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Rabbit model of tracheal stenosis induced by prolonged endotracheal intubation using a segmented tube

Hyoung Shin Lee [a,b,1], Sung Won Kim [a,b,1], Chulho Oak [b,c,*], Yeh-Chan Ahn [b,d], Hyun Wook Kang [b,d], Bong Kwon Chun [e], Kang Dae Lee [a]

[a] Department of Otolaryngology-Head and Neck Surgery, Kosin University College of Medicine, Busan, Korea
[b] Innovative Biomedical Technology Research Center, College of Medicine, Kosin University, Busan, Korea
[c] Department of Internal Medicine, Kosin University College of Medicine, Busan, Korea
[d] Department of Biomedical Engineering and Center for Marine-Integrated Biomedical Technology, Pukyong National University, Busan, South Korea
[e] Department of Pathology, Kosin University College of Medicine, Busan, Korea

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ABSTRACT

Objective: Animal model of tracheal stenosis based on pathophysiology of prolonged endotracheal intubation has been rarely reported. We sought to verify the feasibility of inducing an animal model of tracheal stenosis by segmented endotracheal tube insertion in the New Zealand white rabbit model.
Methods: Tracheal stenosis was induced by inserting a segmented endotracheal tube of 1.5 cm length which was wrapped with a commercialized absorbable hemostat in 15 New Zealand white rabbits, while sham surgery controls ($n = 3$) underwent tracheotomy and direct closure of tracheal exposure. The tube was removed transorally, 1 week after tube insertion. All rabbits were evaluated endoscopically at 1 week, 2 weeks and 3 weeks after the tube insertion. The rabbits were sacrificed 3 weeks after the surgery, and the excised tissue of trachea was processed along with the procedure of standard hematoxylin eosin staining and observed under a microscope.
Results: Tracheal stenosis was induced in all rabbits (range 32–84% stenosis) with no death of rabbits during the study. The histological features of tracheal stenosis demonstrated thickening and fibrosis of lamina propria and submucosa with relatively intact cartilage framework.
Conclusions: We developed a rabbit model of tracheal stenosis induced by endotracheal intubation using a segmented tracheal tube. Since the model is based on the physiologic condition of prolonged endotracheal intubation, it may be used in variable studies related to tracheal stenosis.

1. Introduction

Tracheal stenosis induced by prolonged endotracheal intubation may compromise the airway in variable extents and may result in life threatening conditions. Although conservative management such as repeated dilatation, local or systemic steroid, laser ablation, stent and T-tubes may be successful in highly selective cases [1], aggressive surgical treatment such as the resection of the trachea with end-to-end anastomosis may still be required [2]. Management of patients requiring such aggressive surgery may have high risk of complications and still have possible treatment failure [2,3]. Thus, the optimal management of patients with tracheal stenosis induced by prolonged intubation may require thorough understandings of the pathophysiology of the process, which may lead to development of diagnostic tool for early detection, appropriate methods of treatment and prevention. Therefore, a reliable animal model of tracheal stenosis analogous to the clinical scenario may be required.

Variable methods have been developed to induce tracheal stenosis in animal models. While prolonged endotracheal intubation seems to be the ideal method of inducing the stenosis, it has been considered to be technically difficult with high mortality rate [4]. Recently, Kumar et al. [5] reported an animal model for tracheal stenosis using prolonged intubation. However, the technique requires 2–4 h of anesthesia and manual irritation to tracheal mucosa by tube rotation or up and down movement. As alternative methods, tracheal stenosis was induced by mechanical irritation such as radiofrequency [6], laser [7], electrocautery [8],

* Corresponding author at: Department of Internal Medicine, Kosin University Gospel Hospital Am-Nam Dong 34, Seo-Gu, Busan, 602-702, South Korea. Tel.: +82 51 990 6136; fax: +82 51 245 8539.
E-mail address: oaks70@hanmail.net (C. Oak).
[1] Contributed equally to this work.

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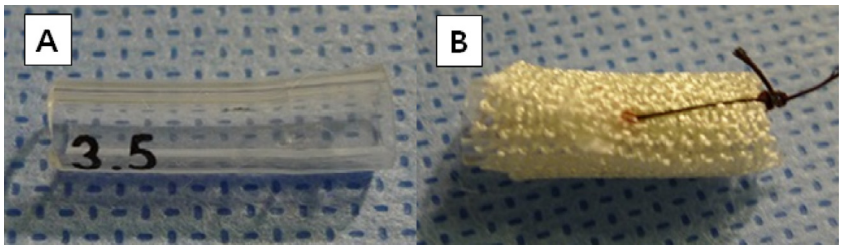

Fig. 1. Segmented tube used for intubation. (A) Segmented endotracheal tube (1.5 cm). (B) Tube is wrapped with Surgicel.

tracheal stents [9] and brushing [10]. On the other hand, variable chemical cauterants such as silver nitrate [11], hydrochloric acid [11] and ethanol [8] have been used with or without mechanical irritation. However, the ranges of stenosis in these studies are still unpredictable and the methods may be complicated or be related to high mortalities. Most of all, these methods of mechanical, thermal or chemical injury may be discrepant to the clinical cause and physiologic conditions of tracheal stenosis in patients with prolonged endotracheal intubation. In this regard, we sought to develop an animal model of tracheal stenosis induced by a segmented endotracheal tube, which may induce similar physiological environment of prolonged endotracheal intubation.

2. Methods

2.1. Study design

All animal procedures were conducted in accordance with the guidelines published in the Guide for the Care and Use of Laboratory Animals (DHEW publication NIH 85–23, revised 2010, Office of Science and Health Reports, DRR/NIH, Bethesda, MD, USA). The study protocol was approved by the Committee on Animal Research of the College of Medicine at Kosin University. Eighteen male New Zealand white rabbits (Taesung Laboratory Animal Science, Busan, Korea) weighing 3.0–3.7 kg were used for the experiment. Three rabbits were allotted for sham surgery to evaluate the impact of tracheostomy. Segmented tracheal tube was intubated to the other 15 rabbits.

2.2. Surgical procedure to induce tracheal stenosis

The rabbits were each intramuscularly anesthetized with 35 mg/kg ketamine and 5 mg/kg xylazine. Each rabbit was placed in the supine position on a heated operating table, and body temperature was maintained at 39 °C by monitoring rectal temperature. Heart rate and respiratory rate were also monitored. To enhance analgesia, 2 ml of 1% lidocaine hydrochloride was injected into the subcutaneous area of the anterior neck. The anterior neck of each rabbit was shaved and disinfected. A midline vertical skin incision was conducted at the anterior neck leading to exposure of the trachea and larynx. Incision via the avascular plane between the strap muscles caused minimal bleeding. After exposure of the anterior wall of trachea, a transverse incision was made between the fifth and sixth tracheal rings at the length of two-thirds of the circumference. Tracheal incision site was closed with a single suture of 4.0 Vicryl to make sham models ($n = 3$).

Initially a segmented pediatric intubation tube (3.5 mm inner diameter, Covidien, MA, USA) at the length of 1.5 cm was wrapped with a commercialized absorbable hemostat namely, Surgicel (Ethicon, Cincinnati, Ohio, USA) (Fig. 1) and was squeezed into the trachea via the tracheostomy site (Fig. 2). The amount of Surgicel was decided so that the tube could fill in the tracheal lumen without any space with adequate pressure to the tracheal mucosa. The tracheal rings were placed into anatomical position and the incision was closed with a single 4.0 silk interrupted suture. The strap muscles and skin tissues were also closed with same technique.

2.3. Evaluation of tracheal stenosis

At 1 week after tube insertion, the tubes were removed transorally under the bronchoscopic view using microforceps (Fig. 3). All rabbits were evaluated endoscopically under the same anesthetic condition to evaluate the degree of tracheal stenosis at 1 week, 2 weeks and 3 weeks after the tube insertion. Three weeks after the surgery, the rabbits were sacrificed and the excised tissue of trachea was processed along with the procedure of standard hematoxylin eosin staining and observed under a microscope. Three sham models were evaluated endoscopically 1–3 week after surgery to evaluate the impact of tracheostomy. Trachea of the sham model was also histologically reviewed 3 weeks after surgery.

The degree of stenosis was measured using photographs of the bronchoscopic view taken at each time points using an index based on area. It was defined as $(1 - s/S) \times 100$ (s indicating the intraluminal area of the trachea after tube removal, and S indicating the relative intraluminal area before tube insertion at the level of sixth tracheal ring). The parameters were measured digitally with Adobe Photoshop CS3 Software (Adobe System Inc., San Jose, CA), dependent upon pixel size.

3. Results

Surgical procedure of tube insertion via the tracheostomy site was quite simple without significant bleeding. Surgicel was wrapped one to three times (median: two times) around the tube, according to the size of the tracheal lumen so that the tube could be tightly fixed within the trachea. The whole procedure took

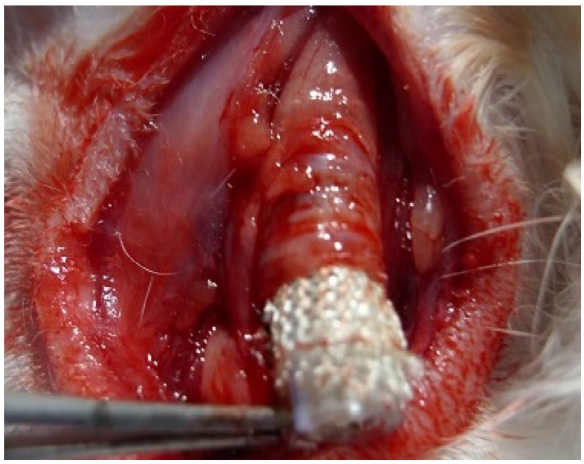

Fig. 2. Insertion of segmented tube via tracheostomy site. Segmented tube is squeezed and inserted into the trachea.