowed to completely level the risk of postoperative failures of air- and hemostasis development, to reduce the general frequency of complications from 14.7% up to 2.9% (χ^2= 8.737; P=0.043) and the necessity of prolonged hospital stay from 32.4% up to 11.4%.

Table 3. Complications frequency in the postoperative period

Complication	Main group		Comparison group	
	abs.	%	abs.	%
Hemostasis failure	0	0.0%	3	8.8%
Airstasis failure	0	0.0%	2	5.9%
Low volume of the lung	1	2.9%	2	5.9%
Acute pleural empyema	0	0.0%	2	5.9%
Total	1	2.9%	5	14.7%
Significance of differences (χ^2 criterion)	8.737; Df=5; P=0.043			

Table 6. The frequency of prolonged hospital stays in the postoperative period

Complication	Main group		Comparison group	
	abs.	%	abs.	%
Discharged in standard period (after 7-9 days)	31	88.6%	23	67.6%
Prolonged hospital stay	4	11.4%	11	32.4%
Total	35	100%	34	100%

DISCUSSION

In surgery, the prevention of postoperative complications has always been and remains relevant. In thoracic operations, it is known that the leading determining factor in the prevention of respiratory disorders and the prevention of infectious complications is the fastest and most complete smoothing of the lung in the postoperative period. One of the most important components contributing to this, in addition to effective drainage, restoration of muscle tone and adequate breathing, is reliable aerostasis and hemostasis.

In a study by Wain et al. [11] showed that a violation of the tightness of the lung suture intraoperatively occurs in 70% of cases. According to the European Society of Thoracic Surgeons (ESTS), the incidence of long-term aerostasis failure after marginal resection of the lung and lobectomy is 3.5% and 8.3%, respectively [12]. Long-term failure of aerostasis is always associated with the need for prolonged drainage of the pleural cavity, an increase in the duration of inpatient treatment, and an increased risk of developing infectious complications. The European Society of Thoracic Surgeons defines the failure of aerostasis as prolonged with air discharge for 5 days or more after surgery. Brunelli et al. [13, 14] in studies on the risk factors for leakage of the seam of the lung, they also determine long-term failure of aerostasis for a period of 7 days or more.

Modern approaches in the prevention of postoperative complications associated with lack of aero- and hemostasis in the literature are based on the use of new technologies to strengthen the bronchial suture. Nevertheless, the literature data on the effectiveness of the use of various patches are contradictory in many respects. Along with the use of traditional materials, there is an active search and development of materials based on bio-base.

The most promising means of biological hemostasis are fibrin polymers. Their main advantage is that they completely consist of biological blood components and, when applied to the damaged area, imitate the physiological mechanism of hemostasis. However, fibrin compositions are usually two-component and are

applied to tissues with the help of injection needles, nebulizers, catheters. Moreover, two-spray applicators are used, which creates certain difficulties in their use in thoracic surgery.

Long-term use of cellulose in the form of a dressing material is experiencing a new period of using its derivatives, which, depending on the type and degree of polymerization, can be widely used in surgery as an independent active principle as a bioinert non-toxic biodegradable implant with certain physical and chemical properties as well as medical properties.

CONCLUSION

The issues of prevention and treatment of air- and hemostasis failure still remain actual in the modern lung surgery. It is especially actual for those patients who have chronic obstructive lung disease, emphysematous injuries and other concomitant diseases of respiratory system. During the lung surgeries in patients with chronic obstructive lung disease, emphysema the risk of these complications development can reach up to 11.8% after lobectomy, after wedge-shaped resections – up to 9.1% and after decortications – up to 33.3%. In whole by all surgeries it makes up 14.7% (airstasis failure – 5.9% and hemostasis failure - 8,8%). The use of the "Geprotsel" biological implant allowed to reduce a necessity of the additional single sewing of the pulmonary tissue for providing air- and hemostasis from 38.2% up to 11.4% and multiple fixing by sutures from 29.4% up to 5.7% (χ^2= 7.706; Df=2; P=0.021).

DECLARATIONS

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Authors' contributions

All authors contributed equally to this work.

Competing interests

The authors declare that they have no competing interests.

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