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A proposed new method of hemostasis for erosive-hemorrhagic complications of the trachea and bronchi

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CASE REPORT
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ABSTRACT: **Ventilator-associated complications are the most frequent ones that prevent the recovery of intensive care patients. This study aimed to evaluate the effectiveness of the endoscopic treatment of acute hemorrhagic lesions of the tracheobronchial tree in patients with ventilator-associated tracheobronchitis. A total of 5 patients (22.4±3.3 mean age, 18 to 36 years) with prolonged mechanical ventilation (>48 hours) in the resuscitation and intensive care unit were monitored. The diagnosis of ventilator-associated tracheobronchitis was established on the basis of clinical signs, radiological and microbiological criteria. Fine-dispersed powder with hemostatic properties (HEMOBEN) was used as a hemostatic agent when applying the method. A morphometric study noted that ventilator-associated tracheobronchitis is accompanied by a pronounced lymphoid-neutrophilic infiltration of the tracheal and bronchial mucosa (signs of diffuse catarrhal inflammation of varying degrees and erosive deforming endobronchitis are verified), and in a complicated course with the presence of a purulent-inflammatory and erosive-hemorrhagic component with its vascularization and metaplastic changes and violations of the integrity of the epithelial lining also leads to a violation of the integrity of tissues due to destruction and necrosis. Hence, a method has been developed to stop bleeding in case of mucosal damage by local application of HEMOBEN, which allows us to quickly cover the bleeding surface with an adequate hemostatic effect.**

KEYWORDS: **Ventilator-associated tracheobronchitis, prolonged mechanical ventilation, clinic, endoscopic treatment, pathomorphological changes**

INTRODUCTION

To date, it has been proven that ventilator-associated infections of the upper and lower respiratory tract are one of the most common complications in patients on prolonged mechanical ventilation [1-6]. Most studies have shown that ventilator-associated tracheobronchitis (VAT) can be considered as an intermediate process leading to ventilator-associated pneumonia (VAP), which has a limited effect on overall mortality, but shows a significant association with increased patient costs, length of stay in the hospital, use of antibiotics and the duration of mechanical ventilation [3, 5, 7]. However, as noted by most researchers, there is no clear evidence to date, especially regarding the clinical course and methods of treatment of VAT [6, 8].

The most difficult problem in VAT is the problem associated with the development of erosive hemorrhagic syndrome with frequent recurrent bleeding [9, 10, 11]. Despite the fact that these bleedings are not fatal with some exceptions, in particular those associated with disseminated intravascular coagulation syndrome nevertheless, for patients with multiple organ failure, this syndrome is a frequent companion in this category of patients. On the other hand, systemic hemostatic therapy often leads to obstructive consequences associated with obturation with thrombotic masses and deforming endobronchitis [12, 13].

In this case, bronchoscopic manipulations themselves can cause contact bleeding. Local hemostasis on the mucosa of the trachea and bronchi almost completely limits the physicochemical effects [2, 7, 14]. In this regard, the search for new good means of local hemostasis is an acute problem. The aim of this study was to evaluate the effectiveness of the method of hemostasis for erosive-hemorrhagic complications of the tracheobronchial tree in patients with ventilator-associated tracheobronchitis.

MATERIALS AND METHODS

The method was used in 5 patients with erosive-hemorrhagic bleeding from the trachea and bronchi, who were on prolonged mechanical ventilation in the intensive care unit of the RSSPMC for surgery named after academician V.Vakhidov. The mean age of the patients was 22.4±3.3 (from 18 to 36) years.

The diagnosis of ventilator-associated tracheobronchitis was established on the basis of clinical signs (body temperature>38°C, leukocytosis>12000/ml, or leukopenia<4000/ml, new appearance of purulent endotracheal secretions or change in sputum pattern), radiological (absence of new or progressive infiltrates) and microbiological (polymorphonuclear lymphocytes with or without bacteria, moderate or severe growth of a potentially pathogenic microorganism) criteria.

HEMOBEN as a hemostatic agent, and a biodegradable polycomposite implant based on carboxymethylcellulose associated with calcium ions in interaction with hydroxycellulose and nanocellulose, was used. For this product, the Agency for the Development of the Pharmaceutical Industry, the State Center for Expertise and Standardization of Medicines, Medical Devices and Medical Equipment received registration certificate No. TV/M 00539/03/22 for "Biodegradable hemostatic implant (powder) – HEMOBEN" dated March 4, 2022. Physical and chemical characteristics of the finished product (HEMOBEN) was A) light gray, light brown fine powder with a particle size of 100 microns; B) at 20°C it dissolves in water with the appearance of flakes; C) in a ratio of up to 4% in an aqueous solution is a gel; D) pH in aqueous solution from 5-7; E) hydrolyzed in an alkaline environment, more stable in an acidic environment.

Biopsies taken by endoscopic biopsy were fixed in 10% neutral formalin solution. At the end of the fixation period, the biopsy was embedded in paraffin. Paraffin blocks were made. Serial sections were made with a thickness of 3-4 µm. Histological preparations were stained with hematoxylin and eosin. For light microscopy, tissue samples were fixed in 10% formalin solution in phosphate buffer. Light-optical micrographs were taken on an Axioscop 40 – ZEISS microscope, coupled with a digital camera. All microphotographs were processed and saved on a computer using Microsoft-"Windows XP-Professional" application programs.

Ethical approval

The review board and ethics committee of the State Institution "Republican Specialized Scientific and Practical Medical Center for Surgery named after academician V.Vakhidov" approved the study protocol and informed consents were taken from all the participants.

RESULTS

To solve the problems associated with erosive hemorrhagic VAT, we have proposed a method for endoscopic treatment of acute hemorrhagic lesions of the mucosa of the trachea and/or bronchi. The method includes a procedure for endoscopic sanitation of tracheobronchial tree with subsequent coverage of the area of damage by the method of application with a composition, characterized in that a therapeutic composition based on substances HEMOBEN, while HEMOBEN is used in the form of a powder, the composition is applied to the affected surface in an amount of 300 mg from a distance of 1 cm from the site of damage. The delivery device in the form of a separate and removable nebulization catheter, the proximal end of which is provided with a cuff for air injection, can be placed in the working channel of the bronchoscope.

The method is carried out as follows: the patient in the supine position is subjected to bronchoscopy in cases of erosive, ulcerative, hemorrhagic tracheobronchitis, in which a defect in the mucosa of the trachea and / or bronchi with signs of bleeding is detected; sanitation is carried out by irrigation with distilled water or saline. Having determined the required amount of the hemostatic drug HEMOBEN, a delivery device is inserted into the working channel of the bronchoscope, consisting of an injecting mechanism and a catheter, through which a therapeutic composition is applied to the affected surface in an amount of 100-300 mg from a distance of 1.0 cm from the injury site.

During endoscopic studies, it was noted that immediately after applying the powdered hemostatic drug HEMOBEN to the bleeding defect, a quick stop of bleeding occurred due to the formation of a uniform layer of the hemostatic drug 1-2 mm thick and a blood clot. Thus, the proposed method is easy to implement through the use of a delivery device for dosed administration and is highly effective in acute hemorrhagic injuries of the trachea and/or bronchi that occur when patients are on long-term mechanical ventilation.

Below is an endophoto of cases from clinical practice in Multiple organ failure (MOF) who were on prolonged invasive mechanical ventilation for more than 15 days and with developed erosive-hemorrhagic VAT (Figures 1-3). Histopathological examination of the bronchial mucosa after insufflation of HEMOBEN demonstrates a pronounced hemostatic effect due to the accumulation of blood cells, erythrocyte detritus (Figure 3A), while the resulting film coating does not cause pathological changes in the tracheal mucosa (Figure 3B).

Against the background of the use of HEMOBEN as a hemostatic agent for erosive-hemorrhagic lesions of the tracheal and bronchial mucosa, on the one hand, an instant hemostatic effect is achieved; on the other hand, there are no destructive changes in tissues leading to degenerative and deforming states of these structures.

It should be noted that an important component of the proposed method of hemostasis is the technique for achieving the technical result: the use of a delivery device consisting of an injecting mechanism and a catheter inserted into the channel of the endoscope or bronchoscope, the sequence of insufflations, the choice of the dose of the drug and the distance to the bleeding defect. The use of a delivery device facilitates controlled and efficient administration of the hemostatic agent and enhances the hemostatic effect.

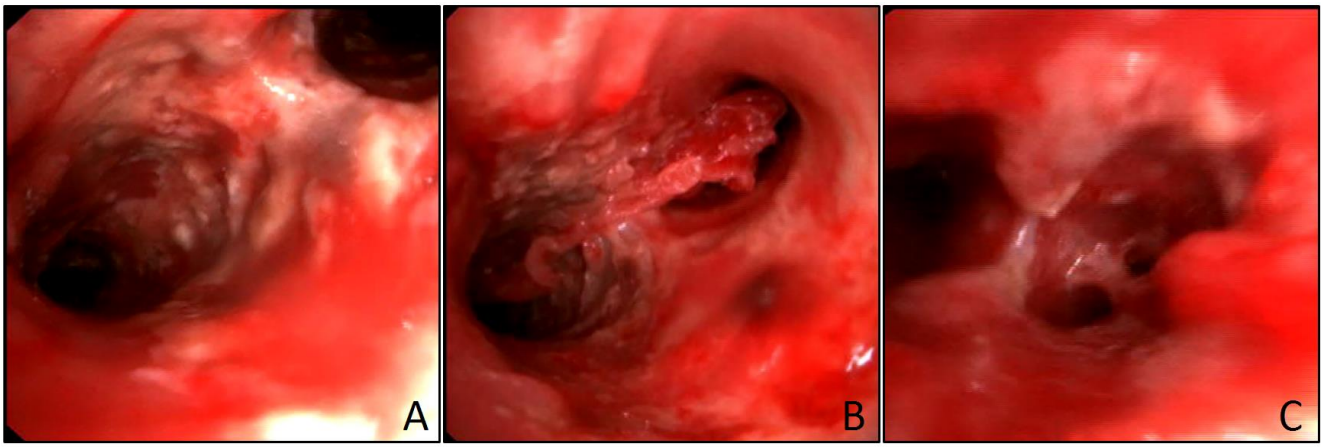

Figure 1. Bronchoscopy picture. An 18-year-old patient after radical correction of Tetralogy of Fallot: A) 16 days on prolonged invasive mechanical ventilation through tracheostomy. The mucosa of the trachea, bronchi on both sides is diffusely hyperemic, edematous, covered with confluent hemorrhagic erosions, loose, bleeds on contact; B) 17 days on prolonged invasive mechanical ventilation. Pronounced bilateral erosive-hemorrhagic endobronchitis. Fibrinous clots in the lumen of the bronchi from 2 sides, when trying to remove - contact bleeding; C) Erosive-hemorrhagic VAT. Active bleeding.

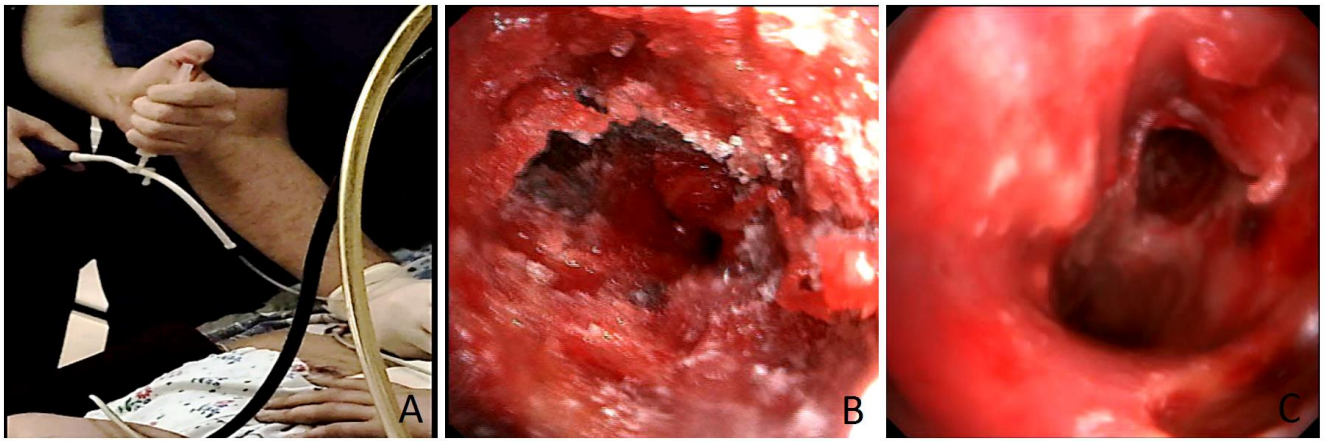

Figure 2. Bronchoscopy picture. An 18-year-old patient after radical correction of Tetralogy of Fallot: A) HEMOBEN delivery technique through a tracheostomy tube. B) Bronchoscopic view of the trachea and bronchi immediately after insufflation of the hemostatic HEMOBEN. Complete coverage of erosive bleeding sites. C) 12 hours after hemostasis. No signs of active bleeding. The stage of epithelization of the mucosa.

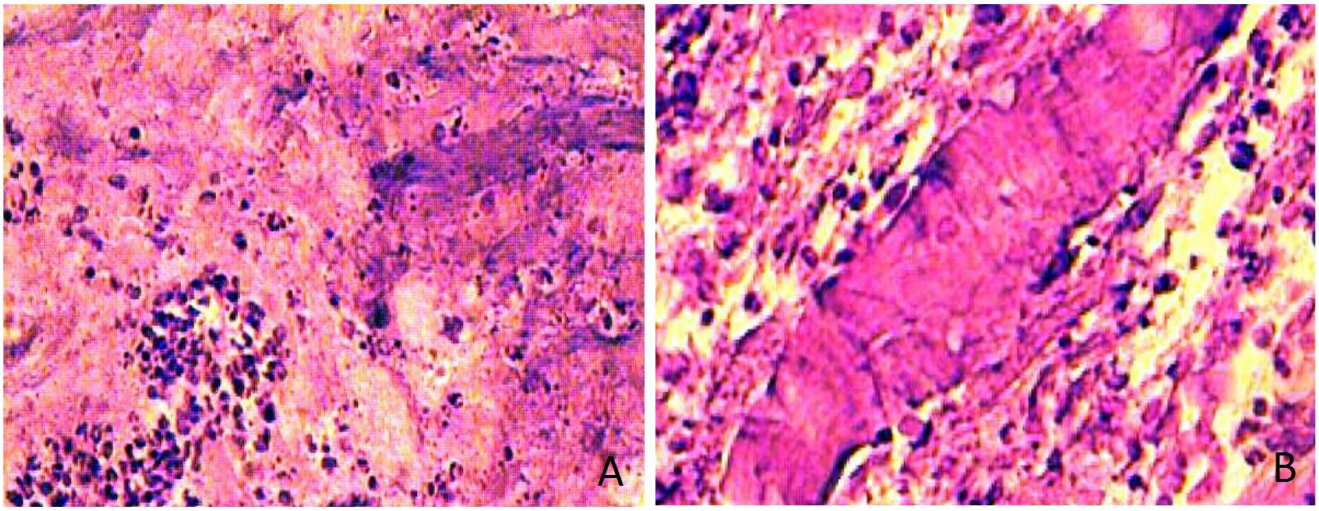

Figure 3. Hematoxylin and Eosin (H&E) Stain, original magnification 10×40: A) Accumulations of blood cells, erythrocyte detritus, remnants of a hemostatic film on the mucosal surface; B) Remains of a hemostatic film on the tissue surface

DISCUSSION

Restoration of reparative processes in tissues is characterized by the development of aseptic inflammation with moderate neutrophilic infiltration at the border of intact and damaged/or necrotic tissue. For example, exposure to blood plasma elements makes it possible to seal large areas of the lung tissue without causing deformation of the remaining part of the lung, its expansion in the postoperative period, and has a hemostatic effect [15-17].

With the development of erosive-hemorrhagic lesions of the mucous membranes of the tracheobronchial tree, the use of physical and chemical methods of hemostasis is associated with negative consequences (aseptic necrosis, perforations). Oxidized cellulose is an interesting material for medical applications due to its biodegradability and antibacterial properties [16, 17]. The results of a clinical study of the use of oxidized cellulose in volumetric lung resections revealed a reduction in the time to achieve hemostasis due to the high density of the implant surface and the presence of free carboxyl groups [16-19].

Spangler et al. [19] in their studies showed that the antibacterial effect of oxidized cellulose, due to the biodegradation of the molecule, is achieved by lowering the pH level on the wound surface. This mechanism indirectly affects gram-positive and gram-negative bacteria, thereby accelerating biochemical processes and, as a result, significantly reduces the time of early healing.

In the studies of Khudaybergenov et al. [20] proved that the composite-polymer biocompatible implant (Geprocel) in case of damage to the lung tissue was not inferior to other analogues "in terms of morphometric and adaptive processes in the lung tissue, demonstrating a pronounced adhesiveness to a wet surface, sufficient aero- and hemostatic effect, high mechanical strength.

One of the promising areas at the present stage of development of medicine is the creation of biological multi-purpose composite materials based on blood components [21]. In terms of tissue sealing, wound dressings made of resorbable materials with high biocompatibility have become the most popular [22-24].

Thus, the developed domestic technologies in ensuring the sealing of wound surfaces in their erosive-hemorrhagic lesions allow us to determine new priorities in the development of these complications in VAT.

CONCLUSIONS

A method has been developed to stop bleeding in case of mucosal damage by local application of HEMOBEN, which allows you to quickly cover the bleeding surface with an adequate hemostatic effect.

DECLARATIONS

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Authors' contribution
All authors contributed equally to this work.

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Competing interests
The authors declare that they have no competing interests.

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