The Laryngoscope

A Simple Mechanical Device Reduces Subglottic Injury in Ventilated Animals

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Objectives/Hypothesis: To test whether a simple inexpensive device that dynamically minimizes endotracheal cuff pressure throughout the respiratory cycle reduces endotracheal cuff pressure-related subglottic injury.

Study Design: Hypoxic animal model with one control and one experimental group.

Methods: Twelve *S. scrofa domesticus* piglets (14–16kg) were intubated with standard endotracheal tubes and maintained in a hypoxic state to accelerate airway injury. Animals in the control group (n = 6) were ventilated with a constant pressure of 20 cm H_2O in the endotracheal tube cuff. Animals in the experimental group (n = 6) were ventilated using a custom-designed circuit that altered the pressure in the endotracheal tube cuff in synchrony with the ventilatory cycle. Larynges were harvested at the end of the experiment and examined histologically to determine the degree of airway injury induced by the endotracheal cuff.

Results: Animals in the experimental group suffered significantly less airway damage than those in the control group. The differences were seen primarily in the subglottis (aggregate damage score 6.5 vs. 12, $P < 0.05$), where the experimental endotracheal tube cuff exerted the least pressure. There was no difference in damage to the glottic or supraglottic structures.

Conclusions: A simple, reliable, and inexpensive means of modulating endotracheal tube cuff pressure with the ventilatory cycle led to a substantial decrease in airway injury in our animal model. Such reduction in cuff pressure may prove important for humans, particularly those in intensive care units who tend to have underlying conditions predisposing them to tracheal damage from the endotracheal tube cuff.

Key Words: Endotracheal tube, airway injury, cuff pressure modulation.

Level of Evidence: N/A.

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INTRODUCTION

Endotracheal intubation and mechanical ventilation are essential elements of modern medical practice. Unfortunately, intubation for even short periods of time carries with it a small but nontrivial risk of laryngeal or tracheal injury.[1] Injury can arise from shear forces or blunt trauma inflicted during the act of placement of the endotracheal tube (ETT) itself, but the more common mechanism of injury is that of pressure necrosis.[2] Whenever the external pressure on the mucosa exceeds the capillary perfusion pressure (considered to be approximately 20–25 cm H_2O), that region suffers from hypoperfusion and ischemia and is susceptible to pressure necrosis.[3] Multiple factors such as airway diameter, ETT shape and cuff pressure, hypoxia, hypotension, and gastroesophageal reflux have all been proposed to impact the rate and degree of injury.[4–6] Injury to the laryngotracheal mucosa and submucosal support can result in granulation, fibrosis, scars, web formation, and stenosis, all of which can have profound functional impact for the patient long after the original process that required intubation has resolved.[2,7,8]

Injury prevention trumps the best treatments. Awareness of intubation-related injury has led to a reduction in rates of subglottic stenosis in children and adults. Changes in intubation practices in adults and children,[9] treatment of gastroesophageal reflux,[10] and trends towards early tracheotomy in adults with chronic comorbidities[11] have all contributed to this decrease. Another approach to reduce injury is to modify the ETT cuff design. The introduction of high-volume, low-pressure cuffs has resulted in a significant decrease in the incidence of tracheal injury and stenosis.[12,13] Alterations in tube shape that allow the ETT to more naturally conform to the contour of the airway have been shown to reduce laryngeal injury.[14] The use of a polyvinyl acetate (Merocel) cuff allows for efficient ventilation and

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Drs. Forte and Fisher have registered for a patent for the pressure modulating in-line valve under the auspices of the Commercialization Offices of the Hospital for Sick Children and the University Health Network, respectively. The authors have no other funding, financial relationships, or conflicts of interest to disclose.

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significantly reduces subglottic injury when compared to a standard inflatable polyvinyl chloride cuff.[15,16]

As opposed to these static alterations in ETT design, a different and new approach is to dynamically modulate ETT cuff pressure. We have previously proposed a means of modulating ETT cuff pressure in a way that inflation of the cuff is synchronized with the ventilator cycle such that the pressure exerted by the cuff on the mucosa is only transiently above 20 cm H_2O,[17] as necessary to maintain cuff seal during peak inspiratory pressures. During the expiratory phase the cuff deflates and allows for reperfusion of the mucosa, thereby maintaining—at least intermittently—mucosal perfusion. Indeed, subglottic injury was reduced in our porcine model using a complex electromechanical device to provide cuff pressure modulation. Here we report the efficacy of a simple mechanical pressure modulating device (PMD) to reduce tracheal injury.

MATERIALS AND METHODS

Our protocol was approved by the Research Ethics Board and the Animal Care Committee at the Hospital for Sick Children.

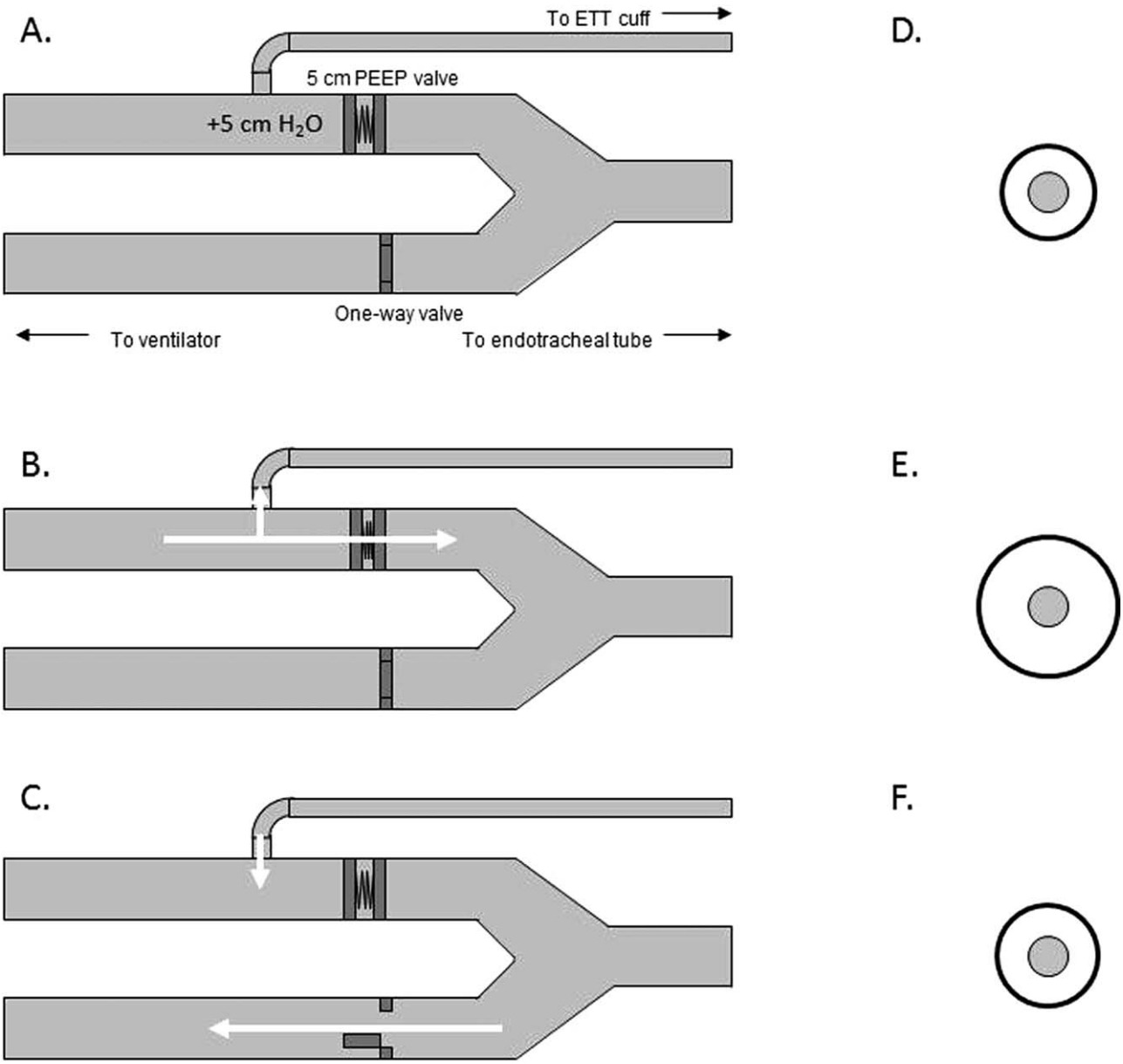

Fig. 1. **Schematic representation of cuff pressure modulation by the in-line mechanical valve. (A)** The device is shown at rest. The connection to the pilot balloon and endotracheal tube cuff is on the high end of the pressure gradient created by the PEEP valve. **(B)** On inspiration air is forced into the cuff and through the circuit to the ETT and patient (airflow is indicated by the white arrow). The PEEP valve ensures that the pressure in the cuff is 5 cm H2O greater than the airway pressure. **(C)** On expiration the pressure in the airway and the cuff decrease and air flows out the expiratory limb of the ventilator circuit. The amount of cuff inflation is shown **(D)** at rest, **(E)** on inspiration, **(F)** and on expiration.

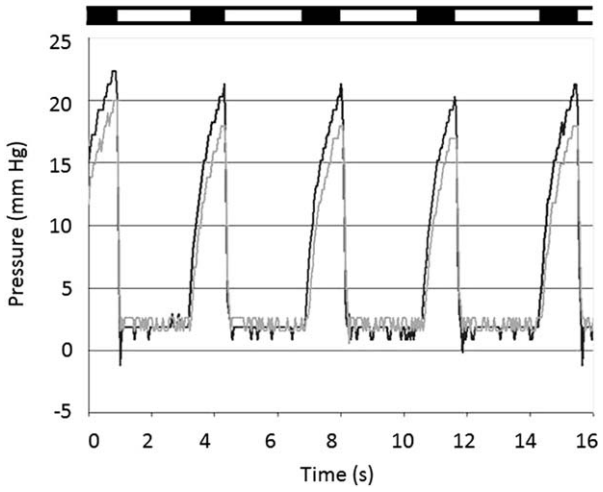

Fig. 2. **Cuff pressure versus airway pressure over multiple ventilator cycles.** Pressure transducers were used to measure the airway and cuff pressures in a bench-top ventilation model using the in-line valve to modulate cuff pressure. During periods of inspiration (solid line above) the cuff pressure can be seen to remain 5 cm H_2O (approximately 3.7 mm Hg) above airway pressure. During expiration (double line above) both pressures drop rapidly and airway pressure is slightly above cuff pressure due to the PEEP inherent in the ventilator.

The Pressure Modulation Device

The schematic representation of the PMD is shown in Figure 1. It consists of a positive end-expiratory pressure (PEEP) valve placed "backward" in the inspiratory limb of the anesthesia circuit, a connector with a female Luer lock valve upstream from the PEEP valve, and a one-way valve in the expiratory limb. Because of the gradient created by the PEEP valve, inspiratory limb pressure and cuff pressure will be maintained at 5 cm H_2O above the airway pressure throughout the inspiratory phase. This will provide a seal and adequate ventilation at any airway pressure. During expiration, the cuff pressure will equal the PEEP setting of the ventilator. The pilot balloon check valve is continuously open when connected to the PMD so that the cuff will inflate on inspiration and will equilibrate with airway pressure during expiration.

We first tested the PMD in a bench-top model, placing it in line with a ventilator circuit ventilating artificial lungs in a pressure-controlled setting. During inspiration, the cuff pressure constantly exceeded the airway pressure (Fig. 2). This pressure gradient, created by the in-line PEEP valve, ensures that the cuff will be able to maintain a seal against the increasing airway pressure during inspiration, thus providing for adequate pulmonary ventilation. Pressures in both the airway and the cuff fall off quickly during expiration. Importantly, cuff pressure does not go to zero, but is instead maintained at the PEEP value set on the ventilator. (Even at ventilator settings of 0, ventilators are considered to be within specifications with inherent PEEP up to 3 cm H_2O). This low but constant PEEP in the airway is important in reducing the theoretical risk of aspiration around a less inflated cuff. In theory, secretions should be kept out of the airway by the positive pressure gradient that exists between the pharynx and the airway distal to the cuff.

The Hypoxic Model of Airway Injury

We used a hypoxic animal model in *S. scrofa* piglets, as previously described.[16,17] The animals were anesthetized by intramuscular injection of 0.15 mL/kg of a sedative mixture (each 1 mL contained ketamine hydrochloride, 58.82 mg; acepromazine maleate, 1.18mg; and atropine sulfate, 0.009 mg). Anesthesia for intubation was achieved by inhalational induction using 3% to 5% isoflurane. All animals were orally intubated using an appropriately sized cuffed polyvinyl chloride ETT (Sheridan; Hudson RCI). We selected the ETT with the largest diameter (usually7.5- to 8.0-mm internal diameter) that would allow an audible air leak with the cuff deflated.

In the control group, the cuff pressure was maintained at 20 cm H_2O using an ETT cuff pressure monitor. In the experimental group, the cuff was initially inflated to 20 cm H_2O and then attached to the PMD, after which the cuff pressure passively followed the pressure in the ventilator circuit. The ETT cuff was placed just below the vocal cords, and insertion depth for both groups was verified under direct vision during direct laryngoscopy. The animal was then placed in the supine position, and the tube was secured to the snout. The oropharynx was filled with 20 mL of a 1% methylene blue solution in order to enable identification of aspiration at the postmortem study.

Animals were ventilated using a volume-cycled ventilator (Air-Shields Ventimeter; Narco Health Co, Hatboro, PA). Maintenance of anesthesia after intubation was achieved using inhaled isoflurane, 2% to 3%. A mixture of oxygen and nitrous oxide was used to lower the FiO_2 and maintain hypoxia. Monitoring during the procedure included electrocardiography, pulse oxymetry, end-tidal carbon dioxide concentration, 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 blood pressure monitoring and arterial blood gas sampling (which were measured every 60 minutes).

Both control and experimental groups were subjected to hypoxic conditions (mean oxygen saturation $\approx$70%). As shown previously, continuous hypoxic conditions accelerate and exacerbate the ETT-related injury in this model.[16,17] The animals were mechanically ventilated for 4 hours. After the final arterial blood gas measurement, the animals were euthanized by an overdose of sodium pentobarbital (25 mg/kg). The ETT was removed and the larynx and trachea were harvested en bloc, and preserved in 10% formaldehyde solution.

Histologic Analysis

Sections were cut from the level of the arytenoids to the trachea, stained with hematoxylin and eosin, and evaluated by a single blinded pathologist (R.C.) The extent of the damage was assessed using a previously published scale as follows (Fig. 3).

0. No damage
1. Compression of the epithelium
2. Epithelial loss
3. Inflammation or necrosis of the submucosal glands
4. Inflammation or necrosis of the perichondrium or cartilage

The subglottis was defined by the cricoid cartilage, and the trachea was defined as any part of the airway that was below the cricoid cartilage.

RESULTS

All animals were appropriately ventilated without a leak. In the animals ventilated with the PMD, no leakage of methylene blue below the level of the cuff was detected upon removal of the larynx, suggesting that the

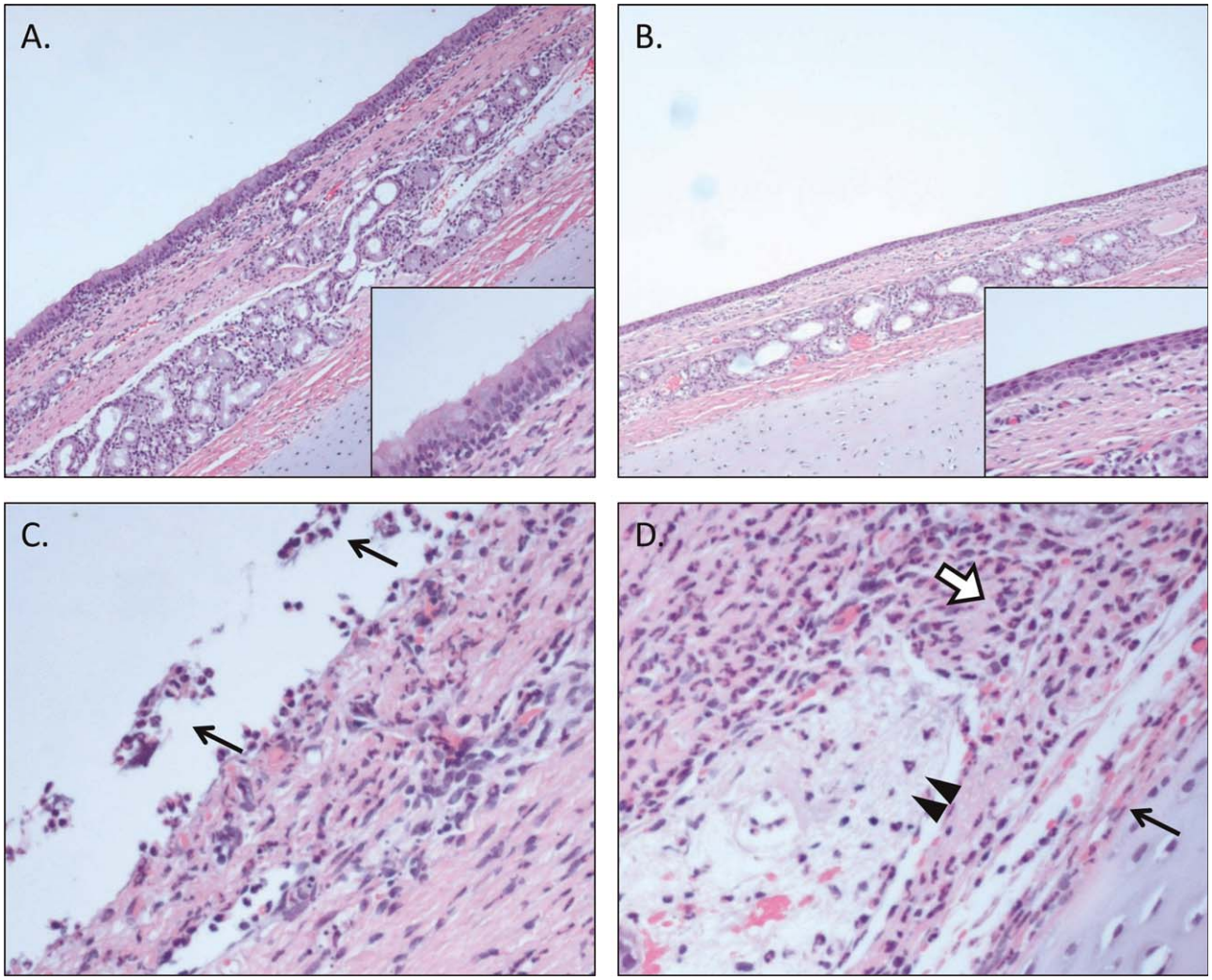

Fig. 3. **Representative examples of damage caused by endotracheal intubation in the hypoxic animal model. (A)** Normal pseudostratified columnar epithelium of the subglottis (100X). Inset at 200X demonstrates the cilia and robust columnar architecture. **(B)** Grade 1 injury (100X). The columnar architecture is compressed and the inset (200X) shows the lack of cilia and goblet cells. **(C)** Grade 2 injury (200X). The epithelium is eroded, and an exudate of fibrin in inflammatory cells is seen (simple arrows). **(D)** Grade 4 injury (200X). There is extensive and deep submucosal inflammation (open arrow), necrosis and inflammation of the submucous mucus glands (double arrowhead), and compression and inflammation of the perichondrium (simple arrow). Color versions of this figure are available online.

PEEP present in the ventilator circuit is successful in preventing aspiration. Baseline characteristics of the animals used in each group and the relevant physiologic and biochemical variables are shown in Table I. Of note, the additional dead space introduced by the pressure modulator required a higher minute ventilation for the animals in the experimental group in order to maintain appropriate $PaCO_2$ and pH levels. Additionally, the experimental group had a statistically significantly lower O_2 saturation than the control group, although this is unlikely to be physiologically significant. The control group of animals had significantly higher degrees of injury in the subglottic region than the animals whose cuff pressures were dynamically modulated (Table II). The median injury score in the subglottis was grade 1 (mucosal compression) in the modulated pressure group and grade 2 (epithelial loss) in the constant pressure group. As in previous experiments using the electromechanical cuff modulation, the degrees of injury between groups were similar in regions of the airway that were not exposed to cuff pressure. Median severity scores across all sections for the indicated region of the airway are shown. Additionally, average aggregate severity scores, in which severity scores over all sections for the indicated region of the airway were combined, are shown.

DISCUSSION

The important finding of our experiment is that ETT cuff pressure modulation with a simple mechanical PMD effectively decreased airway injury in this hypoxic animal model.[17] The PMD demonstrated a similar reduction in airway injury, as shown in a previous study where cuff modulation was performed with an electromechanical device that required active sensors, a separate

TABLE I.
Baseline Characteristics and Physiologic Variables of the Control and Experimental Group *S. Scrofa* Piglets.*

Parameter	Constant Cuff Pressure	Modulated Cuff Pressure
Body weight (kg)	15.4	16.1
Body temperature (degrees C)	37.0	37.2
Pulse (beats per minute)	131	134
Systolic blood pressure (mm Hg)	61	66
Diastolic blood pressure (mm Hg)	36	39
O_2 saturation (%)	69.7†	68.5†
$PaCO_2$ (mm Hg)	39.8†	44.2†
pH	7.42	7.41
Tidal volume (cc)	165†	184†
Respiratory rate (breaths per minute)	20†	22†

*Data are given as mean values.
†Statistically significant differences ($P < 0.05$ by Mann-Whitney test).

pump to inflate and deflate the cuff, and a logic board. We feel that this represents a significant advance compared to our electromechanical device, and the advantages of our mechanical PMD are multiple. Given its simplicity, mechanical components, and passive action, the PMD is likely to be more reliable than the electromechanical device. Since the pressure to inflate the cuff is generated by the ventilator itself, the PMD can easily be included in any ventilator circuit. The main component of the PMD is a commercially available in-line PEEP valve (Intersurgical Inc., supplied through Trudell Medical Marketing, London, ON), which we purchased for $17 (CAD) and adapted to fit "backward" in a ventilator circuit. This is clearly less expensive than the electromechanical device, the components of which cost several hundreds of dollars. Thus the mechanical PMD could be easily adopted as a low-cost option if it proves effective in reducing tracheal trauma during mechanical ventilation in humans. One can envision a scenario in which, through the economy of scale, the PMD could be incorporated into standard ventilator circuits for minimal cost.

TABLE II.
Comparison of Median and Aggregate Injury Severity Scores by Cuff Pressure and Airway Subsite.

Airway Subsite	Constant Cuff Pressure	Modulated Cuff Pressure	
Median injury severity score*			
Supraglottis	0	0	$P = 0.42$
Glottis	0	0	$P = 0.21$
Subglottis	2	1	$P = 0.005$
Trachea	1	1	$P = 0.51$
Average aggregate injury severity score†			
Supraglottis	2.2	1.3	$P = 0.58$
Glottis	2.2	0.8	$P = 0.38$
Subglottis	12	6.5	$P = 0.025$
Trachea	4	5.3	$P = 0.87$

The indicated regions of the airway were examined histologically. Standardized sections were taken of each region of the airway and each slide was scored using the injury scale detailed in the Materials and Methods.
*To determine the median injury severity score for each region of the airway, the scores of all slides of that region for all animals in each arm were grouped and the median value was chosen. *P* values were determined using the Mann-Whitney test for nonparametric distributions.
†To determine the average aggregate injury severity score for each region of the airway, the scores for each slide of that region were summed individually for each animal. The individual scores in each arm were then averaged and *P* values calculated using the Mann-Whitney test.

A reduction in airway injury has been accomplished in previous studies using modified ETTs. Lindholm demonstrated that simply changing the ETT shape to more naturally conform to the curvature of the airway can reduce posterior laryngeal injury.[14] Variation of cuff design has been shown to decrease injury, the first of which was the high-volume, low-pressure cuff .[12,13] A foam-filled latex cuff trialed by Lederman and colleagues in humans and dogs was shown to induce less damage using a similar grading scale to ours.[18] Work by our own group, using a cuff entirely made out of polyvinyl acetate, also showed significantly less propensity to induce injury in the same hypoxic porcine model.[15] Cuff alternatives including a parachute-shaped transglottic cuff[19] and an ultrathin "gill-" style cuff[20] have both been proposed to reduce airway injury. We feel that the PMD presents an advantage over modifying endotracheal tubes themselves as it can be used in line with any available cuffed ETT. One single version of the PMD can be used for any patient and any pattern of ventilation, rather than having to match ETT and cuff configurations to different patients.

Despite high awareness of intubation-related injury, current methods of endotracheal cuff pressure monitoring are inadequate to prevent overinflation. Rates of overinflation can be as high as 38%[21–23]; and although scheduled serial monitoring of cuff pressure can decrease these rates, a significant proportion of patients will still have overinflated cuffs.[24] These studies highlight the need for an automated, continuous means of modulating cuff pressure.

Aspiration is a constant concern in ventilated patients. A theoretical risk of alternating cuff pressure over the course of the ventilator cycle is the increased risk of aspiration. We addressed this in our study by placing methylene blue in the oropharynx of the intubated animals and grossly examining the subglottic and tracheal regions for evidence of aspiration. No evidence of aspiration was seen. Numerous studies have examined the capability of different ETT cuff shapes or materials to prevent aspiration.[25–27] One of the most consistent variables in preventing aspiration is the presence of PEEP, rather than cuff material, shape, or cuff pressure. Thus, we feel that the presence of a small amount of PEEP in our experiments (typically 3–5 cm H_2O) likely was sufficient to prevent aspiration. Further studies to formally assess the risk of aspiration in a bench-top model, as well as in our in vivo hypoxic model, are currently underway in our laboratory.

The animals in the experimental group were able to be ventilated adequately using the PMD, despite the

presence of a cuff that was partially deflated for a large duration of each respiratory cycle. Consistent cuff deflation has been tested in other modes of ventilation, namely high frequency ventilation and CPAP.[28,29] The ability to deliver adequate ventilation was affected in the case of high frequency ventilation, but there was minimal effect in the instance of CPAP. We feel that in our study, adequate ventilation without a detectable leak was achieved under volume-controlled settings because the cuff inflated and created a seal during inspiration. It is reasonable to assume that the PMD would work equally well under pressure-controlled settings, although this was not formally tested in our model.

Traditionally, cuffed ETTs are avoided in children until the age of 8 or 10 years. This allows for a larger diameter tube to be used and has been proposed to reduce subglottic injury.[30] Recently, however, this dogma has come under scrutiny. The advantages of using cuffed ETTs, especially in the intensive care unit combined with technical advances in ETT and cuff design, have led some to advocate for the routine use of cuffed ETTs in children.[3,31] It should be noted that head-to-head trials comparing complications following intubation with modern cuffed ETTs or uncuffed tubes in children do not exist. The PMD presented here might allow for safer use of cuffed ETTs in children, particularly children at risk of tracheal injury, such as those with hypotension, hypoxia, malnutrition, and prolonged intubation.

Limitations

The PMD was tested in healthy normotensive pigs in which ventilation was adequate at relatively low peak airway pressures (20–25 cm H_2O) and low respiratory rates (18–24 breaths per minute). Although the PMD should theoretically work with rapidly oscillating ventilation, it has not been tested under these conditions, and it is unclear whether pressure in the cuff can subside rapidly enough during a very brief expiration to allow reperfusion before the next inspiration. Furthermore, because reperfusion of the mucosa theoretically occurs during expiration, modes of ventilation that decrease expiration time, such as high frequency ventilation or inverse ratio ventilation or very high peak pressures, might not allow for adequate reperfusion times to prevent injury, but would still seem to be better than continuous pressure as it presently occurs. Finally, if PEEP pressures are high during expiration (e.g., above 25 cm H_2O), then the cuff may not deflate sufficiently to allow reperfusion of the mucosa. Other devices that have been developed to maintain constant cuff pressure,[32,33] but do not rely on the ventilator as the source of cuff pressure may be more suitable for these situations. Nevertheless, further testing of all devices—PMD included—under these ventilatory conditions is needed before any conclusions can be drawn in this regard.

CONCLUSION

We have developed a simple and inexpensive mechanical valve-based device that reliably modulates ETT cuff pressure during mechanical ventilation. This device is a simpler and less expensive version of a device that we previously designed to perform a similar function, but it was as effective in reducing subglottic injury. The PMD is a simple low-risk modification of the ventilator circuit that shows promise under normal ventilatory conditions. Testing under more extreme conditions, as suggested above, is warranted to establish limits of the PMD prior to clinical trials.

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BIBLIOGRAPHY

1. Mendels EJ, Brunings JW, Hamaekers AE, Stokroos RJ, Kremer B, Baijens LW. Adverse laryngeal effects following short-term general anesthesia: a systematic review. *Arch Otolaryngol Head Neck Surg* 2012;138:257–264.
2. Streitz JM Jr, Shapshay SM. Airway injury after tracheotomy and endotracheal intubation. *Surg Clin North Am* 1991;71:1211–1230.
3. Veyckemans F. New developments in the management of the paediatric airway: cuffed or uncuffed tracheal tubes, laryngeal mask airway, cuffed oropharyngeal airway, tracheostomy and one-lung ventilation devices. *Curr Opin Anaesthesiol* 1999;12:315–320.
4. Colton House J, Noordzij JP, Murgia B, Langmore S. Laryngeal injury from prolonged intubation: a prospective analysis of contributing factors. *Laryngoscope* 2011;121:596–600.
5. Esteller-More E, Ibanez J, Matino E, Adema JM, Nolla M, Quer IM. Prognostic factors in laryngotracheal injury following intubation and/or tracheotomy in ICU patients. *Eur Arch Otorhinolaryngol* 2005;262:880–883.
6. Gomes Cordeiro AM, Fernandes JC, Troster EJ. Possible risk factors associated with moderate or severe airway injuries in children who underwent endotracheal intubation. *Pediatr Crit Care Med* 2004;5:364–368.
7. Duynstee ML, de Krijger RR, Monnier P, Verwoerd CD, Verwoerd-Verhoef HL. Subglottic stenosis after endolaryngeal intubation in infants and children: result of wound healing processes. *Int J Pediatr Otorhinolaryngol* 2002;62:1–9.
8. Wei JL, Bond J. Management and prevention of endotracheal intubation injury in neonates. *Curr Opin Otolaryngol Head Neck Surg* 2011;19:474–477.
9. Choi SS, Zalzal GH. Changing trends in neonatal subglottic stenosis. *Otolaryngol Head Neck Surg* 2000;122:61–63.
10. Jindal JR, Milbrath MM, Shaker R, Hogan WJ, Toohill RJ. Gastroesophageal reflux disease as a likely cause of "idiopathic" subglottic stenosis. *Ann Otol Rhinol Laryngol* 1994;103:186–191.
11. Volpi D, Lin PT, Kuriloff DB, Kimmelman CP. Risk factors for intubation injury of the larynx. *Ann Otol Rhinol Laryngol* 1987;96:684–686.
12. Pearson FG, Goldberg M, da Silva AJ. A prospective study of tracheal injury complicating tracheostomy with a cuffed tube. *Ann Otol Rhinol Laryngol* 1968;77:867–882.
13. Whited RE. A prospective study of laryngotracheal sequelae in long-term intubation. *Laryngoscope* 1984;94:367–377.
14. Lindholm CE. Experience with a new orotracheal tube. *Acta Otolaryngol* 1973;75:389–390.
15. Gordin A, Chadha NK, Campisi P, Luginbuehl I, Taylor G, Forte V. Effect of a novel anatomically shaped endotracheal tube on intubation-related injury. *Arch Otolaryngol Head Neck Surg* 2010;136:54–59.
16. Gordin A, Chadha NK, Campisi P, Luginbuehl I, Taylor G, Forte V. An animal model for endotracheal tube-related laryngeal injury using hypoxic ventilation. *Otolaryngol Head Neck Surg* 2011;144:247–251.
17. Chadha NK, Gordin A, Luginbuehl I, et al. Automated cuff pressure modulation: a novel device to reduce endotracheal tube injury. *Arch Otolaryngol Head Neck Surg* 2011;137:30–34.
18. Lederman DS, Klein EF, Jr., Drury WD, et al. A comparison of foam and air-filled endotracheal-tube cuffs. *Anesth Analg* 1974;53:521–526.
19. Nordin U, Lyttkens L. New parachute cuff and positive end-expiratory pressure to minimize tracheal injury and prevent aspiration. *Arch Otorhinolaryngol* 1979;222:119–125.
20. Reali-Forster C, Kolobow T, Giacomini M, Hayashi T, Horiba K, Ferrans VJ. New ultrathin-walled endotracheal tube with a novel laryngeal seal design. Long-term evaluation in sheep. *Anesthesiology* 1996;84:162–172; discussion 127A.
21. Duguet A, D'Amico L, Biondi G, Prodanovic H, Gonzalez-Bermejo J, Similowski T. Control of tracheal cuff pressure: a pilot study using a pneumatic device. *Intensive Care Med* 2007;33:128–132.
22. Morris LG, Zoumalan RA, Roccaforte JD, Amin MR. Monitoring tracheal tube cuff pressures in the intensive care unit: a comparison of digital palpation and manometry. *Ann Otol Rhinol Laryngol* 2007;116:639–642.

23. Sole ML, Penoyer DA, Su X, et al. Assessment of endotracheal cuff pressure by continuous monitoring: a pilot study. *Am J Crit Care* 2009;18:133–143.
24. Sole ML, Su X, Talbert S, et al. Evaluation of an intervention to maintain endotracheal tube cuff pressure within therapeutic range. *Am J Crit Care* 2011;20:109–117; quiz 118.
25. Dave MH, Koepfer N, Madjdpour C, Frotzler A, Weiss M. Tracheal fluid leakage in benchtop trials: comparison of static versus dynamic ventilation model with and without lubrication. *J Anesth* 2010;24:247–252.
26. Kolobow T, Cressoni M, Epp M, Corti I, Cadringher P, Zanella A. Comparison of a novel lycra endotracheal tube cuff to standard polyvinyl chloride cuff and polyurethane cuff for fluid leak prevention. *Respir Care* 2011;56:1095–1099.
27. Zanella A, Scaravilli V, Isgro S, et al. Fluid leakage across tracheal tube cuff, effect of different cuff material, shape, and positive expiratory pressure: a bench-top study. *Intensive Care Med* 2011;37:343–347.
28. Allan PF, Thurlby JR, Naworol GA. Measurement of pulsatile tidal volume, pressure amplitude, and gas flow during high-frequency percussive ventilation, with and without partial cuff deflation. *Respir Care* 2007;52:45–49.
29. Conway DH, Mackie C. The effects of tracheostomy cuff deflation during continuous positive airway pressure. *Anaesthesia* 2004;59:652–657.
30. Black AE, Hatch DJ, Nauth-Misir N. Complications of nasotracheal intubation in neonates, infants and children: a review of 4 years' experience in a children's hospital. *Br J Anaesth* 1990;65:461–467.
31. Fine GF, Borland LM. The future of the cuffed endotracheal tube. *Paediatr Anaesth* 2004;14:38–42.
32. Howard WR. Bench study of a new device to display and maintain stable artificial airway cuff pressure. *Respir Care* 2011;56:1506–1513.
33. Valencia M, Ferrer M, Farre R, et al. Automatic control of tracheal tube cuff pressure in ventilated patients in semirecumbent position: a randomized trial. *Crit Care Med* 2007;35:1543–1549.