Effect of a Novel Anatomically Shaped Endotracheal Tube on Intubation-Related Injury

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Objectives: To develop an anatomically shaped endotracheal tube (ETT) and to compare the degree of induced laryngeal injury of this ETT with that of a standard ETT using an animal model.

Design: Randomized controlled animal study.

Subjects: Eight Sus scrofa piglets (15-20 kg) randomly intubated with either a standard or a modified uncuffed ETT.

Interventions: The modified ETT was handcrafted by gluing and then trimming dry polyvinyl acetate foam circumferentially to the distal end of a standard uncuffed ETT. After intubation, the foam quickly self-expanded as it absorbed the secretions of the laryngopharynx and adopted the shape of the intraluminal airway. This conforming shape also sealed the larynx to allow for positive pressure ventilation. Both groups were intubated for 4 hours under constant hypoxic conditions (mean oxygen saturation <70%) to enhance and accelerate intubation damage. They were then humanely killed, and the larynx and trachea were harvested for histologic examination.

Main Outcome Measures: The severity of laryngeal injury graded on a scale from 0 to 4 (0 indicates normal; 1, epithelial compression; 2, epithelial loss; 3, subepithelial and glandular necrosis; and 4, perichondrium involvement).

Results: All of the specimens histologically demonstrated areas of inflammation and epithelial loss. The standard ETT caused substantial deep damage, with a mean (SD) severity score of 2.79 (0.74). The modified ETT caused mainly superficial damage, with a mean (SD) severity score of 1.65 (0.56) (P < .001).

Conclusion: The modified ETT objectively caused less laryngotracheal damage compared with the standard ETT and may be of potential clinical benefit.
cuffed ETT that included a foam-filled cuff at the laryngeal level in addition to the standard distal tracheal cuff. The rationale behind the design was to decrease lateral pressure by increasing the contact surface area. His prototype tube showed decreased mucosal injury compared with a conventional ETT in an animal model and in clinical trials.5,11

Endotracheal tube-related mucosal damage can be demonstrated even after short intubation periods. In 1969, Donnelly12 found that the first signs of laryngeal injury could be detected after 3 hours of intubation and that deep ulcerations could be present after 48 hours. In a canine model, Weymuller13 demonstrated that ischemic injury due to an ETT could be seen within 6 hours of intubation.

We previously demonstrated that intubation under hypoxic conditions can accelerate and exacerbate ETT-related airway injury, and we have developed a porcine animal model for measuring ETT-related laryngeal injury.13,14 The primary objective of the present study is to develop an anatomically shaped ETT and to compare the degree of laryngeal injury related to this novel tube with the degree of injury from a standard ETT using a hypoxic animal model.

**METHODS**

This trial was approved by the Research Ethics Board and the Animal Care Committee at The Hospital for Sick Children, Toronto, Ontario, Canada. Eight Sus scrofa piglets each weighing 16 to 20 kg were randomly assigned to a standard cuffed ETT group (n=4) or an anatomically modified ETT (mETT) group (n=4).

**mETT PREPARATION AND TESTING**

The mETT was handcrafted by broadening and gluing a 5-cm length of dry polyvinyl acetate (PVA) foam (Merocel; Medtronic Xomed, Jacksonville, Florida) circumferentially on the distal portion of a standard uncuffed ETT (Sheridan; Hudson RCI, Temecula, California), with a 5-mm internal diameter. The foam was subsequently trimmed and smoothed to achieve an even circular surface, with an external diameter of 10 mm (thereby equaling the external diameter of a standard 7.5-mm–internal diameter ETT). Insertion and removal of the tube was pilot tested using a semirigid stylet. The insertion depth was verified under direct vision. The mETT was positioned with most of the foam below the vocal cords. All intubations were performed successfully. The animal was then placed in the supine position, and the tube was secured to the snout. Ventilation was accomplished using a volume-cycled ventilator (Air-Shields Ventimeter; Narco Health Co, Hatboro, Pennsylvania). Maintenance of anesthesia after intubation was achieved using inhaled isoflurane, 2% to 3%

Monitoring during the procedure included electrocardiography, oxygen saturation, end-tidal carbon dioxide, body temperature (rectal), systolic and diastolic blood pressure, respiratory rate, inspired fractions of oxygen and nitrous oxide, and cuff pressure in the standard ETT group.

The right auricular vein was cannulated for fluid administration, and the left carotid artery was cannulated for arterial reference sample withdrawal, blood pressure monitoring, and arterial blood gas sampling (which were measured every 60 minutes). Immediately after intubation, the animals were paralyzed by intravenous injection of pancuronium bromide (Pavulon; Organon USA Inc, Roseland, New Jersey) (a bolus dose followed by a maintenance dose of 0.2 mg/kg/h) to prevent any ETT movement during the procedure.

We used hypoxic conditions (mean oxygen saturation <70%) in both groups of animals. As shown previously,13 continuous hypoxic conditions accelerate and exacerbate the ETT-related injury in this model. This allowed us to use relatively short intubation periods (4 hours). Hypoxia was achieved by ventilating with a mixture of air and nitrous oxide. We maintained the animals at the lowest oxygen saturation level that would still allow adequate ventilation without severely compromising the hemodynamic status of the animal. The animals were mechanically ventilated for 4 hours.

After the final arterial blood gas measurement, the animals were humanely killed by a lethal injection of sodium pentobarbital (25 mg/kg). The larynx and the trachea were exposed through a midline incision. The trachea was incised at the lower section, below the edge of the ETT, and the position of the tube was confirmed. The tube was sutured to the larynx and trachea to prevent movement. The larynx and the trachea were harvested en bloc while the ETT remained in the lumen, and 10% formaldehyde solution was used as a fixative. This allowed histologic sectioning to be performed with the tube in situ. Serial axial sections of the specimen were cut from the level of the epiglottis to the distal trachea (below the distal edge of the ETT), and digital photographs were taken (Figure 1).

**HISTOLOGIC EVALUATION**

All histologic evaluations were conducted by a single senior pathologist (G.T.). The specimens were evaluated for the severity and extent of tissue damage. The severity of laryngeal injury was graded on a scale from 0 to 4 (0 indicates normal [no damage]; 1, epithelial compression; 2, epithelial loss; 3, subepithelial and glandular inflammation or necrosis; and 4, perichondrium inflammation or loss), as previously described.15 The extent of damage was calculated as the involved proportion of the airway circumference. Examples of pathology specimens are shown for the standard tube (Figure 2) and for the mETT (Figure 3).
The statistical methods used for data analysis were determined a priori using $\alpha = .05$ for exploring the statistical significance. Overall severity and overall extent of histologic damage (using the described grading systems) were compared between the standard ETT and mETT groups using the Mann-Whitney test. Severity and extent were compared between the standard ETT and mETT groups allowing for different section levels using a factorial analysis of variance test. Where this test demonstrated a statistically significant relationship, subgroup analyses were performed to compare severity and extent between the 2 ETT groups at each histologic section level (supraglottic, glottic, subglottic, and trachea) using the Mann-Whitney test.

**RESULTS**

The baseline characteristics of the animals and the measured experimental physiologic and biochemical variables are summarized in Table 1. All 8 animals completed the 4-hour intubation protocol, and all were included in the data analysis. The mETT was found to be relatively easy to insert and, after intubation, the foam quickly self-expanded as it absorbed the secretions of the laryngopharynx to allow it to adopt the shape of the intraluminal airway. The initial airway leak, thereby, disappeared within 2 to 3 minutes of intubation.

All the histologic specimens demonstrated areas of inflammation and epithelial loss. The standard ETT caused substantial deep damage, with a mean (SD) severity score of 2.79 (0.74), whereas the mETT caused mainly superficial damage, with a mean (SD) severity score of 1.65 (0.56) ($P < .001$) (Figure 4A). The mean extent of damage (as a percentage of the airway circumference) was not significantly different between the 2 study groups (31% for the standard ETT and 40% for the mETT, $P > .05$) (Figure 4B). Using the factorial analysis of variance test, severity was significantly related to tube type and section level ($P < .001$ for both), so subgroup analyses were performed. At all levels, the severity score was statistically significantly higher in the standard ETT vs the mETT group (Table 2).

**COMMENT**

Laryngeal injury is a well-recognized sequela of endotracheal intubation. Since the introduction of high-volume low-pressure cuffs, tracheal injuries caused by
extreme pressure from tubes are seldom seen, but there has been no corresponding decrease in the incidence of laryngeal damage.\textsuperscript{15} The pressure that the tube exerts on the laryngeal wall is probably the most important factor that contributes to laryngeal injury.\textsuperscript{16} When the pressure exerted by the tube exceeds mucosal capillary pressure, ischemia occurs.\textsuperscript{17} Mucosal injury first manifests with erythema and edema, then progresses to ulceration, which leads to perichondritis, chondritis, and, eventually, the formation of scar tissue and stenosis.\textsuperscript{7,8} Owing to the relatively small contact area between the ETT and the larynx, the pressure at these contact points may be extremely high (several hundred millimeters of mercury), well above capillary occlusion pressure. Because the ETT rests in the posterior part of the larynx, sites most vulnerable to injury include the medial surfaces of the arytenoids, the cricoarytenoid joints, the interarytenoid region, and the posterior cricoid cartilage.\textsuperscript{1,3,6} Weymuller et al\textsuperscript{11} demonstrated that the area of ischemia correlates with the size of the ETT (because the lateral force exerted by the tube increases with tube diameter).

Benjamin\textsuperscript{1} stated that the ideal ETT should be inexpensive; should be made of a synthetic material with a smooth, nonirritating surface; should have no potentially toxic components; and should be thermoplastic at body temperature to mold itself to body contours. In addition, the tube should disperse pressure over a large surface contact area, thereby minimizing posterior and lateral intralaryngeal surface pressure and remaining below the capillary perfusion pressure. The present mETT fulfilled these requirements while remaining relatively inexpensive and straightforward to manufacture. The PVA foam that covers the tube expands when coming in contact with the local secretions and, hence, takes the anatomical shape of the airway. The tube then demonstrated an excellent airway seal, without any audible or measurable air leaks. We, thereby, found that the mETT allowed us to achieve 2 desirable goals: to dramatically increase the surface contact area and to obviate the need for a tracheal cuff. The mETT foam was in contact with the airway circumferentially, thereby reducing the lateral pressure exerted on the airway. This was evidenced by the significantly lower severity score for the mETT compared with the standard ETT, especially in the glottic and subglottic areas.

Several previous attempts to improve ETT design have been reported in the literature. Grimm and Knight\textsuperscript{18} modified an ETT by surrounding it with a rubber condom from the level of the vocal cords to the middle of the trachea. Weymuller\textsuperscript{11} used a double-cuffed ETT that included a foam-filled cuff at the laryngeal level in addition to the standard distal tracheal cuff. Using a canine model, he showed that his prototype tube caused very mild laryngotracheal injury compared with the severe damage caused...
by the standard ETT for short- and long-term intubation. Lederman et al\textsuperscript{19} designed an ETT in which the regular cuff was replaced by polyurethane foam coated in latex at the level of the trachea. This tube caused significantly less tracheal injury compared with the standard low-pressure cuffed tube but was not designed to reduce damage at the glottic and subglottic levels. Non-PVA polyurethane foam cuffs have also been marketed for use in tracheostomy tubes. Here again, the foam cuff was designed to address the issues of high lateral tracheal wall pressures that lead to complications such as tracheal necrosis and stenosis, but the larynx and subglottis were not addressed. None of these previous modified tubes have gained widespread popularity.

In most cases, acute loss of mucosa from the larynx and the trachea is reversible.\textsuperscript{20} Healing commonly occurs primarily through reepithelialization. In contrast, perichondrial and cartilaginous ulceration heal by reparative fibrosis and could lead to the formation of subglottic and posterior glottic stenosis.\textsuperscript{7} The severest damage that the mETT caused was epithelial loss. This injury would be expected to heal without any long-term sequelae. In contrast, animals intubated with the standard tube demonstrated at least subepithelial necrosis, with most having perichondrial involvement. Those injuries could potentially lead to laryngeal and tracheal stenosis. In the present study, we are limited to pathologic evidence of mucosal changes after relatively short periods of intubation, without a clinical correlation. Future studies will include animal recovery after the intubation period to compare the longer-term effects on laryngotracheal mucosa after a period of repair.

In addition to a decrease in lateral pressure, the second achievement of the mETT was the avoidance of a tracheal cuff. As discussed earlier, although the incidence of tracheal cuff injury dramatically reduced after introduction of the high-volume low-pressure cuff, damage to tracheal mucosa may be seen with relatively low cuff pressures. Nordin et al\textsuperscript{21} demonstrated in a rabbit model that superficial damage to mucosa occurs within 15 minutes of intubation at a cuff pressure of 20 mm Hg (27 cm H\textsubscript{2}O). At cuff pressures exceeding 50 mm Hg, there was evidence of hindered perfusion of the capillary bed in contact with the cuff. Seegobin and van Hasselt\textsuperscript{22} found evidence of obstruction to mucosal blood flow in the human trachea when lateral wall pressure was raised above 30 cm H\textsubscript{2}O, with total occlusion of flow to the mucosa over the tracheal rings and posterior tracheal wall at a lateral wall pressure of 50 cm H\textsubscript{2}O. Ideally, cuff pressure should be measured frequently and adjusted to appropriate levels. In reality, in the intensive care setting, cuff pressure may be checked rarely, only by manual palpation, and it is often overinflated to prevent an air leak.\textsuperscript{23} Duguet et al\textsuperscript{24} measured the cuff pressure in intubated patients receiving intensive care. They demonstrated that despite manual control of the endotracheal pressure with a portable manometer, the mean (SD) proportion of time that the cuff pressure was greater than 30 cm H\textsubscript{2}O was 30% (25%).

The tracheal cuff area had a significantly higher severity of injury in the control group than in the group receiving the mETT despite cuff pressure being maintained below 20 cm H\textsubscript{2}O. This finding confirms that substantial damage to the tracheal cuff area could be seen even with very low cuff pressures. A partial explanation for this finding was the hypoxic condition in which the animals were ventilated, rendering them vulnerable to ischemic damage even with very low lateral pressures. The mETT sealed the airway at the glottic and subglottic levels, thereby eliminating the need for a tracheal cuff.

To our knowledge, this is the first study to report the use of PVA in the laryngotracheal region. We did not demonstrate any adverse or toxic reactions to the PVA during the experiments. Although the PVA is used extensively in the nasal cavity, there is a scarcity of information in the literature about its effects on normal nasal mucosa. One study\textsuperscript{25} using an animal model of surgically injured nasal mucosa demonstrated that mucosal healing in PVA-packed animals was similar or better than that in unpacked controls. In the nasal cavity and in the airway animal model, the PVA foam is inflated by the absorption of contact fluid.

The long-term effects of the PVA foam on the airway mucosa are unknown. As discussed previously herein, longer intubation studies are needed to explore potential benefits and adverse effects of the foam. It is theoretically possible that the PVA foam could increase bacterial growth, the infection rate, or granulation tissue formation. Available data from PVA use in nasal surgery does not support an increased infection rate with its use in nasal packing.\textsuperscript{26} Previous work has shown some ingrowth of granulation tissue directly into PVA foam when used in the nose,\textsuperscript{27} but the relevance of this to the airway is unclear.

Systemic corticosteroids are widely used in the periextubation period and in the treatment of laryngeal edema, and associated adverse effects are often of substantial concern, particularly in neonates.\textsuperscript{27} The mETT may, therefore, allow the administration of topical corticosteroids, thereby potentially achieving the local laryngeal effect of systemic corticosteroids without the adverse systemic effects.

These initial results are encouraging and demonstrate that the mETT may be beneficial in reducing laryngotracheal damage after short periods of intubation. This may be clinically applicable to patients with chronic hypoxia (eg, congenital cardiac disease, prematurity, and chronic lung disease) or those who have failed previous attempts at extubation.

Submitted for Publication: March 29, 2009; final revision received June 26, 2009; accepted September 21, 2009. Correspondence: Arie Gordin, MD, Department of Otolaryngology–Head and Neck Surgery, The Hospital for Sick Children, 555 University Ave, Toronto, ON M5G 1X8, Canada (a_gordin@rambam.health.gov.il).

Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Gordin, Campisi, Luginbuehl, Taylor, and Forte. Acquisition of data: Gordin, Luginbuehl, Taylor, and Forte. Analysis and interpretation of data: Gordin, Chadda, and Forte. Drafting of the manu-
Critical revision of the manuscript for important intellectual content: Gordin, Chadha, and Taylor. Statistical analysis: Gordin and Chadha. Obtained funding: Forte. Administrative, technical, and material support: Luginbuehl and Taylor. Study supervision: Campisi and Taylor. Financial Disclosure: None reported.

Previous Presentations: This study was presented at the American Society of Pediatric Otolaryngology Annual Meeting; May 24, 2009; Seattle, Washington.

REFERENCES