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ORIGINAL ARTICLE

The lowest effective intracuff pressure of the esophagus obstruction tube to prevent reflux of gastric contents: a study on rabbits

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Abstract

Purpose To determine the lowest effective cuff pressure of the esophageal obstruction tube to prevent reflux of gastric contents in rabbits.

Methods Twenty-two New Zealand white rabbits (2.0–2.5 kg) were anesthetized. An esophageal obstruction tube, an esophageal observation tube, and a gastric tube were inserted into the esophagus and stomach, respectively. Normal saline containing methylene blue was injected into the stomach for an animal model of gastric contents reflux. Possible saline reflux was observed through the esophageal observation tube. It was considered "regurgitation" when the saline flowed out, and "no regurgitation" when the saline did not. When a "regurgitation" result was obtained in a particular rabbit, the intracuff pressure was increased by 10 cm H_2O in the following rabbit and vice versa. The trial was not terminated until six crossover points were observed from "no regurgitation" to "regurgitation." A probit regression model was used to analyze the effective intracuff pressure of the esophagus obstruction tube after 50 % and 95 % of the rabbits showed no reflux.

Results The lowest effective intracuff pressure to prevent reflux of gastric contents in 50 % of rabbits from the Dixon up-down method was 61.67 ± 8.16 cm H_2O. The intracuff pressures at which there was 50 % and 95 % probability of lack of gastric contents reflux from a probit regression model were 61.95 and 74.39 cm H_2O, respectively.

Conclusion The insertion of an esophageal obstruction tube before endotracheal intubation can be an acceptable method for preventing the reflux of gastric contents in most rabbits under light anesthesia.

Keywords Intracuff pressure · Reflux · Esophagus · General anesthesia

Introduction

Reflux and aspiration of gastric contents can cause serious complications, including pulmonary obstruction, chemical pneumonitis, and secondary infection, and can even be life threatening [1, 2]. Aspiration of the gastric contents can occur in patients under pharmacosedation and general anesthesia. The induction of anesthesia in patients who are at risk for pulmonary aspiration is challenging, and aspiration and reflux during the induction of anesthesia have long been a concern for anesthetists. In clinical practice, rapid sequence induction and endotracheal intubation are the "gold standard" technique for preventing aspiration of gastric contents during the induction of anesthesia in non-fasted patients [3, 4].

However, tracheal intubation after rapid sequence induction of anesthesia is indicated only in patients at risk for aspiration of gastric contents without suspicion of

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difficult intubation [5]. In patients with a suspicion of difficult intubation, other techniques may be necessary to induce anesthesia. Experimental findings in animals and test subjects have shown that inserting a nasogastric balloon tube can prevent gastroesophageal reflux under provocation of vomiting and regurgitation [6]. Nonetheless, the effectiveness and safety of the esophageal obstruction tube at preventing reflux primarily depends on the lateral pressure of the cuff on the esophageal wall and might not be fully related to the intracuff volume. An excessively high intracuff pressure of the tracheal tube can result in tracheal wall ischemia and perforation in a short time; in contrast, excessively low pressure may not prevent aspiration [7, 8]. This effect is similar to that of intracuff pressure on tracheal and esophageal mucosa. Inappropriate intracuff pressure of the esophageal obstruction tube can lead to ischemia and perforation in the esophageal wall or reflux. The lowest effective pressure inside the cuff of the esophageal obstruction tube to prevent reflux of gastric contents has not yet been determined. Therefore, in the present study, we designed a rabbit reflux model and measured the lowest effective intracuff pressure of the esophageal obstruction tube to prevent reflux of gastric contents.

Materials and methods

After obtaining approval from the Ethics Committee of Sichuan University Hospital (Chengdu, Sichuan, China), New Zealand white rabbits, half males and half females, weighing 2.0–2.5 kg, were injected intramuscularly with 20 mg/kg ketamine and 0.5 mg/kg midazolam. After the onset of anesthesia, propofol was administered by continuous intravenous injection at the edge of the ear at an infusion rate of 30 mg/kg/h to maintain anesthesia.

Rabbits were placed in a lateral recumbent position with the four limbs fixed on the experimental table. A self-made tubular fixator was inserted into the rabbit's mouth to prevent movement and damage to the tube and fixed at the back of the rabbit's head using a plastic belt. A regular 3.5-mm internal diameter cuffed endotracheal tube (Intermediate Hi-Lo, cylindrical polyurethane cuff; Mallinckrodt Medical, St. Louis, MO, USA) was intubated through the tubular fixator into the esophagus as an esophageal obstruction tube; the tube was inserted to the lowest position in the esophagus at a depth of approximately 15 cm from the incisor. The cuff of the esophageal obstruction tube was inflated to block the esophagus. A T-tube was applied to connect the cuff of the esophageal obstruction tube to a pressure-monitoring device (Mallinckrodt). The other end of the T-tube was covered with a heparin cap connected to a 2-mL syringe. The pressure inside the cuff

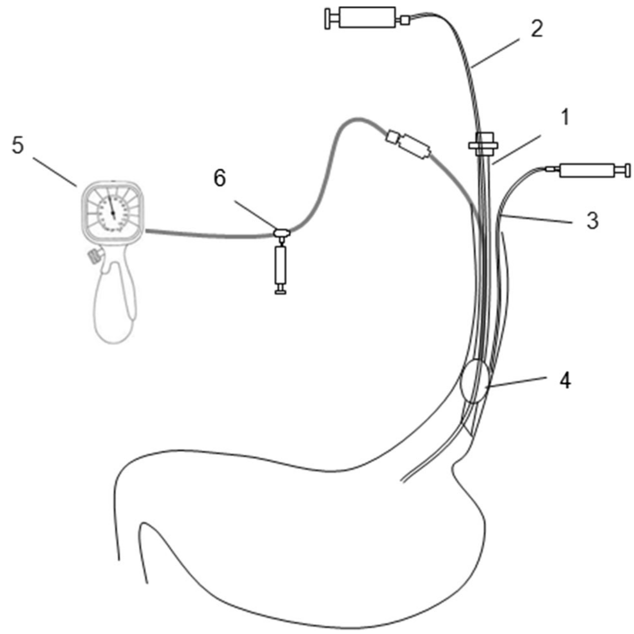

Fig. 1 Schematic representation of an esophageal obstruction tube in a rabbit. *1* A cuffed esophageal obstruction tube was intubated into the esophagus ending at the lowest position of the esophagus; *2* a gastric tube connected to a 20-mL syringe was inserted into the stomach through the esophageal obstruction tube; *3* an observation tube connected to a 10-mL syringe was inserted into the esophagus, and its tip ended at 1–2 cm from the upper margin of the obstructive cuff for observation of gastric content reflux; *4* inflatable cuff; *5* pressure monitoring device; and *6* a T-tube connected to the cuff, a 2-mL syringe, and the pressure monitoring device

was measured with the pressure-monitoring device and regulated using the syringe to maintain the intracuff pressure at a predetermined level. After positioning of the esophageal obstruction tube, a plastic catheter 2 mm in diameter was inserted into the stomach through the esophageal obstruction tube as the "gastric tube" to a depth of approximately 20 cm from the incisor. Then, another plastic catheter with the same diameter as the "observation tube" was inserted along the exterior wall of the esophageal obstruction tube with its tip positioned at 1–2 cm from the upper margin of the obstructive cuff to enable observation of gastric contents reflux; the insertion depth was approximately 10 cm from the incisor (Fig. 1). The size and depth of the esophageal obstruction tube and the plastic catheter were confirmed in preliminary experiments on anatomic models and in the context of autopsies. Normal saline (15–20 ml) stained with methylene blue dye was slowly infused into the "gastric tube" to simulate gastric contents until it flowed out from the esophageal obstruction tube and showed fluctuations with respiratory movement, thus generating an animal model of gastric contents reflux. Because of gastric expandability and gastric emptying during the experiment, methylene blue-dyed normal saline was infused into the stomach intermittently every 5 min to maintain the conditions associated with increased risk of gastric contents reflux.

After maintaining the intracuff pressure at a predetermined level for 5 min, repeated attempts were made to aspirate for at least 10 s with a 10-mL syringe connected to the "observation tube" to determine whether the methylene blue-dyed normal saline flowed out to the upper margin of the obstructive cuff. If methylene blue-dyed normal saline was detected, the result of the reflux trial was defined as "regurgitation," and the opposite effect was defined as a "no regurgitation" result. A single measurement was obtained for each animal. The intracuff pressure of the esophageal obstruction tube blocking off the esophagus was initially set at 120 cm H_2O, and was increased or decreased by 10 cm H_2O each time. In essence, the result obtained from the preceding rabbit determined the intracuff pressure applied to the succeeding rabbit. If the result of the reflux trial was "regurgitation" in the preceding rabbit, the intracuff pressure of the esophageal obstruction tube was increased by 10 cm H_2O in the succeeding rabbit; if the result of the reflux trial was "no regurgitation" in the preceding rabbit, the pressure was decreased by 10 cm H_2O in the succeeding rabbit. A crossover pair represented a unique set of sequential rabbits in which the first rabbit refluxed and the next rabbit did or did not reflux. All the trials were terminated when six crossover pairs were observed from "no regurgitation" to "regurgitation."

Statistical analysis

Data were analyzed using a standard statistics software package (SPSS version 15.0; SPSS, Chicago, IL, USA). The lowest effective intracuff pressure of the esophageal obstruction tube to prevent reflux of gastric contents in 50 % of rabbits was determined by the Dixon up-down method by averaging the midpoints of independent crossover pairs for each result [9, 10]. The intracuff pressure of the esophageal obstruction tube at which there were 50 % and 95 % probabilities of no gastric contents reflux in rabbits was defined using a probit regression model. Data are presented as mean ± SD and 95 % confidence intervals (CI).

Results

A total of 22 New Zealand white rabbits weighing 2.2 ± 0.75 kg were used in this study. Methylene blue-dyed normal saline reflux was not observed when intracuff pressure was maintained at 80–120 cm H_2O. A "regurgitation" result of the reflux trial was obtained for the first time when the intracuff pressure was 70 cm H_2O, and twice when the intracuff pressure was 60 cm H_2O, as well as three times when the intracuff pressure was 50 cm H_2O. The results of the reflux trials on each rabbit under different intracuff pressures are shown in Fig. 2. The lowest effective intracuff pressure of the esophageal obstruction tube for preventing reflux of gastric contents in 50 % of rabbits as determined by the Dixon up-down method was 61.67 ± 8.16 cm H_2O. The results of the probit regression model showed that the intracuff pressure of the esophageal obstruction tube at which there was a 50 % probability of "no regurgitation" of gastric contents was 61.95 cm H_2O (95 % CI, 50.91–69.57 cm H_2O). The intracuff pressure at which there was a 95 % probability of "no regurgitation" of gastric contents was 74.39 cm H_2O (95 % CI, 67.42–184.81 cm H_2O). The regression curve for the

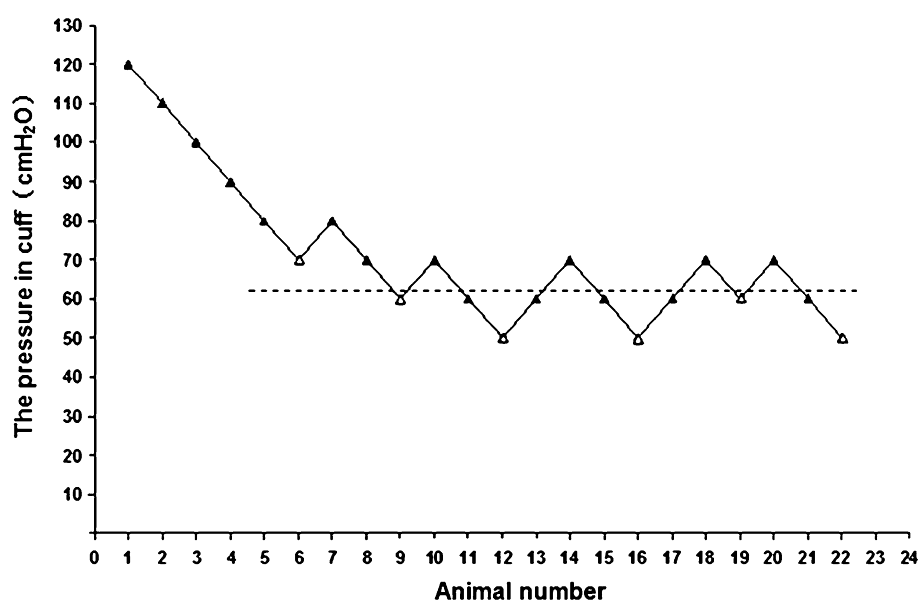

Fig. 2 Individual responses of 22 consecutive rabbits to intracuff pressure according to the up-and-down sequence. Each rabbit's data are represented with a *triangle*. When a rabbit showed reflux in the observation tube, the intracuff pressure given to the next rabbit was increased by 10 cm H_2O [regurgitation (*open symbols*)], whereas in the absence of a reflux, the intracuff pressure given to the next rabbit was decreased by 10 cm H_2O [no regurgitation (*filled symbols*)]. The lowest effective pressure in the cuff for preventing gastric reflux in 50 % of the rabbits was 61.67 ± 8.16 cm H_2O

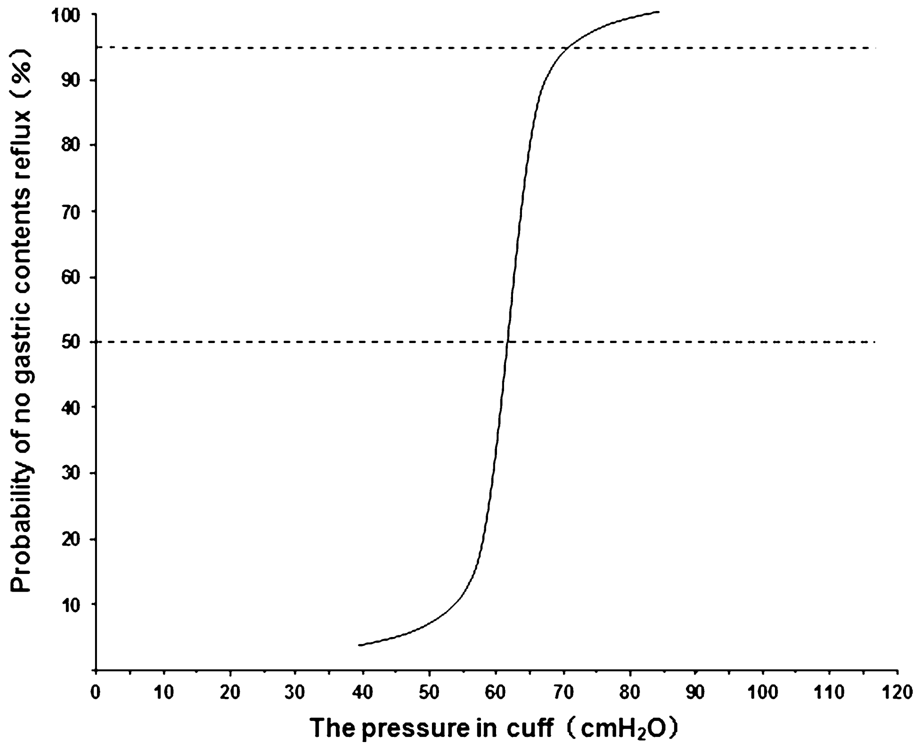

Fig. 3 Pressure–response curve of the probability of no regurgitation of gastric contents. This curve was plotted according to the results of logistic regression analyses of individual intracuff pressure and the respective responses to intracuff pressure in rabbits. The pressure at which there were 50 % and 95 % probabilities of no regurgitation of gastric contents was 61.95 cm H_2O [95 % confidence interval (CI), 50.91–69.57 cm H_2O] and 74.39 cm H_2O (95 % CI, 67.4–184.81 cm H_2O), respectively

possibility of "no regurgitation" of gastric contents is shown in Fig. 3.

Discussion

The present study showed that the insertion of an esophageal obstruction tube into the esophagus can be an acceptable method for preventing reflux of gastric contents in most rabbits within a short period before endotracheal intubation. In addition, it indicated that the reflux prevention effect was pressure dependent within the range of 50–80 cm H_2O. Furthermore, an intracuff pressure >74.40 cm H_2O may prevent gastric contents reflux in most rabbits. In a previous study, a disposable nasogastric balloon tube was developed to prevent the reflux of gastric contents by blocking the cardia with a balloon. The results of that study showed that the nasogastric balloon tube can prevent gastroesophageal reflux under provocation of vomiting and regurgitation. The balloon pressure was set at 46 ± 2 to 86 ± 4 cm H_2O, which was similar to the results from our study [6]. However, in this research a standard tracheal tube was used as an esophageal obstruction tube and the tube cuff was positioned at the lower esophagus, which is different from the study mentioned earlier. Therefore, the underlying mechanism to prevent reflux may be different between the two studies.

In this study, whether the esophageal obstruction tube can effectively prevent reflux depends on the sealing efficacy of the contact surface between the cuff and esophagus, which is mainly determined by the lateral pressure of the cuff on the esophageal wall. When the two closely adhere to each other and the cuff is not excessively filled, the intracuff pressure is equivalent to the lateral pressure of the cuff on the esophageal wall [11]. Therefore, the measured intracuff pressure can be considered to represent the lateral pressure of the cuff on the esophageal wall, which indirectly reflects the degree of sealing of the contact surface between the cuff and the esophagus, and the efficacy of the cuff for preventing reflux under different filling pressures. The underlying mechanism to prevent reflux by blocking the cardia with a balloon was as follows: the nasogastric tube counteracts gastric reflux by means of a gastric balloon that was inflated after the transnasal insertion of the nasogastric tube into the stomach and was then placed under tension at the cardia in such a way that the reflux of residual gastric contents into the esophagus is prevented [6].

Whether intracuff pressure may differ depends on the device or balloon used or may even be affected by the cuff shape and material. High-volume, low-pressure endotracheal tubes cuffs can seal the trachea at lower intracuff pressures. Cylindrical and conical cuffs lead to different compliance of volume and sealing efficacy. Polyurethane, polyvinyl chloride, and guayule latex also caused different results to prevent fluid leakage. Standard polyvinyl chloride endotracheal tube cuffs do not protect from aspiration across the cuff [12]. Cuffs made of polyurethane showed the best short- and long-term sealing efficacy compared with the polyvinyl chloride endotracheal tube [11]. Guayule latex cuffs always prevented fluid leakage. Both cylindrical and conical polyurethane cuffs showed limited leakage. Among all the polyvinyl chloride cuffs, the conical shape ensured higher sealing properties [13]. In this study, a high-volume, low-pressure, cylindrical polyurethane cuff was used, which showed a short-term effect for preventing fluid leakage in most rabbits when the intracuff pressure was more than 74.39 cm H_2O. The intracuff pressure for preventing fluid leakage might be higher in conical cuffs and polyvinyl chloride cuffs but lower in the guayule latex cuffs in the same animal model. However, it is not clear whether the characteristics of the cuff just mentioned in the esophagus and trachea were the same when cuffs of different shape and material were used.

In previous studies investigating the effect of inflation pressure of the endotracheal tube cuff on the occurrence of liquid aspiration, visual observation of the anatomy was commonly used to check for evidence of dye leaking past the cuff. Aspiration was considered to have occurred if the dye reached the area distal to the cuff through the contact surface between the cuff and the cavity wall [14], which criterion was also used in the preliminary experiments in our study. However, we found that the esophageal anatomy method was not suitable for the rabbit model. The trachea has a cartilaginous ring, and the position of the endotracheal tube can be relatively fixed; therefore, the morphological specificity of trachea would not be affected by the traction from the surrounding tissues when we anatomized the trachea. Nevertheless, because the esophagus is a pipe of smooth muscle, anatomical traction from the surrounding tissues around the esophagus may induce morphological changes in the esophagus, leading to intraesophageal catheter movement and dye overflow. This result could mistakenly be interpreted as gastric contents reflux in the animal, possibly leading to false-positive results. In subsequent experiments, we observed that when the dye leaked past the cuff, methylene blue-dyed normal saline could be aspirated out through the transparent observation tube inserted into the upper margin of the cuff of the esophageal obstruction tube. Therefore, in the present study, we used this new method based on the aspiration of methylene blue-dyed normal saline instead of the esophageal anatomy method previously used.

Previous studies have shown that unit volume-induced intracuff pressure changes differ between the esophagus and trachea. It has been shown that unit volume-induced intracuff pressure changes are greater in the esophagus than in the trachea when volumes are greater than 3 mL [15]. This finding seems to conflict with the fact that the expandability is greater in the esophagus than in the trachea. However, it appears to be related to the anatomical characteristics of the esophagus. The esophagus is a muscular pipe without a cartilaginous ring, and its smooth muscle undergoes reflex contraction when the cuff dilates within the esophagus, bringing a counter-acting force on the surface of the cuff and increasing the intracuff pressure. However, this reflex contraction is not observed in the trachea [16]. These anatomical characteristics lead to unit volume-induced intracuff pressure changes that are greater in the esophagus than in the trachea. Therefore, esophageal compliance is generally less than tracheal compliance. Moreover, the esophagus can closely adhere to most of the outer surface of the cuff through morphological changes and reflex contraction, whereas the trachea can only closely adhere to a few parts of the cuff because of anatomical characteristics, which may explain why the pressure preventing reflux is less in the esophagus than in the trachea. The characteristics may be related to the difference in compliance with esophagus and trachea. The Dixon up-down method, which is commonly used to determine the lowest effective dosage or the lowest effective concentration of a drug, can be used to obtain precise results with a comparatively small sample size [9, 10]. It has been reported that the study process can be terminated when at least four crossover pairs from "negative" to "positive" are observed [17]. To ensure the precision of the results, most studies have used six crossover pairs for termination [18, 19]. In the present study, the lowest effective intracuff pressure of the esophageal obstruction tube for preventing reflux of gastric contents in 50 % of the rabbits was defined as the average of the crossover midpoints in each pair.

To simulate the conditions leading to reflux of gastric contents, approximately 15–20 mL methylene blue-dyed normal saline was injected slowly into the gastric tube until the saline flowed out from the esophageal obstruction tube and fluctuated with respiration. This method ensured that the methylene blue-dyed normal saline was present in the area distal to the cuff of the esophageal obstruction tube. During the trial, methylene blue-dyed normal saline was intermittently injected into the stomach to maintain constant gastric swelling and tension, which ensured that the rabbits were at risk of gastric contents reflux. Nevertheless, because the stomach and lower part of the esophagus were open to the outside through the esophageal obstruction tube, gastric pressure could have been lower than that in a sealed system. Therefore, when a catheter that cannot be opened to the outside is used as an esophageal obstruction tube, the actual intracuff pressure needed for reflux prevention might be higher than the pressure measured in this study. A better reflux prevention effect could be obtained under lower intracuff pressure when a catheter that is open to the outside is used as the esophageal obstruction tube.

The present study had several limitations. The gastric pressure and lower esophageal pressure were not measured simultaneously; therefore, it is difficult to determine the ideal gastric pressure to which our result is applicable. In addition, because the lower esophageal sphincter of the rabbits used in the study may have been relaxed under anesthesia, our results might be more applicable to subjects under sedation, and the necessary pressure may be higher than that measured when a subject is fully awake. Moreover, it is difficult to distinguish the active vomiting and swallowing action in the rabbit under anesthesia. Reflux resulting from active vomiting was not observed, and esophageal dilation after active vomiting was not considered in this model. In the present study, the cuff of the esophageal obstruction tube was not inserted into the stomach but rather into the esophagus, which differed from the position of the nasogastric balloon tube used in previous studies [6]. Therefore, our findings may not be suitable for blocking the cardia and may only be applicable to esophageal blocking. Moreover, the use of swine as research subjects is more significant because their esophagus is more similar to that of humans [20]. Although the intracuff pressure of the esophageal obstruction tube was not too high in this model, the risk of esophageal rupture or perforation caused by the obtained intracuff pressure still could not be excluded.

In conclusion, the present study showed that the insertion of an esophageal obstruction tube into the esophagus before endotracheal intubation can be an acceptable method for preventing reflux of gastric contents in most rabbits under light anesthesia. Moreover, within a short period before endotracheal intubation, the maintenance of intracuff pressure of the esophageal obstruction tube could prevent reflux of gastric contents without active vomiting in most rabbits.

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Conflict of interest The authors declare no conflicts of interest.

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