Mechanical Ventilation Weaning Methods And Extubation Success

Steven Y. Chang

A. Statement Of Study Purpose And Rationale

The severely ill patient experiencing respiratory failure often requires mechanical support for ventilation. After the resolution of the acute event necessitating mechanical ventilation, patients need to be weaned off support. In a recent study by Esteban et al. (1994) of Spanish hospitals, it was found that the mean duration of mechanical ventilation in ICUs was 27.1 ± 1.4 days (range 1 to 168 days). 95% of patients required ~!3 days of support. When the patients' physicians felt that they were ready to be weaned off the ventilators, it took an average of 10.9 ± 1.1 days to eventually extubate the patients. That is, weaning took an average of 41% of ventilator time. In a study by Ely et al. (1996) in U.S. hospitals, the duration of mechanical ventilation was 4.5 to 6 days. In carefully monitored groups, the duration of weaning was decreased from 50 to 22% of the total ventilatory time. Even after extubation, 3 to 22.6% of patients require reintubation (Brochard et al., 1994; Esteban et al., 1995; Ely et al., 1996). Complications of reintubation include nosocomial pneumonia, prolonged duration of hospitalization, poor outcome and increased mortality (Torres et al., 1995). In the study by Brochard et al., (1994), low rates of reintubation were associated with strict extubation criteria in breathing trials lasting up to 24 hours. It seems possible, however, that the period of mechanical ventilation is likely increased with rigid criteria, so it would seem prudent to try to reduce the reintubation rate in order to decrease associated complications while not prolonging excessively the duration of respiratory support.

Before patients can be weaned off mechanical ventilation, several conditions must be met (Hall and Wood, 1987). The identification and normalization of neuromuscular (central or peripheral), chest wall, lung, airway and hemoglobin abnormalities must be achieved. The patient should be hemodynamically stable. Ventilatory demand should be decreased by minimizing C02 production (addressing fever, shivering, pain/agitation, trauma/burns, sepsis, overfeeding, work of breathing), and ventilatory drive and strength should be optimized (via nutrition, good mental status, correcting metabolic derangements and psychological support). Once these parameters are achieved, adequate gas exchange must be ensured. Generally accepted parameters of gas exchange might include 02 Sat ~!90% with an Fi02:!~ 40% or a Pa02/FiO2 > 200 with a PEEP of:!~ 5 cmH20 (Mancebo, 1996). After patients meet these criteria, one of two things happen: a) extubation or b) continuation to weaning which may or may not be successful.

In recent years, two notable studies have been published examining various methods of weaning from mechanical ventilation (Brochard et al., 1994; Esteban et al., 1995). At present, common modes of weaning include: spontaneous breathing on a T-piece (usually for two hours), Intermittent Mandatory Ventilation (IMV) and Pressure Support Ventilation (PSV). Brochard et al. (1994), in comparing these 3 modes of weaning, found that the use of PSV resulted in a lower number of failures, a lower probability of remaining on mechanical ventilation a shorter duration of weaning when compared to T-piece trails or IMV-based strategies. Esteban et al. (1995) examined 4 weaning techniques, IMV, PSV, intermittent two-hour trials of T-piece breathing conducted several times per day and a once-daily two-hour trial of T-piece breathing. They found that trials of spontaneous breathing were significantly better than either PSV or IMV based modes as the mean duration of weaning was shorter and the rate of successful extubations higher. What was clear from these two trials is that IMV gave consistently poor weaning results. It is not evident whether T-piece trials or PSV based protocols are equivalent or whether one is superior to the other. It is also not evident whether duration of T-piece breathing can help predict the likelihood of extubation.

With this in mind, I propose to examine the effect of duration of spontaneous T-piece breathing on predicting success of extubation. I hypothesize that an increased duration of spontaneous breathing will increase the likelihood of successful extubation. Patients will be selected when they meet pre-defined criteria for weaning and will be randomized to either undergo a 2 hour or a 4 hour spontaneous breathing trial on a T-piece on a once daily basis.

B. Description Of Study Design And Statistical Analysis

The study shall be a prospective, randomized trial that will be undertaken in the Columbia-Presbyterian Medical Center Medical Intensive Care Unit (MICU) and the Allen Pavilion ICU.

The primary endpoints of this study will be the rate of successful extubation (defined as remaining off ventilatory support ~! 48 hours or avoidance of tracheostomy) and the number of days of mechanical ventilation.

The study population will consist of patients who have received mechanical ventilation for more than 24 hours because of acute respiratory failure. To be enrolled in the protocol, patients should show an improvement in or resolution of the inciting event resulting in respiratory failure, adequate gas exchange as indicated by an 0_2 saturation ≥ 90% with an $FiO_2 \leq 40\%$ or a $PaO_2/ FiO_2 \geq 200$ with a PEEP of: ≤ 5 cmH_20; a core body temperature of ≅38'C (100.4ºF); a hemoglobin level >9 g per deciliter; and no further need for sedation or vasopressors. Clinically, physicians will need to feel that patients are stable and ready to undergo weaning from mechanical support. Patients with a tracheostomy or who have been ventilated > 14 days, and those under the age of 18 years will be excluded from the trial. Likewise, patients intubated electively for procedures, surgical or otherwise, will be excluded from the study.

Patients who are deemed appropriate for the weaning protocol will be stratified according to etiology of the primary disease process responsible for difficult weaning. Broadly, these categories will include: 1) patients with chronic pulmonary diseases (ea. - COPD, bronchiectasis, interstitial/restrictive diseases, poorly controlled asthma), 2) patients with cardiac disease (congestive heart failure, ischemic heart disease), 3) patients with neuromuscular disorders, and 4) patients with other disease processes resulting in ARDS. The patients will be assigned to undergo either two or four hour trials of breathing in a random fashion with the use of sealed envelopes, opened after patients meet weaning criteria. After enrollment in the weaning protocol, patients will be required to breathe spontaneously through a T-tube circuit with the FiO_2 to be held at the same level as during mechanical support. Tidal volume and respiratory frequency will be monitored and negative inspiratory force (NIF) will be measured three times prior to the end of the trials.

Subjects who meet at least one of the two following criteria: 1) a tidal volume of greater than 5 mL per kilogram of body weight or 350 mL (whichever is less) or 2) a ratio of respiratory rate/tidal volume of ≤ 105 AND at least one of the two following additional criteria: 3) respiratory rate of less than 38 breaths per minute or 4) NIF of at least -20 cmH20 (on the best attempt) will be extubated if they can sustain spontaneous breathing for the entirety of the 2 or 4 hour trial to which they were randomized. The trial will be terminated if the patient shows the following signs of distress: a respiratory rate of > 38 breaths per minute, 02 saturation of <90%, tachycardia >140 bpm or a sustained change in either direction of HR of >20%, systolic BP of >180 mmHg or <90 mmHg, agitation, diaphoresis, or anxiety. Assist-control or IMV ventilation (at a sufficiently high rate to allow for rest) will be reinstituted for another 24 hour period at which time another identical trial will be attempted. Subjects will then continue to undergo once daily trials of spontaneous breathing in the manner just described comparing 2-hour and 4-hour trials of spontaneous breathing via T-pieces. On the day that patients tolerate the two or four hour trial, they will be extubated. No crossovers will occur between the two groups.

Weaning will be considered a failure if reintubation is necessary within a 2 day period or if patients require tracheostomy. Weaning will be considered a success if reintubation is avoided within the 2 day period after extubation and if tracheostomy is avoided.

It is estimated that a total of 400 patients (200 in each arm) will be need to be enrolled in order to ensure 80% power on a two-tailed test to look for significance at the level of $p < 0.05$ assuming a baseline failure rate of 20% and a failure rate of only 10 % with the four hour trial of PSV.

C. Description Of Study Procedures

Informed consent is not deemed necessary for the following reasons. The research involves nominal, if any, risk to the study subjects. The weaning protocol will proceed as per published guidelines, and patients will need to meet strict criteria for entry into the study. These criteria, in fact, are often more stringent that found in practice in the MICUs of many hospitals. Patients rights will not be affected by the protocol as all subjects must eventually undergo weaning from mechanical ventilation and at present, there is not a clear cut gold standard weaning protocol. It is often difficult, if not impossible to assess the capacity of patients on ventilators as they are unable to communicate in an easy manner, and they are often on medications which may preclude clarity of thought. Finally, if there arises pertinent information, patients will be advises after participation in the study.

Once the inciting event requiring mechanical ventilation resolves, and patient meet entry criteria, they will be randomized to weaning trials consisting of spontaneous, breathing on a T-tube circuit for either two or four hour periods on a daily basis. Patient vital statistics, ABGs, 02 Saturation will be kept in accordance with standard MICU practices so this will not add any extra work for the nursing staff. All records to be copied from the patient's chart, laboratory computer system, or other patient data sources shall be performed by the investigator(s). The medical housestaff will make all decisions regarding weaning in accordance with study protocol. If there is confusion, the investigator(s) will be available to clarify issues.

Maximum duration of participation in the trial will be determined by the time that it requires for a patient to receive a tracheostomy (generally 2 to 3 weeks) in those instances in which weaning cannot be accomplished. Time of participation, in most instances, will be significantly shorter as the trial will end on an individual basis when successful extubation occurs.

Additional instrumentation of patients beyond that of the typical intubated MICU patient w ill not be necessary. For mechanically supported patients, standard procedure is to place an indwelling arterial line for blood pressure monitoring, blood drawing and arterial blood gas determinations. A noninvasive pulse oximeter will be used to monitor 02 saturation during the weaning protocol as is standard for all intubated patients.

D. Study Drugs

Not applicable.

E. Medical Devices

Not applicable, other than those standard to an ICU.

F. Study Questionnaire

Not applicable.

G. Study Subjects And Methods Of Recruitment

Potential study subjects will be identified by the attending physician or medical housestaff of the ICU as per the guidelines established under Description of Study Design and Statistical Analysis. Once identified, the subject will be evaluated for eligibility for entry into the study based on predetermined criteria.

H. Confidentility

All collected data will be strictly confidential. Patients will be assigned a study number when enrolled into the study protocol. All data will be designated by this study number. A copy of the study number and corresponding CPMC Medical Record number will be kept in a confidential file separate from the data collected and used for analysis.

I. Location Of Study

The study will be performed within the CPMC Medical Intensive Care Unit and the Allen Pavilion Intensive Care Unit.

J. Risks And Benefits

There are few added risks to the weaning protocol, given the fact that all patients must be weaned off mechanical ventilation or must be admitted to chronic ventilator facilities. The most obvious risk is that patients will not be weaned off mechanical support, but this risk is more appropriately attributed to being intubated rather than any particular weaning protocol. The once-daily trial of spontaneous T-piece breathing was shown by Esteban et al (1995) to be the most efficacious method of discontinuation of ventilator support and patients will be weaned in this manner.

The benefit to patient participation is discontinuation of mechanical ventilation in accordance to published guidelines rather than in an anecdotal and empiric manner.

K. Alternative Therapies

Other weaning modes include Pressure Support Ventilation (PSV) and Intermittent Mandatory Ventilation (IMV). IMV has been shown to be a poor weaning method by both Esteban et al. (1995) and Brochard et al. (1994). PSV, it could be argued, is equivalent to once-daily trials of spontaneous breathing on a T-tube circuit. However, T-piece breathing on a once daily basis offers ease, simplicity, and generally good patient tolerance.

L. Compensation And Costs To The Subjects

There will be no compensation for participation in this study nor shall any extra costs be accrued.

M. Minors And Research Subjects

Not applicable.

N. Radiation And Radioactive Substances

Not applicable.

O. Bibliogrgphy

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