Corticosteroid Treatment of Intubated Patients at High Risk for Post-extubation Stridor

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A. Statement of Study Purpose and Rationale

Endotracheal intubation for the purposes of mechanical ventilation is a common procedure in critically-ill patients. As a patient's condition improves, the clinician must decide when it is appropriate to extubate. There are several standard weaning strategies which are followed and respiratory parameters which are measured prior to extubation. These serve to predict patients who are more likely to succeed/fail extubation and to minimize post-extubation complications.

One of the complications which occurs after extubation is upper airway edema which manifests as stridor. Estimates of the incidence of post-extubation stridor has varied from 15-40 % depending on the population studied (1,2). If the ' stridor cannot be alleviated with treatments such as racemic epinephrine and nebulizers, the patients often require re-intubation. Mortality associated with re-intubation has been estimated as high as 30-40% (3,4). Several small studies have shown that the presence of a small endotracheal cuff leak volume can predict stridor after extubation (2, 5-7).

Corticosteroids are routinely used in the treatment of conditions associated with airway inflammation like asthma and COPD. However, controversy exists regarding the effectiveness of steroid therapy prior to extubation for patients considered at high risk for stridor. There have been few prospective trials in adults investigating this therapy. Most studies that have looked at post-extubation stridor have retrospectively analyzed outcomes for sub-groups of patients who were receiving steroids during their intubation with inconclusive and some negative results (7-9). One study which investigated adults intubated for more or less than 36 hours and randomized patients in both groups to receive dexamethasone found no difference with steroid treatment in the incidence of upper airway edema (10). Another study conducted in intubated neonates at high risk for airway edema showed significantly improved outcome in the group treated with corticosteroids prior to extubation (11).

The purpose of this study is to investigate whether prophylactic treatment with corticosteroids of patients at high risk for post-extubation airway edema would reduce the incidence of stridor and its associated complications, including re-intubation and mortality. The hypothesis is that pre-treatment with corticosteroids of patients with a small endotracheal cuff leak, that is patients with evidence of upper airway edema, would improve their post-extubation outcome.

B. Study Design and Statistical Analysis

Adult patients admitted to the Medical Intensive Care Unit who are intubated will have an endotracheal cuff leak volume measured within 48 hours of their planned extubation. Those patients with a leak volume less than 150 cc Will be identified. The value of 150 cc is drawn from Miller's study which calculated a mean value of 115 cc ± 96 in patients with post-extubation stridor. Information regarding the circumstances of the patient's intubation (traumatic intubation, multiple intubations, self-extubation history) will be recorded. The decision to extubate will be made by the ICU team without input from the investigators. The patients will be randomized by an independent investigator to one of two groups, the treatment group or the control group. The treatment group will receive Solumedrol 60mg/50cc normal saline intravenously every six hours for 24 hours prior to their planned extubation (asthma sources for this) . The control group will receive placebo. The make-up of the drug and placebo will be arranged by the independent investigator to ensure blinding.

One hundred subjects will be enrolled over a one-year period. This is based on an incidence of post-extubation stridor in high risk groups of 30% (5,6,11). The expected treatment effect was drawn

from data in Couser's study. The expected risk reduction is conservatively estimated at 60%, although the study showed a relative risk reduction of 84% (11). The absolute required number of study subjects calculated from the above data is 88. A power of 80 and an alpha of 0.05 were used. A two-tailed chi square test will be used to compare the difference between the two groups.

C. Study Procedures and Study Drug

The cuff leak volume will be measured in patients who are deemed candidates for extubation. This determination will be made by the ICU team. Patients will be placed on the assist-control mode of ventilation, to insure adequate inspiratory tidal volumes (standard volume is I 0cc/kg). The patient will have endotracheal and oral secretions suctioned prior to measuring the cuff leak. The inspiratory and expiratory volumes will be recorded with the cuff s balloon inflated Then the cuff s balloon will be deflated and the inspiratory volume (which should not change) and the expiratory volume (which will change proportionately to the cuff leak) will be measured over 3 respiratory cycles. The difference between these two values will be the leak volume. The above measurements should take about 10 seconds with the cuff deflated. No discomfort is expected to be perceived by the patient, nor will it affect their plan of care.

Those patients with a leak volume less than 150cc will then be randomized to the treatment or placebo group. The treatment group will receive Solurnedrol 60mg in a 50cc bag of normal saline intravenously every 6 hours for the 24 hours prior to planned extubation. This dose is based on the standard treatment for airway inflammation in asthma. The length of treatment is much shorter than that used in asthmatic patients.

The placebo group will receive 50ccof normal saline every 6 hours prior to their extubation.

We do not anticipate any serious side effects of such a short term course of corticosteroids, unlike those seen in longer courses. All patients who are intubated in the MICU have existing intravenous access so they will not endure any extra painf~l stimuli associatedwith insertion of intravenous access.

For 24 hours after their extubation patients will then be monitored in the ICU with hourly vital signs including interval subjective assessment by the primary nurse. Any sign of respiratory distress will be fully evaluated by a physician including a lung exam to detect stridor. Stridor will be appropriately treated by the ICU staff. This is standard of care in the ICU. The patients enrollment in the study is not expected to lengthen their stay in the ICU, or interfere in their care.

D. Medical Devices

N/A

E. Study Questionnaire

N/A

F. Study subjects, inclusion and exclusion criteria

All intubated patients admitted to the MICU will be screened for the volume of their endotracheal cuff leak 48 hours prior to their planned extubation. Patients with a leak volume less than 150cc and planned extubation within the next 48 hours will be enrolled.

Patients already receiving steroids for other conditions, patients with tracheostomies, hemodynamically unstable patients, unstable ventilatory or oxygenation parameters, pregnant women, minors will be excluded.

G. Confidentiality

All data accrued will be kept in a secure location and available to investigators only.

H. Location of the study

The study will be conducted at the Columbia-Presbyterian Medical Center in the Medical Intensive Care Unit.

I. Potential Risks and Benefits

The cuff leak test is not expected to cause any harm to the patient. The only theoretical risk is that of aspiration which is minimized by suctioning of endotracheal and oral secretions prior to the test.

The administration of steroids for 24 hours is not associated with known risks of longer term steroid use. Treatment with steroids is not standard of care in patients with a small cuff leak so the control subjects are receiving the currently accepted standard of care for intubated patients.

J. Alternative therapies

There are no alternative therapies at this time.

K. Compensation and Cost to Subjects

No monetary compensation will be awarded to the patients. The patients will incur no costs.

L. Minors

N/A

M. Radiation or radioactive substances

N/A

N. References

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