CHEST

Endotracheal Tubes for Critically Ill Patients

An In Vivo Analysis of Associated Tracheal Injury, Mucociliary Clearance, and Sealing Efficacy

Gianluigi Li Bassi, MD, PhD; Nestor Luque, MD; Joan Daniel Martí, PhD, RPT; Eli Aguilera Xiol, MSc; Marta Di Pasquale, MD; Valeria Giunta, MD; Talitha Comaru, PhD, RPT; Montserrat Rigol, DVM, PhD; Silvia Terraneo, MD; Francesca De Rosa, MD; Mariano Rinaudo, MD; Ernesto Crisafulli, MD, PhD, FCCP; Rogelio Cesar Peralta Lepe, MD; Carles Agusti, MD, PhD; Carmen Lucena, MD; Miguel Ferrer, MD, PhD; Laia Fernández, PhD; and Antoni Torres, MD, PhD, FCCP

BACKGROUND: Improvements in the design of the endotracheal tube (ETT) have been achieved in recent years. We evaluated tracheal injury associated with ETTs with novel high-volume low-pressure (HVLP) cuffs and subglottic secretions aspiration (SSA) and the effects on mucociliary clearance (MCC).

METHODS: Twenty-nine pigs were intubated with ETTs comprising cylindrical or tapered cuffs and made of polyvinylchloride (PVC) or polyurethane. In specific ETTs, SSA was performed every 2 h. Following 76 h of mechanical ventilation, pigs were weaned and extubated. Images of the tracheal wall were recorded before intubation, at extubation, and 24 and 96 h thereafter through a fluorescence bronchoscope. We calculated the red-to-green intensity ratio (R/G), an index of tracheal injury, and the green-plus-blue (G+B) intensity, an index of normalcy, of the most injured tracheal regions. MCC was assessed through fluoroscopic tracking of radiopaque markers. After 96 h from extubation, pigs were killed, and a pathologist scored injury.

RESULTS: Cylindrical cuffs presented a smaller increase in R/G vs tapered cuffs ($P = .011$). Additionally, cuffs made of polyurethane produced a minor increase in R/G ($P = .012$) and less G+B intensity decline ($P = .022$) vs PVC cuffs. Particularly, a cuff made of polyurethane and with a smaller outer diameter outperformed all cuffs. SSA-related histologic injury ranged from cilia loss to subepithelial inflammation. MCC was 0.9 ± 1.8 and 0.4 ± 0.9 mm/min for polyurethane and PVC cuffs, respectively ($P < .001$).

CONCLUSIONS: HVLP cuffs and SSA produce tracheal injury, and the recovery is incomplete up to 96 h following extubation. Small, cylindrical-shaped cuffs made of polyurethane cause less injury. MCC decline is reduced with polyurethane cuffs. CHEST 2015; 147(5):1327-1335

Manuscript received June 13, 2014; revision accepted November 13, 2014; originally published Online First December 11, 2014.

ABBREVIATIONS: ETT = endotracheal tube; G+B = green plus blue; HVLP = high volume low pressure; MCC = mucociliary clearance; PVC = polyvinylchloride; R/G = red-to-green intensity ratio; SSA = subglottic secretions aspiration; VAP = ventilator-associated pneumonia

AFFILIATIONS: From the Division of Animal Experimentation (Drs Li Bassi, Luque, Martí, Di Pasquale, Giunta, Comaru, Rigol, Terraneo, De Rosa, Rinaudo, Crisafulli, Peralta Lepe, Ferrer, Fernández, and Torres and Ms Aguilera Xiol), Department of Pulmonary and Critical Care Medicine, Thorax Institute, Hospital Clínic, Barcelona, Spain; Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) (Drs Li Bassi, Rigol, Ferrer, Fernández, and Torres), Barcelona, Spain; Centro de Investigación Biomedica En Red-Enfermedades Respiratorias (CIBERES) (Drs Li Bassi, Martí, Rigol, Ferrer, Fernández, and Torres and Ms Aguilera Xiol), Barcelona, Spain; University of Milan (Drs Di Pasquale, Giunta, Terraneo, and De Rosa), Milan, Italy; Division of Bronchoscopy (Drs Agusti and Lucena), Department of Pulmonary Medicine, Thorax Institute, Hospital Clínic, Barcelona, Spain; and University of Barcelona (Dr Torres), Barcelona, Spain.

Drs Li Bassi and Luque contributed equally to this work.

Part of this article has been presented in abstract form [De Rosa F, Li Bassi G, Martí JD, et al. Histological evaluation of the recovery of cuff-induced tracheal injury: assessment at 72 hours from extubation. *Intens Care Med*. 2013;39(suppl 2):0680; Li Bassi G, Marti JD, Aguilera Xiol E, et al. Effects of high-volume low-pressure cuff designs and materials on mucociliary clearance. *Crit Care Med*. 2012;40(12)(suppl 1):440; and Li Bassi G, Aguilera Xiol E, Marti JD, et al. Assessment of cuff-induced

Several improvements in the design of the endotracheal tube (ETT) have been achieved in recent years.[1] Critically ill patients are often intubated with ETTs comprising tapered[2] or polyurethane cuffs.[3] These novel cuffs have shown enhanced sealing effectiveness[2-8] compared with standard high-volume low-pressure (HVLP) cuffs of cylindrical shape and made of polyvinylchloride (PVC). Additionally, some ETTs are designed for subglottic secretions aspiration (SSA). In two clinical studies,[9,10] patients intubated with ETT comprising polyurethane cuffs were at lower risk of developing ventilator-associated pneumonia (VAP). Likewise, there is compelling evidence that SSA decreases the risk of VAP.[11]

Nevertheless, the safety of these novel ETTs has not been extensively evaluated. We have demonstrated[7] that HVLP cuffs inflated at the clinically recommended pressure range might transmit high pressure against the trachea. In particular, we found that folds form along the cuff's surface, and the tracheal mucosa adjacent to a fold could be subject to potentially harmful transmitted pressure. As for the safety of SSA, only a few studies have shown tracheal injury associated with SSA, particularly when few secretions are present within the subglottic region[12] or when continuous aspiration is applied.[13,14] Finally, inflation of the cuff impairs the mucociliary escalator.[15] The effects of these novel cuffs on the mucociliary clearance (MCC) rate, however, is largely unknown. Thus, we designed this prospective randomized study to evaluate in tracheally intubated pigs the effects of commercially available HVLP cuffs on tracheal injury, MCC, and prevention of leakage across the cuff. Additionally, injury associated with intermittent SSA was assessed.

Materials and Methods

The institutional ethics committee approved the protocol. Animals were managed according to the guidelines for the use and care of laboratory animals.[16] Further methodologic details are provided in e-Appendix 1.

Randomization and Animal Handling

Large White-Landrace pigs (37.3 ± 3.6 kg) were randomized to be intubated with one of the ETTs listed in Table 1 connected to a mechanical ventilator (SERVO-i; MAQUET Holding BV & Co KG) and ventilated as previously reported.[17] Anesthesia was maintained through infusion of propofol and remifentanil. Gases were conditioned to 37°C with a heated humidifier (Hudson RCI Conchatherm III; Teleflex Incorporated). The internal ETT cuff pressure was maintained at 28 cm H_2O through a mechanical device[18] to optimize sealing efficacy[7] while avoiding tracheal ischemia.[19-24] In ETTs with SSA, the patency of the suction lumen was tested every 2 h and secretions aspirated with a syringe. In case of resistance upon aspiration, 10 mL air was insufflated into the suction lumen, and aspiration was attempted one additional time only. Importantly, the cuff was deflated every 6 h and the ETT gently rotated to ensure that the evacuation port was directed toward the most-dependent tracheal regions. Following 76 h of mechanical ventilation, pigs were weaned, extubated, and housed with water and food ad libitum (e-Fig 1).

Tracheal Injury

Fluorescence Bronchoscopy: At baseline, extubation, and 24 and 96 h thereafter, images of the tracheal region where the cuff was located were recorded through a fluorescence bronchoscope (Pentax SAFE-3000; Ricoh Imaging Deutschland GmbH). White-light and fluorescence pictures were concomitantly recorded. Upon laser activation, normal tracheal regions appeared bluish/greenish, whereas injured regions were darker and brownish.[25] We calculated through image analysis software (ImageJ; National Institutes of Health) the red-to-green intensity ratio (R/G),[26,27] an index of injury, and the green-plus-blue (G+B) intensity, an index of normalcy, of the most injured tracheal region (100 × 100 pixels). Thus, tracheal injury was expected to increase R/G and decrease G+B intensity values. To correct for intersubject fluorescence variability, all values were adjusted per baseline values as follows: ([current – baseline value] / baseline value) × 100, namely R/G and G+B intensity differentials, and reported as percentage. Upon imaging analysis, the observers were blinded to treatment allocation.

White-Light Bronchoscopy: The white-light bronchoscopy pictures were scored by two bronchoscopists blinded to treatment allocation (Fig 1).

Histopathology: After 96 h from extubation, the pigs were killed, and the length of the trachea adjacent to the cuff was measured. The worst histologic injury of the first and last tracheal rings in contact with the cuff and every other ring between these two segments were scored (0, no injury; 1, epithelial layer compression; 2, cilia loss; 3, epithelial denudation; 4, subepithelial/glandular inflammation; 5, perichondrium inflammation) by a pathologist (e-Fig 2) blinded to treatment allocation. Injury of the area adjacent to the SSA opening was also studied by gross examination and microscopy.

Mucociliary Clearance

Following 28 h of mechanical ventilation, MCC was measured through fluoroscopic tracking of radiopaque markers, as previously described.[17,28]

Cuff Leakage

At 52 and 73 h from intubation, animals were placed prone, the bed was oriented 30° above horizontal, and positive end-expiratory pressure was reduced to 0 cm H_2O. We instilled 2 mL methylene blue and 3 mL phosphate buffer solution with 1.5 μL of 2.0-μm Invitrogen fluorescent microspheres (Thermo Fisher Scientific Inc) into the subglottic region. One hour from instillation, leakage was estimated by the presence of methylene blue and quantification of microspheres in tracheal secretions.[29] We calculated the percentage of recovered microspheres per gram of tracheal secretions per the total amount of instilled microspheres (aspirated microspheres).[29]

tracheal injury by commercially available endotracheal tubes. *Crit Care Med*. 2012;40(12 suppl 1):443].

FUNDING/SUPPORT: Support was provided by Covidien Ltd.

CORRESPONDENCE TO: Antoni Torres, MD, PhD, FCCP, Department of Pulmonary and Critical Care Medicine, Hospital Clínic, Calle Villarroel 170, Esc 6/8 Planta 2, 08036 Barcelona, Spain; e-mail: atorres@clinic.ub.es

DOI: 10.1378/chest.14-1438