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Original Article

Effect of Calcium Alginate Stopper on Persistent Air Leakage in the Lung of Rats

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ABSTRACT

Background and Aim: A number of adverse consequences of Persistent Air Leakage (PAL) account for the morbidity and mortality associated with this condition. Calcium Alginate is known as an effective and bioactive occlusion material, but the effect of Calcium Alginate stopper on air leakage has not yet been investigated *in vivo*. Here, we aim to examine the efficiency of Calcium Alginate stopper in the prevention of air leakage in the lung of rats. **Methods:** A total of 24 rats were included in the study. Comparable tissue injury was induced in all groups by performing right anterior thoracotomies. The control group received no treatment at the injury site, the standard surgery group underwent conventional suturing, and the experimental group was treated with a calcium alginate stopper. **Results:** At a positive airway pressure of 5 cmH_2O, air leakage was detected in the isolated lungs of the control group but was absent in both the standard surgery and study groups. The mean airway pressure required to induce air leakage was 6.1 ± 0.5 cmH_2O in the control group, 17.3 ± 3.1 cm H_2O in the standard surgery group, and 21.6 ± 3.5 cmH_2O in the study group, respectively. **Conclusion:** The calcium alginate stopper effectively prevented air leakage in rat lungs, with no significant difference observed when compared with the standard surgery group.

Keywords: Persistent air leakage, Calcium alginate stopper, Lung parenchymal injury, Bronchial occlusion, Experimental rat model, Thoracic surgery.

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INTRODUCTION

Persistent Air Leakage (PAL) is defined as air leakage more than 5-7 days after intercostal drainage, which is a serious postoperative complication that threatens patients' lives after thoracic surgery.[1-3] It is an important clinical problem associated with significant morbidity and mortality.[4] According to Ali *et al*., prolonged air leakage represents the second leading cause of extended hospital stays.[5] Major contributors to persistent air leakage include radiotherapy and/or chemotherapy, surgical treatment of infectious pulmonary lesions, and decortication of pleural thickening associated with diseases such as tuberculosis.[6,7]

To reduce or prevent these complications, thoracic surgeons have investigated the use of several adjunctive materials, such as fibrin sealants, synthetic polyethylene glycol-based hydrogel adhesives, coated adhesives, and stapling devices with supportive reinforcements.[5] But, many polymers such as cyanoacrylates are cytotoxic in their liquid form, which can lead to an undesirable immune response and tissue inflammation.[8]

Alginate is a natural polysaccharide hydrogel extracted from seaweed.[9] Alginate is a nontoxic liquid material dissolved in water and is biocompatible in both its liquid and solid forms. Alginate possesses a high degree of biocompatibility and mechanical stability compared with many existing materials. Many studies show that Calcium alginate stopper is a non-adhesive material with high mechanical strength in its reacted solid form, low viscosity in its unreacted liquid form.[9-11] Another promising property of alginate is that it can be absorbed in the graft body hardly leaving any harmful effect. These facts encouraged many researchers to use alginate as a potential material for many areas including occlusion therapy or cosmetic medicine. Optimization

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of Calcium alginate as an effective and bioactive occlusion material for endovascular occlusion has been described previously.[10,11]

Despite the positive effects of Calcium alginate for bioactive occlusion, the efficiency of calcium alginate stopper on air leakage is not fully revealed and, for many, their use as a treatment modality is still controversial. In present study, we experimentally investigated the efficiency of Calcium Alginate on stopping air leakage in the lung of rats.

MATERIALS AND METHODS

Calcium Alginate

Calcium alginate was obtained from Mannyon Pharmaceutical Company, DPR Korea and identified by comparison with the voucher specimen deposited at National Drug Certification Institute of Pyongyang, DPR Korea.

Animals and Groups

Male Wistar rats weighing 240±20 g were provided by Laboratory Animal Centre of Pyongyang University of Medical Sciences and adapted in a lab environment before experiments for a week. All rats were randomly chosen and feed and water were available to rats at any time during the experiment. The temperature was maintained at 21±3 °C and the humidity was 56%. The study was approved by the Ethics Committee for Animal Experimentation, Faculty of Basic Medicine, Pyongyang University of Medical Sciences.

A total of 24 rats were used in our study. No interventions were made on the tissue injury in control group, suturing was performed in standard surgery group, and calcium alginate stopper was applied to study group.

Surgical Procedure and Calcium Alginate administration

All rats were anesthetized with ketamine hydrochloride (60 mg/kg) in combination with xylazine hydrochloride (10 mg/kg). The animals were positioned supine, and the operative fields were prepared and disinfected under sterile conditions. Tracheostomy was performed through a cervical incision, followed by endotracheal intubation. The rats were randomly divided into three groups, each consisting of eight animals. The right thoracic area was shaved and sterilized, and a right-sided thoracotomy was performed via an anterolateral approach through the sixth intercostal space with the animals in the lateral position. A uniform injury approximately 5 mm long and 2 mm deep was created in the right lung parenchyma using a scalpel. In the control group, the lung injury was left untreated, and air leakage was monitored at 5-sec intervals using a compress. In the standard surgery group, the injury was closed with 6-0 polyglactin (Vicryl) sutures, and the time required for air leakage to cease was recorded. In the experimental group, intubation was performed with a 16G catheter, and 1 mL of a calcium alginate stopper was instilled into the right bronchus through the catheter. All animals were sacrificed on the fifth postoperative day.

Positive airway pressure and threshold of positive airway pressure for air leakage

To avoid further damage to the lungs, a midline sternotomy was performed. Following meticulous dissection of the tissues surrounding the trachea, the lungs were removed together with the trachea as a single unit. A cannula was introduced into the trachea and firmly secured to prevent air escape at the cannula-trachea interface.[6]

To measure positive airway pressure, a three-way stopcock was used, with one outlet connected to a pressure gauge and the other to a syringe. The isolated lungs were submerged in 0.9% saline solution. The pressure at which air bubbles were first observed emerging from the injured site was designated as the "threshold air leakage pressure."

Histopathological Analysis

Lung biopsy specimens were taken from the damaged regions and histopathological examination was performed. The sampled lung tissue was fixed with formalin solution (10%). Paraffin cross sections were obtained after routine follow-up and analysed after staining with haematoxylin-eosin.

Statistical Analysis of Data

Quantitative results are presented as the Mean ± Standard Error of the Mean (SEM). Differences in baseline characteristics among groups were analyzed using one-way Analysis of Variance (ANOVA) and Student's *t*-test for continuous variables. A p value of less than 0.01 was regarded as statistically significant. All statistical analyses were conducted using SPSS software version 16.0.

RESULTS

Evaluation of Air Leakage

As shown in Table 1, all rats in the control group exhibited air leakage at an airway pressure of 5 cmH_2O, while no leakage occurred in either the standard surgery group or the study group at this pressure. The airway pressure needed to initiate air leakage was significantly greater in both the standard surgery and study groups than in the control group ($p < 0.01$). The mean threshold pressures were 6.1 ± 0.5 cmH_2O for the control group, 17.3 ± 3.1 cmH_2O for the standard surgery group, and 21.6 ± 3.5 cmH_2O for the study group. In contrast, there was no significant difference in threshold air leakage pressure between the standard surgery and study groups.

Evaluation of Histopathological Finding

Figure 1 demonstrates the effect of the calcium alginate stopper on air leakage. Clusters of hemolyzed clot were observed in areas of

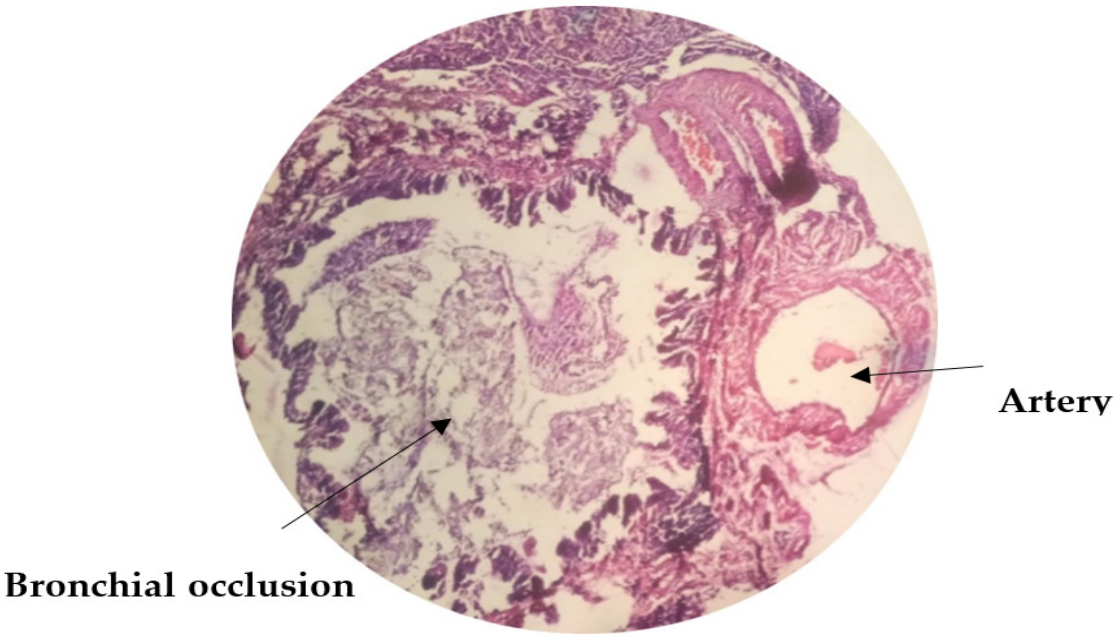

Figure 1: Bronchial occlusion by calcium alginate (H-E, magnification ×200).

Table 1: Air leakage in each group.

Groups	Air leakage at 5 cm H_2O pressure	Threshold air leakage pressure (cm H_2O)
Control group	+	6.1± 0.5
Standard surgery group	-	17.3± 3.1*
Study group	-	21.6±3.5*

+: positive, -: negative, Each value represents the Mean ± SEM of 8 rats per group. *p< 0.01 as compared with control group.

the rat lung treated with calcium alginate, suggesting obstruction of the bronchus associated with the fistula. Furthermore, newly formed fibrin plugs induced by calcium alginate were identified in the upper bronchial segments adjacent to the pulmonary fistula.

DISCUSSION

Persistent air leakage is defined as air leakage more than 5-7 days after intercostal drainage, which are common with thoracic surgery.[2] Despite the application of numerous surgical approaches and biological materials, the rate of air leakage from lung parenchyma remains high. Surgical suturing or the use of stapling devices is the conventional method for preventing air leaks. Alternative strategies include the use of fibrin sealants, synthetic polyethylene glycol-based hydrogel adhesives, Tachocomb, coated sealants, and stents of various dimensions.[3,5,8,12-14]

Alginate has been employed in both food and medical products since the 1950s and is regarded as a highly versatile and biocompatible hydrogel.[9,10] Owing to its non-adhesive, non-toxic, and biologically active properties, alginate may represent a suitable material for the management of Persistent Air Leaks (PAL). Accordingly, we proposed that the use of calcium alginate for PAL occlusion, given its ability to promote cell growth and tissue repair, would yield better outcomes than conventional therapeutic methods.

In the present study, all rats in the control group exhibited air leakage at a positive airway pressure of 5 cmH_2O, whereas no leakage was observed in either the standard surgery group or the study group at this level. The airway pressure needed to initiate air leakage was significantly higher in both the standard surgery and study groups compared with the control group ($p < 0.01$). However, there was no statistically significant difference in threshold air leakage pressure between the standard surgery and study groups. Histopathological analysis demonstrated the presence of newly formed fibrin plugs induced by calcium alginate in the proximal bronchial areas adjacent to the pulmonary fistula.

As a conclusion, calcium alginate can prevent air leakage in the lung of rats effectively and we suggest that this material may be used for the treatment of PAL as a newer stopper. Further experimental and clinical studies are needed to investigate the effect of Calcium Alginate in the lung.

Careful assessment is essential before clinical application, considering the difference between experimental animal models and human patients in wound healing; nevertheless, we think that bronchoscopic occlusion with calcium alginate is an effective therapy for PAL.

CONCLUSION

Calcium alginate stopper effectively prevents air leakage in rat lung parenchyma by significantly increasing the threshold airway pressure for leakage. Its efficacy is comparable to standard surgical

suturing. Histopathological findings support bronchial occlusion and fibrin plug formation at the injury site. Calcium alginate may represent a promising alternative for managing persistent air leakage, warranting further clinical evaluation.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

PAL: Persistent Air Leakage; **cmH_2O:** Centimeters of Water.

REFERENCES

1. How CH, Hsu HH, Chen JS. Chemical pleurodesis for spontaneous pneumothorax. J Formos Med Assoc. 2013;112(12):749-55.
2. Anile M. Treatment of persistent air leakage with endobronchial one-way valves. J Thorac Cardiovasc Surg. 2006;132(3):711-2.
3. Santana-Rodríguez N, Llontop P, Clavo B, Camacho R, Quintana A, Fiuza MD, *et al.* Autologous platelet-poor plasma decreases the bronchial stump necrosis in rat. J Surg Res. 2013;183(1):68-74.
4. Travaline JM, McKenna RJ Jr, Byrne J, *et al.* Endobronchial valve treatment for prolonged air leaks of the lung: a case series. Ann Thorac Surg. 2011;91(1):270-3.
5. Kılıçgün A, Sarıkaş NG, Korkmaz T, Saydam Ö, Boran Ç, Boztaş G. Effect of Ankaferd Blood Stopper on air leakage in the lung and prevention of bleeding: an experimental study. J Cardiothorac Surg. 2011;6:20.
6. Sanli A, Aktas S, Dundar M, *et al.* Glutamine administration enhances the healing of lung parenchymal injuries and reduces air leakage in rats. Tohoku J Exp Med. 2006;210:239-245.
7. Jantra N, Phattharayuttawat S, McMillan K. Computed tomographic features of pneumothorax secondary to a bronchopleural fistula in two dogs. J Am Anim Hosp Assoc. 2014;50(4):284-290.
8. Ono K, Oka M, Ishihara M, *et al.* Experimental evaluation of photocrosslinkable chitosan as a biologic adhesive with surgical applications. Surgery. 2001;130(5):844-850.
9. Iwata Y, Nakamura M, Nakai S, *et al.* Cholesterol-lowering effect of calcium alginate in rats. Biol Pharm Bull. 2016;39(1):62-67.
10. Becker TA, Brinjikji W, Lanzino G, *et al.* Calcium alginate gel as a biocompatible material for endovascular arteriovenous malformation embolization: six-month results in an animal model. Neurosurgery. 2005;56(4):793-801.
11. Becker TA, Siddique M, Thielen KR, *et al. In vivo* assessment of calcium alginate gel for endovascular embolization of a cerebral arteriovenous malformation model using the swine rete mirabile. Neurosurgery. 2002;51(2):453-458.
12. Petrella F, Carofino BC, DiGemma N, *et al.* Stem cell transplantation effectively occludes bronchopleural fistula in an animal model. Ann Thorac Surg. 2014;97(2):480-483.
13. Tao H, Seder CW, Reza N, *et al.* Bronchoscopic treatment of postpneumonectomy bronchopleural fistula with a collagen screw plug. J Thorac Cardiovasc Surg. 2006;132(1):99-104.
14. Shaikhrezai K, Sharif K, Mohyuddin A, *et al.* Bronchopleural fistula: an update for intensivists. J Crit Care. 2010;25(1):47-55.

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