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Impact of Balloon Diameter on Dilation Outcomes in a Model of Rabbit Subglottic Stenosis

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OBJECTIVE: To determine the appropriate balloon size for dilation using a previously described reproducible survival animal model of subglottic stenosis.

STUDY DESIGN: Prospective animal study.

METHODS: We conducted a prospective study including 16 New Zealand White rabbits. The airway of each animal was sized with an endotracheal tube (ETT), and subglottic stenosis (SGS) was endoscopically induced using Bugbee electrocautery to 75% of the circumference of the subglottis, followed by 4-hour intubation. Two weeks postoperatively, the rabbits’ airways were sized and then dilated using a 6-, 7-, 8-, or 9-mm balloon, with four animals in each experimental group. Following dilation, animals were again sized and subsequently euthanized. The cricoid lumen was measured microscopically in each animal.

RESULTS: Prior to inducing stenosis, all animals were sized with a 3.5 ETT. After inducing injury but prior to dilation, airways showed grade 2 SGS that sized with a 2.5 ETT with no leak. Postdilation, animals dilated with 6- or 7-mm balloons (n = 8) sized with a 3.0 ETT, and animals dilated with an 8- or 9-mm balloon (n = 8) sized with a 3.5 ETT. Postdilation median cricoid lumen measurements were 12.5 mm² (6-mm balloon), 13.92 mm² (7-mm), 16.83 mm² (8-mm), and 17.15 mm² (9-mm); two cricoid fractures occurred in the 9-mm group.

CONCLUSION: The postdilation cricoid lumen diameter increased with increased balloon size, and the use of an 8-mm balloon achieved the largest cricoid lumen diameter without causing fracture. Further research is necessary to determine the ideal duration of dilation and optimal intervals between dilations.

KEY WORDS: Subglottic stenosis, rabbit, animal model, balloon, dilation.

LEVEL OF EVIDENCE: NA

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INTRODUCTION

Over the past several years, endoscopic techniques such as balloon dilation have become an invaluable tool for the management of acquired subglottic stenosis (SGS). A number of case series and two recent systematic reviews have reported positive outcomes for patients who have undergone balloon dilation, either as the sole therapy for SGS or in conjunction with other management approaches.

Study Description

Currently, however, there are no evidence-based guidelines for selecting balloon parameters such as balloon diameter. In several published case series, authors do not explain their rationale for choosing a particular balloon diameter. In other reports, authors select different diameters corresponding to the normal age-appropriate airway size, 1-mm larger than an age-appropriate endotracheal tube (ETT), 2- to 4-mm larger than the normal airway diameter, or 100% to 125% of the normal airway. The lack of consensus concerning balloon size implies that the histopathological and biomechanical effects of balloon dilation are poorly understood and that animal studies are necessary to determine the effects of balloon dilation both on the stenosis and on the cricoid cartilage.

With these issues in mind, our aim was to determine the appropriate balloon size for dilation using an animal model of SGS.

MATERIALS AND METHODS

Experimental Study Groups

Our study included 16 New Zealand White rabbits with an average weight of 3.44 kg (range 3.14–3.8 kg). All animals were given at least 3 days to acclimate to our animal facility prior to airway intervention. They were then divided into four experimental groups, with each group undergoing dilation with one of four different balloon sizes: group 1 (6-mm balloon), group

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2 (7-mm balloon), group 3 (8-mm balloon), and group 4 (9-mm balloon).

**Anesthesia Induction and Endoscopy**

General anesthesia induction for all groups was carried out using intramuscular ketamine (35 mg/kg) and xylazine (5 mg/kg) and was maintained with inhaled 2% isoflurane. Isoflurane was continued during the 4-hour period of intubation.

The larynx was exposed using a Miller size 1 laryngoscope and assessed using a 2.7-mm Hopkins Rod telescope (Karl Storz, Tuttingen, Germany). The vocal folds were anesthetized with 0.5 mL of atomized lidocaine (1 mg/mL). The telescope was advanced into the airway to assess laryngeal and tracheal anatomy. Next, sizing of the airway with ETTs was performed.13

**Inducing Subglottic Stenosis**

Subglottic stenosis induction was carried out following a previously described protocol.14 Bugbee monopolar cautery was inserted under endoscopic visualization and used to injure 75% of the circumference of the posterior subglottic area with 7 watts of power for approximately 5 seconds. Intubation was carried out with a 3.5-mm cuffed Portex ETT (Smiths Medical, Dublin, OH) under direct vision. After the 4-hour period of intubation, rabbits were extubated and monitored in a temperature-controlled chamber for 1 to 2 hours. They were then transferred to their respective cages, where they were monitored for the 14-day follow-up period. Buprenorphine (0.03 mg/kg) was given for analgesia every 6 to 12 hours postoperatively.

**Balloon Dilation and Sacrifice**

At day 14, endoscopy and sizing of the airway in each group were again performed using the anesthesia induction method described above. Images from airway endoscopies were recorded.

Following sizing, we performed balloon dilation in all groups. The balloon (Aeris Balloon Dilation Catheter; Bryan Medical Inc., Cincinnati, OH) was inserted through the larynx, centered on the area of the SGS, inflated with 30 seconds with a pressure of 17 atmospheres (recommended pressure for this specific balloon), and then deflated. Each rabbit underwent a single dilation. Airway sizing with an ETT was performed immediately after dilation.

The animals were euthanized with sodium pentobarbital (100 mg/kg), which was administered directly into the heart while the animals remained under general anesthesia.

The larynx and trachea from the level of the hyoid bone to 2 cm below the cricoid were then harvested. Each specimen was sectioned and fixed in 10% buffered formalin, embedded in paraffin, and sectioned into 5-μm sections. Thirty slides of each cricoid stenotic segment were made. A hematoxylin and eosin stain was used for histologic analysis. Pathology slides were analyzed under an optical microscope (Carl Zeiss Microscopy, Thornwood, NY). The circumference of the cricoid lumen was manually demarcated with an AxioVision software SE64 Rel. 4.9.1 tool (Carl Zeiss), and the inner area was calculated by this software. A single measurement of the narrowest part of the airway after dilation was considered for analysis purposes.

All procedures were conducted in accordance with a protocol approved by the Institutional Animal Care and Use Committee at Cincinnati Children’s Hospital Medical Center, and all procedures were conducted at an approved animal surgical facility. The care and handling of the animals were done in accordance with guidelines specified by the National Institutes of Health.

**Data Analysis**

The following parameters were documented in each of our four experimental groups: respiratory symptoms, endoscopic airway sizing, grade of stenosis before and after dilation, and histologic analysis of cricoid areas. We examined distributions of cricoid areas in each group. Descriptive statistics (medians and range) are reported.

The Kruskal-Wallis test was used to compare distributions of cricoid areas between experimental groups. Exact P-values are reported. SAS (SAS institute, Cary, NC) was used to conduct all analyses.

**RESULTS**

Prior to inducing stenosis, all rabbits were sized with a 3.5 ETT. All tolerated induction of SGS and recovered without evidence of respiratory difficulties in the immediate postcauterization period. All animals received extra doses of buprenorphine for pain control following cauterization. One animal from group 1 (6-mm balloon) developed fever and poor oral intake in the first few days after cauterization and had to be sacrificed on postoperative day 4. This rabbit showed a grade 1 SGS with no stridor and underwent dilation before sacrifice. All other animals (n = 15, 93.75%) survived the planned 14-day follow-up period.

After inducing injury but prior to dilation, one animal from group 1 (6-mm balloon) and one from group 3 (8-mm balloon) developed grade 2 SGS that could not be sized with an ETT. All other animals developed grade 2 SGS, sizing with a 2.5 ETT with no leak (Fig. 1). All animals experienced oxygen desaturations as low as 60% during balloon dilation, with complete and quick recovery after balloon withdrawal.

After balloon dilation, all animals dilated with a 6- or 7-mm balloon (n = 8) sized with a 3.0 ETT. The animals dilated with an 8- or 9-mm balloon (n = 8) sized with a 3.5 ETT (Figs. 2 and 3).

The appearance of the hematoxylin and eosin-stained cricoids is demonstrated in Figures 4 to 7. After

Fig. 1. Group 3 (8-mm balloon): subglottis before dilation. [Color figure can be viewed at wileyonlinelibrary.com]
balloon dilation, the median (range) cricoid lumen measurements were 12.46 (9.78, 12.77) mm² (6-mm balloon), 13.92 (8.72, 15.91) mm² (7 mm), 16.84 (13.49, 20.13) mm² (8 mm), and 17.15 (16.23, 21.43) mm² (9 mm) (Fig. 8), with an overall statistical difference between these measurements (P = 0.005).

Cricoid fracture occurred in two animals in group 4 (9-mm balloon). Both fractures occurred in the anterior lamina of the cricoid. Because the animals were sacrificed immediately after balloon dilation, they did not present any symptom related to the fracture.

**DISCUSSION**

In our study of balloon dilation in 16 New Zealand White rabbits, we found that of the four balloon sizes used (6, 7, 8, and 9 mm), the 8-mm balloon was the most effective in achieving an improved postdilation cricoid lumen diameter (both endoscopically and histologically) without causing cricoid fractures. Our findings suggest that, in the setting of established stenosis, the cricoid may be less prone to fracture with a larger (8-mm) balloon diameter. Increasing the size of the balloon (9 mm), however, resulted in a 50% increase in fractures. It is our hope that these findings may be helpful in establishing guidelines for optimal balloon sizes used in the setting of airway stenosis in humans.

Although recent systematic reviews have concluded that airway balloon dilation is effective in treating SGS, there is no consensus regarding optimal balloon-diameter size in humans. It is, however, known that excessively large balloons can damage or rupture the airway, and
balloons that are too small can reduce the effectiveness of the procedure, which results in the need for repeated procedures to achieve clinical improvement. The overall body of literature pertaining to balloon-diameter size is sparse, and current surgical practice frequently depends on surgeon experience regarding balloon sizing, inflation pressures, and length of inflation time rather than evidence-based data.

A number of previous studies have sought to determine the effects of balloon dilation on the normal subglottis of rabbits. Visaya et al. found that dilation in rabbits with a balloon diameter 4.6-mm larger than the measured subglottis resulted in cardiopulmonary arrest in nearly 50% of study animals. These authors concluded that balloon dilation is not necessarily a benign procedure and that guidelines are needed to select an appropriate balloon diameter and pressure. In our model, dilation with a 9-mm balloon would equate to approximately 4.8-mm larger than the subglottis of a rabbit; these animals did not have cardiopulmonary arrest during dilation.

Cricoid fractures can occur with larger balloons in the normal rabbit subglottis. Modi et al. dilated the airways of 39 normal rabbits using balloon diameters ranging from 6 to 10 mm with between 5 and 15 atmospheres of pressure. Fractures occurred in six (66.7%) of nine rabbits dilated with an 8-mm balloon and in eight (88.9%) of nine rabbits dilated with a 9-mm balloon. Ang et al. found that the minimum parameter required to generate a cricoid fracture was a balloon that was 1.6-mm larger than the subglottis at 6 atmospheres of pressure. Despite using younger rabbits, our cricoid fracture rate was 0% (0 of 4) with the 8-mm balloon and 50% (2 of 4) with the 9-mm balloon. The two fractures in our rabbits occurred in the anterior lamina of the cricoid—a finding that is consistent with those reported in other rabbit studies that describe a cricoid fracture. Interestingly, postdilation endoscopic evaluation of the airway did not reveal a cricoid fracture but rather a greater extent of exposed cartilage (Fig. 3). Given our findings as compared to the collective findings of earlier studies in uninjured rabbits, we suspect that an induced stenosis may provide some degree of “protection,” or at the very least may decrease the risk of cricoid fracture during balloon dilation.

Currently, experts advocate the use of a balloon that is 1- to 2-mm larger than the outer diameter for the age-appropriate ETT. As an example, a 6-mm balloon for dilating the subglottis of a neonate (appropriate ETT for this age: 3.5 ETT, with a 4.2 outer diameter). However, we found that when dilating a rabbit subglottis, it is efficient and safe to dilate with a larger (8-mm) balloon.

A limitation of this study is that it is an animal model. We must use caution in translating the results to humans because the human subglottis may not necessarily respond in the same manner as the subglottis of the animals in our model and may not be as accommodating to larger balloons.
CONCLUSION

We found that in 16 New Zealand White rabbits, the postdilation cricoid lumen diameter increased with increased balloon size. The use of an 8-mm balloon achieved the largest cricoid lumen diameter without fracturing the anterior lamina of the cricoid. Our results suggest that SGS may offer some degree of “protection” from cricoid fractures when using an 8-mm balloon. Further research is necessary to define the ideal duration of balloon inflation during dilation, the optimal interval between dilations, and the role of adjunctive therapies in the management of acquired SGS.

BIBLIOGRAPHY