POSTEXTUBATION STRIDOR IN ADULT ICU PATIENTS

SUMMARY

Post-extubation stridor secondary to laryngeal edema may occur in up to 37% of extubated patients and is associated with increase cost, morbidity and mortality. The risk of laryngeal edema may be evaluated by the cuff leak test. Patients with a leak volume of <10% of the inhaled volume are at increased risk of having significant laryngeal edema and developing post-extubation stridor and respiratory distress. Little may be done following the development of post-extubation stridor, but recent studies have shown that prophylactic steroids, in a variety of dosing strategies, administered at least 4-6 hours prior to extubation may be of benefit in properly selected patients.

RECOMMENDATIONS

- **Level 1**
  - ➢ **Steroid therapy decreases post-extubation stridor and need for reintubation in patients at increased risk for extubation failure due to airway edema.**
  - ➢ **Steroid therapy should be administered >6 hours prior to extubation to be effective in reducing airway edema.**

- **Level 2**
  - ➢ **Patients at risk for laryngeal edema include:**
    - **Traumatic intubation**
    - **Female gender**
    - **Prolonged intubation (>7 days)**
    - **Traumatic injury**
    - **Oversized endotracheal tubes**
    - **Self extubation**
    - **Failed cuff leak test**
  - ➢ **The cuff leak test is an adequate test to assess for laryngeal edema.**

- **Level 3**
  - ➢ **A leak of greater than 30% of the administered tidal volume upon deflation of the endotracheal tube cuff is suggestive of successful extubation.**
  - ➢ **When steroids are administered to decrease post-extubation stridor, recommend:**
    - **Methylprednisolone 40 mg IV x 1 at least 4 hours prior to extubation OR**
    - **Dexamethasone 4 mg IV every 6 hours**

INTRODUCTION

Laryngeal edema is a common cause of airway obstruction in the recently extubated intensive care unit (ICU) patient. Depending upon the severity of edema, patients may go on to develop "a high pitched

EVIDENCE DEFINITIONS
- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS
- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

noisy respiration" known as "stridor" (1). Stridor has been documented to occur in 3.5-36.8% of the ICU population, depending on the definition used (2). Stridor not only leads to anxiety for the patient and family, but may progress to acute respiratory failure requiring reintubation and resulting in increased mechanical ventilation days, ICU days, patient care costs, morbidity, and mortality.

The etiology of laryngeal edema in intubated ICU patients is likely pressure and ischemia from the endotracheal tube cuff during prolonged intubation (2). Nearly all intubated patients will develop some level of edema; however, >50% narrowing of the tracheal lumen is needed before respiratory distress develops (3,4). The most typical location of edema leading to stridor and reintubation is at the level of the vocal cords. This edema is transient and most times will resolve within one month (2).

LITERATURE REVIEW

Risk factors
An early study by Colice et al. prospectively evaluated risk factors for post-extubation stridor in a limited population (4). The authors observed 82 patients that had undergone prolonged intubation for mostly medical indications. Entry criteria were intubation for greater than four days, no prior laryngeal abnormality, and no prior intubation within the last 6 months. The 82 patients consisted of only men admitted to medical, surgical and respiratory ICUs in a Veteran's Administration Medical Center. Only 17% of the population consisted of surgical or trauma patients. The authors identified some level laryngeal edema in 94% of the population by direct laryngoscopy and noted that moderate to severe edema was associated with an increased duration of intubation. Most patients' symptoms were resolved by 8 weeks.

Darmon et al. evaluated risk factors for laryngeal edema in a double blinded, placebo controlled, multicenter trial (5). The authors attempted to determine whether pre-extubation steroid therapy would decrease post-extubation edema. Seven hundred consecutive ICU patients were randomized and further categorized into either short-duration intubation (<36 hours) or long-duration intubation (>36 hours). The authors found no difference between the treatment groups. Laryngeal edema was defined as laryngeal dyspnea or stridor and had an overall incidence of 4.2%. They found the incidence of edema was increased within the long duration group (7.2% vs 0.9%) and that no patients within the short duration group required reintubation. Female gender was noted to be a risk factor (70% of patients with laryngeal edema) with a relative risk of 3.3.

Jaber et al. evaluated risk factors in an observational study to evaluate the cuff leak test (6). The authors defined laryngeal edema by the evidence of stridor. They analyzed 112 patients within a 14 month period. Patients were identified as either having stridor or not. They noted an increased risk of stridor in patients with increased severity of illness (SAPS II of 50 vs. 38), traumatic intubation (54% vs. 7%), self extubation (38% vs. 4%), and duration of intubation (median of 10.9 vs.5.5 days).

Tadie et al. prospectively gathered data on patients within six hours of their extubation by using a laryngeal nasofibroscope (7). One hundred thirty-six patients were evaluated over the course of one year. Overall, 73% of the patients had at least one laryngeal abnormality upon examination. Of these, 53% had one abnormality, 36% had two abnormalities, and 11% had 3 or 4 abnormalities. Risk factors for laryngeal injury were length of intubation, use of myorelaxant medications, and elevated APACHE II score. Eighteen percent of patients went on to develop post-extubation stridor and 3% were reintubated. This was mostly due to laryngeal edema at the level of the vocal cords. Risk factors for edema were longer duration of intubation, female gender, height/endotracheal tube size ratio and emergency intubation.

Cuff leak test
The gold standard for determination of laryngeal edema would be direct laryngoscopy of the airway prior to extubation. Unfortunately, this is not possible prior to extubation due to the endotracheal tube which is well below this area. Due to this fact, the cuff leak test has been advocated has a test for the determination of possible laryngeal edema. It's a simple test that involves placing the patient on a set

tidal volume by setting the mechanical ventilator on assist control mode. After the endotracheal tube has been thoroughly suctioned, the cuff is deflated. The expiratory volumes are measured over the course of several breaths after the patient has ceased coughing. The expiratory volumes are subtracted from the inhalatory volumes and this is defined as "the cuff leak volume".

Miller and Cole were the first to attempt to correlate the volume of leak with the possibility of post-extubation stridor (8). Their study population consisted of 100 extubation attempts in 88 patients admitted to a medical ICU. Patients had to be intubated for >24 hours. Patients underwent a cuff leak test 24 hours after intubation and those deemed appropriate for extubation underwent a cuff leak test within 24 hours of extubation. The result of the cuff leak test was blinded to the managing physicians. All assessments for stridor and the need for intubation were made by the managing physicians. Patient characteristics were similar between the two groups. Patients that developed stridor had lower cuff leaks (180 ± 157 mL vs. 360 ± 157 mL; p=0.012) and were more likely to have self-extubated (5.2% vs. 20%). By using a receiver operating characteristic (ROC) analysis,, the authors predicted that a cuff leak less than 110 mL provided a positive predictive value (PPV) of 0.80 for the presence of stridor post-extubation and PPV of 0.98 for the absence of stridor if the volume was greater than 110 mL. They also concluded that this would give a specificity of 0.99, but a sensitivity of only 0.67.

Jaber et al. likewise evaluated the cuff leak test in order to quantify what volume would have predicted an increased risk of stridor (6). The authors selected a volume of 130 mL or 12% of the inspiratory volume based upon their ROC plot. They calculated a sensitivity of 85% and specificity of 95% with a PPV of 69% and a negative predictive value (NPV) of 98%.

Chung et al. examined 95 patients after undergoing percutanous tracheotomy with bronchoscopy to evaluate cord edema compared to a cuff leak test (9). The vocal cords were evaluated upon removal of the endotracheal tube and evidence of severely swollen vocal cords was considered confirmation of severe laryngeal edema. The authors selected a volume of 140 mL after examining the ROC plot. This provided a PPV and NPV of 83.8% and 93.1% respectively. The sensitivity and specificity were 88.6% and 90.0%.

Sandu et al. conducted a similar study to that of Miller and Cole with similar results (10). The authors found that a percentage of the cuff leak volume was more advantageous in determining complications from laryngeal edema. The mean cuff leak in patients with uneventful extubations was 408 ± 201 mL (57.2% ± 23.9% of tidal volume before cuff deflation) while the mean cuff leak for patients who required reintubation had a mean cuff leak of 68 ± 75 mL (9.2% ± 9.9% of tidal volume before cuff deflation), with a range of 0 to 190 mL (0% to 24% of tidal volume before cuff deflation). They noted that a cuff leak of less than 10% gave a specificity of 96% for predicting failed extubation.

Steroid Therapy
Several studies have evaluated the use of steroid therapy immediately prior to extubation in an attempt to reduce airway edema and stridor with poor results (5,11,12). Several more recent studies have shown steroids are potentially effective if given at least four hours prior to extubation.

Lee et al., in a randomized, placebo controlled double-blind trial conducted on adult medical ICU patients, evaluated the use of dexamethasone on patients who had leak volumes of <110 mL and had been intubated for >48 hours (13). Eighty-six patients were identified and received dexamethasone 5 mg IV every six hours for four doses vs. placebo on the day prior to extubation. The cuff leak test was performed prior to injection, one hour after injection, and 24 hours after the fourth injection of steroids. Demographically the patients were the same. A dramatic increase in leak volume was seen in the steroid vs. placebo arm beginning around six hours prior to extubation. The steroid arm showed a decreased incidence of stridor (10% vs. 27.5%, p=0.037) and reintubation (2.5% vs. 5%, p=0.56). The absolute risk reduction and number needed to treat (NNT) were calculated as 18% and 5.7 respectively. No patients demonstrated evidence of gastrointestinal (GI) bleeding, gastric pain or irritation, psychiatric disturbances, or Cushingoid features as a result of the steroid therapy.

Francois et al. performed a large randomized, placebo controlled double-blind trial of 698 surgical and trauma patients who received methylprednisolone vs. placebo. Patients were mechanically ventilated for more than 36 hours with a planned extubation during their ICU stay. Methylprednisolone 20 mg IV was initiated 12 hours prior to planned extubation and continued every four hours with the last injection immediately prior to extubation. Patients in the steroid arm showed significantly less laryngeal edema (3% vs. 22%; p<0.0001) and need for reintubation (4% vs. 8%; p=0.005). The authors also identified female gender, shorter height, traumatic injury, and an oversized endotracheal tube as risk factors in univariate analysis (14).

Cheng et al performed a small randomized control rial of 71 patients in medical and surgical ICUs who had been intubated >24 h and had failed a cuff leak test (<24% tidal volume). Patients received either single 40 mg IV dose of methyprednisolone or normal saline 4 hours prior to extubation. They were observed for 48 h post-extubation for stridor and need for reintubation. Results showed significant reduction in post-extubation stridor and reintubation rate in the treated group compared to placebo group (15.8% vs. 39.4%, P=0.025, and 7.9% vs. 30.3%, P=0.015, respectively). They secondarily found decreased length of stay in the ICU in the treated group vs placebo (8.6±5.2 vs. 13±6.8 days, P=0.004). (15)

Three recent meta-analyses have confirmed these findings. Through the Cochrane collaboration, Khemani et al. evaluated six studies and noted a significant reduction in stridor (RR 0.47, CI= 0.22-0.99) but could only show a non-significant trend in reintubation rate (12). However, in a post hoc analysis, studies that incorporated a multiple dosing strategy did show a decreased re-intubation rate. Jaber et al. identified seven randomized controlled trials. The authors noted a decreased risk of stridor (RR 0.48, CI=0.26-0.87) with steroids and a decreased risk of re-intubation (RR 0.58, CI=0.41-0.81) (11). When patients at high risk for reintubation were selected, this benefit became more pronounced with rates decreasing from 19.8% to 8.6% (RR 0.38, CI=0.21-0.72). McCaffrey et al., incorporating both pediatric and adult populations, noted that the benefit of steroid therapy was more pronounced if given greater than 12 hours prior to extubation (16). The authors calculated the NNT one patient for stridor as 11 patients and the NNT was 28 for re-intubation; this fell to only 9 if only high risk patients were included. Based upon this data, steroid therapy would this prevent 35 reintubations and 84 instances of laryngeal edema per 1000 patient extubations.

The American Thoracic Society and American College of Chest Physicians published a clinical practice guideline including recommendations regarding performance of cuff leak tests and administration of steroids prior to extubation. They found 14 observational studies looking at post-extubation stridor and reintubation rates after performing a cuff leak test. Due to the small size of the studies and observational design, they concluded there is low certainty in the evidence but recommend performing a cuff leak test prior to extubation in patients who are high risk for post-extubation stridor. They reviewed three randomized trials evaluating the effect of systemic steroid therapy in patients who failed a cuff leak test and found reduced rate in reintubation (5.8 vs. 17.0%; RR, 0.32; 95% CI, 0.14–0.76) and post-extubation stridor rate (10.8 vs. 31.9%; RR, 0.35; 95% CI, 0.20–0.63). Their recommendation, with moderate certainty in the evidence, is for systemic steroid administration at least 4 h prior to extubation in patients who have failed a cuff leak test (17).

Complications of Steroid Therapy
Complications associated with steroid therapy have been well documented and their use should be considered carefully prior to administration. However, currently there is no clear data evaluating the long term effects of steroid therapy for laryngeal edema. Lee et al. noted no complications associated with steroid administration in their study (13). Khemani et al. was unable to identify any major complications through the Cochrane database (12). McCaffrey et al. noted increased glycosuria, but noted no discernable difference in mortality, incidence of sepsis, or hyperglycemia in their meta-analysis (15). It remains clear that a long-term study evaluating the risk of steroid therapy in this patient population is needed.

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