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Weaning from mechanical ventilation in pediatric intensive care patients

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Abstract *Objective:* The development of weaning predictors in mechanically ventilated children has not been sufficiently investigated. The purpose of this study was to evaluate the accuracy of some weaning indices in predicting weaning failure.
Design: Prospective, interventional study.
Setting: University-affiliated children's hospital with a 19-bed intensive care unit.
Patients: 84 consecutive infants and children requiring mechanical ventilation for at least 48 h and judged ready to wean by their primary physicians.
Interventions: Patients who met the criteria to start weaning underwent a trial of spontaneous breathing lasting up to 2 h. Bedside measurements of respiratory function were obtained immediately before discontinuation of mechanical ventilation and within the first 5 min of spontaneous breathing. The primary physicians were blinded to those measurements, and the decision to extubate a patient at the end of the spontaneous breathing trial or reinstitute mechanical ventilation was made by them. Failure to wean was defined as the requirement for mechanical ventilation at any time during the trial of spontaneous breathing (trial failure) or needing reintubation within 48 h of extubation (extubation failure).
Measurements and main results: Seventy-five patients had neither signs of respiratory distress nor deterioration in gas exchange during the trial and were extubated. Twelve patients required reintubation within 48 h. In 9 patients, mechanical ventilation was reinstituted after a median duration of the spontaneous breathing trial of 35 min. The only independent predictor of trial failure was tidal volume indexed to body weight [odds ratio 2.60, 95 % confidence interval (CI) 1.40 to 24.9]. The only independent predictor of extubation failure was frequency-to-tidal volume ratio indexed to body weight (odds ratio 1.23, 95 % CI 1.11 to 1.36). The sensitivity, specificity, and positive and negative predictive values to predict weaning failure were calculated for each of the above variables. These values were 0.48, 0.86, 0.53, and 0.83, respectively, for a frequency-to-tidal volume ratio higher than 11 breaths/min per ml per kg and 0.43, 0.94, 0.69, and 0.83, respectively, for a tidal volume lower than 4 ml/kg.
Conclusions: Three-quarters of ventilated children can be successfully weaned after a trial of spontaneous breathing lasting 2 h. Both tidal volume and frequency-to-tidal volume ratio indexed to body weight were poor predictors of weaning failure in the study population.

Key words Weaning · Mechanical ventilation · Children · Weaning indices

Introduction

Mechanical ventilation is frequently lifesaving but it also involves the risk of serious complications, which markedly increases the cost of care for ventilator-dependent patients and their morbidity [1]. Therefore, every effort should be made to discontinue mechanical ventilation as soon as the patient can protect the airway and sustain spontaneous ventilation. Selecting what is the most appropriate time for extubation is one of the most difficult decisions that physicians must make. On the one hand, mechanical ventilation is unnecessarily prolonged and the risk for nosocomial pneumonia increased if extubation is not performed at the appropriate time. On the other hand, premature extubation involves the risk of emergent reintubation.

The purpose of having weaning parameters is to identify those patients who are likely to fail a weaning trial or will need reintubation, so as to avoid the risks associated with each of the above events. The criteria for successful weaning are fairly homogeneous in the majority of studies evaluating weaning parameters (patient remains exubated for 24 to 72 h after mechanical ventilation is discontinued). However, the criteria for weaning failure are different from study to study. Whereas in several studies weaning failure refers only to patients needing reintubation [2–6], in other series it refers to patients who were not extubated because they fulfilled objective criteria for termination of a weaning trial and to patients who were reintubated [7–11], and the rate of reintubation is not given in some papers [9–11].

There is little information about weaning parameters in mechanically ventilated children [6, 12, 13]. It is possible that the accuracy of indices predicting weaning failure substantially differs according to what these indices are predicting, whether it is the failure of a weaning attempt or the need for reintubation. To investigate this, some indices associated with weaning failure were evaluated prospectively in mechanically ventilated infants and children, with the aim of determining their accuracy in predicting weaning failure and whether predicting weaning trial failure is different from predicting extubation failure.

Patients and methods

Eighty-four infants and children requiring mechanical ventilation for at least 48 h and judged ready to wean by the primary physicians were recruited from the medical-surgical intensive care unit of the Children's Hospital R. Gutierrez, Buenos Aires, from March 1995 to April 1996. The median age was 7.5 months (25th, 75th percentiles: 4, 28 months). There were 43 males and 41 females. The median weight of the patients was 7.3 kg (25th, 75th percentiles: 4.5, 13.2 kg).

The clinical diagnoses of the patients were as follows: pneumonia ($n = 19$), bronchiolitis ($n = 21$), acute respiratory distress syndrome ($n = 2$), pulmonary contusion ($n = 2$), septic shock ($n = 12$), postoperative state ($n = 8$), meningitis or encephalitis ($n = 5$), status epilepticus ($n = 3$), head trauma ($n = 3$), other ($n = 9$).

The patients received mechanical ventilation for a median of 8.5 days (25th, 75th percentiles: 5, 14.5 days) before weaning was started. At the time of disconnection, patients were being ventilated in assist-control ventilation ($n = 36$) or intermittent mandatory ventilation ($n = 48$) with any of the following ventilations: Bird 6400 (Bird, California), Dräguer Evita (Dräguer, Germany), Sechrist IV-100B (Sechrist, California). The decision to start weaning was made by the primary physicians and was based on the following criteria: improvement or resolution of the underlying cause of acute respiratory failure; pharmacological control of bronchoconstriction; absence of respiratory acidosis; a fractional inspired oxygen of (FIO_2) ≤ 0.40, a positive end-expiratory pressure of PEEP ≤ 5 cmH_2O, and a peak inspiratory pressure < 25 cmH_2O; body temperature $< 38.5\,^{\circ}C$; no sedation, correction of electrolyte disorders; and absence of neuromuscular blockade 24 h prior to the start of weaning. Patients with neuromuscular disease or a tracheostomy were excluded. The study was approved by the institutional ethics committee of our hospital and the need for informed consent was waived.

Protocol

Patients enrolled in the study underwent a trial of spontaneous breathing through a T-piece circuit lasting up to 2 h. The FIO_2 was set at the same level as that used during mechanical ventilation (0.38 ± 0.09) and held constant over the trial.

The following variables were measured during mechanical ventilation: peak inspiratory pressure, tidal volume, respiratory rate, FIO_2, heart rate, and blood pressure. Tidal volume and peak inspiratory pressure delivered by the ventilator to the patient were measured by a pneumotachograph (Bicore CP 100, Irving, Calif., USA) connected to the endotracheal tube and were standardized to body weight. None of the above measured variables were included in the data analysis because there were no differences among patients failing weaning and patients successfully weaned. A sample of arterial blood was collected for blood analysis while the patient was receiving mechanical ventilation, and pulmonary gas exchange was assessed by calculation of the arterial oxygen tension (PaO_2)/FIO_2 ratio and the PaO_2/alveolar oxygen tension (P_AO_2) ratio.

The following measurements were taken within the first 5 min of spontaneous breathing through a T-piece after mechanical ventilation was discontinued: respiratory rate, exhaled minute volume, and maximal inspiratory pressure. Exhaled minute volume was measured with a Wright spirometer (Ferraris Medical, London, UK) over 1 min. Tidal volume was calculated by dividing exhaled minute volume by respiratory frequency and was indexed to body weight. Maximal inspiratory pressure was measured by occluding the airway for at least 20 s using a one-way valve [14]. Frequency-to-tidal volume ratio (f/V_T ratio) was calculated by dividing respiratory rate during spontaneous breathing by tidal volume indexed to body weight.

The primary physicians were blinded to the measurements taken within the first 5 min of spontaneous breathing, and they made the decision to extubate the patient at the end of the spontaneous breathing trial or to reinstitute mechanical ventilation. They terminated the spontaneous breathing trial if a patient had any of the following signs: (1) respiratory rate of more than 62, 52, or 40 breaths/min in patients aged 12 months or less, 13 to 48 months, and 49 to 180 months, respectively; (2) mean blood pressure lower than 45, 55, or 65 in patients aged 12 months or less, 13 to

Table 1 Characteristics of the study population at baseline according to weaning outcome. Values are median (25th centile, 75th centile)

Characteristics	Successful extubation ($n = 63$)	Reintubation ($n = 12$)	Trial failure ($n = 9$)	p
Age (months)	8 (4–33)	3 (3–5.5)	8 (4–31)	< 0.04[a]
Body weight (kg)	7.5 (5.5–14.5)	4.3 (3.7–5.9)	5.8 (4.5–14)	< 0.03[b]
Duration of ventilator support before weaning (days)	8 (4–13)	9.5 (8–17)	15 (10–23)	< 0.03[b]
PaO_2/FIO_2 ratio	295 (213–377)	327 (272–504)	235 (222–280)	0.23
PaO_2/PAO_2 ratio	0.48 (0.4–0.6)	0.55 (0.5–0.6)	0.40 (0.4–0.4)	0.27
Tidal volume (ml/kg)	6.8 (4.8–8)	4.3 (3.8–5.6)	3.8 (2.6–4.4)	< 0.0002[a,b]
Minute volume (ml/kg)	245 (180–320)	245 (175–304)	204 (100–233)	0.61
Respiratory frequency (breaths/min)	40 (31–50)	50 (39–62)	40 (32–54)	0.23
Maximal inspiratory pressure (cmH_2O)	45 (36–60)	35 (27–50)	40 (40–60)	0.16
f/V_T ratio (breaths/min per ml per kg)	6.5 (4.3–8.7)	10.9 (8.3–13.7)	10 (8–15)	< 0.001[a,b]

[a] Significant difference for the comparison of successful extubation with reintubation groups
[b] Significant difference for the comparison of successful extubation and trial failure groups

48 months, or 49 to 180 months, respectively; (3) increase in heart rate of more than 20 % with respect to the heart rate on mechanical ventilation; (4) signs of increased respiratory work; (5) PaO_2 < 60 mm Hg or arterial oxygen saturation < 90 %; (6) arterial pH ≤ 7.30; (7) partial pressure of arterial carbon dioxide > 50 mm Hg or an increase ≥ 8 mm Hg. The decision to reintubate was based on clinical examination, blood gases, or both.

Classification of weaning outcomes

Weaning was considered successful if extubation was performed after a 2-h trial of spontaneous breathing and reintubation was not required within 48 h of extubation (successful extubation group).

Failure to wean was defined as requiring reinstitution of mechanical ventilation at any time during the trial of spontaneous breathing (trial failure group) or needing reintubation within 48 h of extubation after a successful breathing trial (reintubation group).

Data analysis

Data are shown as medians with the first and third quartiles, or proportions with 95 % confidence intervals (CI). The chi-square test with Yates' correction was used to compare categorical data. The Kruskal-Wallis test was used to compare continuous variables among the following group: successful extubation group, trial failure group, reintubation group.

Multivariate logistic regression analysis was used to determine which variables were useful to predict failure of spontaneous breathing and which were useful to predict reintubation. A stepwise discriminant analysis was used including the following covariates: age, sex, number of days of ventilatory support prior to weaning, PaO_2/FIO_2 ratio, PaO_2/PAO_2 ratio, spontaneous tidal volume, spontaneous respiratory frequency, spontaneous exhaled minute volume f/V_T ratio, and maximal inspiratory pressure. Backward elimination was used to reduce the model to the subgroup of factors that made statistical contributions to reconnection and reintubation. Predictive value was calculated for those factors associated with trial failure or extubation failure. The values selected to evaluate the accuracy of tidal volume and f/V_T ratio as predictors of weaning failure were those that yielded the least false classifications. The predictive value is represented as sensitivity (TP/TP + FN), specificity (TN/TN + FP), positive predictive value (TP/TP + FP), and negative predictive value (TN/TN + FN), where TP (true positive) is defined as occurring when a patient's test predicted weaning failure and weaning actually failed, TN (true negative) when a test predicted weaning success and weaning actually succeeded, FP (false positive) when a test predicted weaning failure but weaning succeeded, and FN (false negative) when a test predicted weaning success but weaning failed.

The data were processed using the software CSS/Statistical 3.1 (StatSoft, Tulsa, Okla., USA) and True Epistat 5.0.

Results

Of the 84 patients, 75 (89 %; 95 % CI: 80 to 95 %) successfully underwent a 2-h trial of spontaneous breathing and were immediately extubated. Of these 75 patients, 12 (16 %; CI 9 to 27 %) required reintubation within 48 h. The reasons for reintubation were as follows: pneumonia in 2 patients, atelectasis 2, upper airway obstruction 2, and decreased level of consciousness 4. In 2 patients it was thought that the original respiratory process was the reason for reintubation.

In 9 patients, the trial of spontaneous breathing was stopped after a median time of 35 min (25th, 75th percentiles: 30, 120 min) and mechanical ventilation was reinstituted. The reasons for trial failure were as follows: arterial oxygen saturation < 90 % in 4 patients, respiratory frequency > 62 in 2, mean arterial pressure < 45 mm Hg in 1, and signs of increase respiratory work in 2.

The characteristics of the patients according with the weaning outcomes are shown in Table 1. Reintubated patients were significantly younger than patients suc-

Table 2 Accuracy of the frequency-to-tidal volume ratio f/V_T indexed to body weight to predict weaning failure (*NPV* negative predictive value, *PPV* positive predictive value)

	Trial failure		Trial success
$f/V_T > 11$	4 (TP)		15 (FP)
$f/V_T \leq 11$	5 (FN)		60 (TN)
Sensitivity	Specificity	PPV	NPV
0.44	0.80	0.21	0.92
	Extubation failure		Extubation success
$f/V_T > 11$	6 (TP)		9 (FP)
$f/V_T \leq 11$	6 (FN)		54 (TN)
Sensitivity	Specificity	PPV	NPV
0.50	0.86	0.40	0.90
	Weaning failure		Weaning success
$f/V_T > 11$	10 (TP)		9 (FP)
$f/V_T \leq 11$	11 (FN)		54 (TN)
Sensitivity	Specificity	PPV	NPV
0.48	0.86	0.53	0.83

Table 3 Accuracy of tidal volume V_T indexed to body weight to predict weaning failure (*NPV* negative predictive value, *PPV* positive predictive value)

	Trial failure		Trial success
$V_T \leq 4$ ml/kg	5 (TP)		8 (FP)
$V_T > 4$ ml/kg	4 (FN)		67 (TN)
Sensitivity	Specificity	PPV	NPV
0.55	0.89	0.38	0.94
	Extubation failure		Extubation success
$V_T \leq 4$ ml/kg	4 (TP)		4 (FP)
$V_T > 4$ ml/kg	8 (FN)		59 (TN)
Sensitivity	Specificity	PPV	NPV
0.33	0.94	0.50	0.88
	Weaning failure		Weaning success
$V_T \leq 4$ ml/kg	9 (TP)		4 (FP)
$V_T > 4$ ml/kg	12 (FN)		59 (TN)
Sensitivity	Specificity	PPV	NPV
0.43	0.94	0.69	0.83

cessfully extubated and were not different from patients failing the spontaneous breathing trial. The duration of ventilatory support before weaning was longer in patients who failed the spontaneous breathing trial compared to patients who were successfully extubated. There were no differences in the pulmonary gas exchange variables among the three groups. Tidal volume was significantly lower and f/V_T ratio, both indexed to body weight, was significantly higher in patients reintubated and in patients failing the trial of spontaneous breathing when compared with patients successfully extubated.

The multivariate regression analysis revealed one factor that was associated with the risk of trial failure: tidal volume indexed to body weight (odds ratio 2.60; 95 % CI 1.40–24.9, for each decrement of 1 ml/kg), and one factor that was associated with the risk of reintubation: f/V_T ratio indexed to body weight (odds ratio 1.23; 95 % CI 1.11–1.36, for each increment of 1 point). These results mean that the probability of failing a trial of spontaneous breathing increases 2.6 times as tidal volume decreases by 1 ml/kg and the probability of needing reintubation after discontinuation of mechanical ventilation increases 23 % as f/V_T ratio indexed to body weight increases by 1 breath/min per ml per kg.

The accuracy of tidal volume and f/V_T ratio to predict trial failure, extubation failure, or weaning failure is shown in Tables 2 and 3. The threshold values we used seem to be useful to identify patients with a high probability of trial success and extubation success. However, they are not useful to identify patients who will fail the trial of spontaneous breathing or will need reintubation, since almost half of patients who had an f/V_T ratio > 11 breaths/min per ml per kg or a tidal volume > 4 ml/kg tolerated the spontaneous breathing trial and were not reintubated after extubation.

Discussion

This study produced two major findings. First, ventilator support can be discontinued in three-quarters of ventilated children after a trial of spontaneous breathing lasting 2 h. Second, the f/V_T ratio and tidal volume, both indexed to body weight, are poor predictors of weaning failure.

It has been recently reported by several authors that extubation can be safely performed in adult patients when they are able to undertake a trial of spontaneous breathing lasting 2 h without respiratory distress or significant deterioration in gas exchange [15–20]. The current study is the first one to report those findings in adult patients in children. The extubation failure rate within 48 h after extubation that we found is very similar to that reported in infants and children, which has ranged from 16 to 22 % [6, 13].

Patients receiving mechanical ventilation are at risk of several complications [1]. The best way to prevent those complications is to reduce the duration of ventilatory support as much as possible. This should not be achieved at the expense of premature extubations, because it is known that reintubation increases the risk of nosocomial pneumonia [21] and is associated with an increase in mortality [19]. Some weaning parameters allow clinicians to identify patients with a probability of weaning success higher than 70 % [10]; thus, deciding to attempt weaning in patients who fulfill those parameters is an easy task. The problem is how should we deal

with patients who, according to clinical judgment, are ready for weaning but who don't fulfill the weaning parameters. If the weaning parameters are poor predictors of weaning failure, most patients would be ventilated for an unnecessarily long period in the case where an attempt at weaning was delayed because of the lack of favorable weaning criteria. To avoid this, it would be desirable to have weaning parameters which will identify patients with a high probability of weaning failure.

Khan et al. [6] evaluated the predictors of extubation success and failure in a group of 208 mechanically ventilated infants and children. They found that the f/V_T ratio did not show any trend in failure rate with decreasing or increasing values. On the contrary, extubation failure increased significantly with decreasing tidal volume indexed to body weight, from 10% with a tidal volume ≥ 6.5 ml/kg to 26% with a tidal volume ≤ 3.5 ml/kg. However, from a clinical point of view, this latter cutoff value does not seem to be a helpful threshold to identify patients with a high risk of extubation failure.

A consistent finding in all the studies evaluating the f/V_T ratio as a predictor of weaning outcome is that it has a high positive predictive value ranging from 0.78 to 0.92 [5, 7, 10, 15, 16], which means that an f/V_T ratio ≤ 100 breaths/min per l is helpful to identify patients with a high probability of weaning success or extubation success. We have also found that children with an f/V_T ratio indexed to body weight ≤ 11 breaths/min per ml per kg have a probability of successful weaning trials and successful extubation higher than 0.9.

Yang and Tobin [10] demonstrated, in a group of 64 medical patients, that the f/V_T ratio measured while patients breathed spontaneously for 1 min through an endotracheal tube had a very high negative predictive value for predicting weaning outcome. Ninety-five percent of patients (19 out of 20 patients) with an f/V_T ratio > 105 failed weaning. Several subsequent reports have noted lower negative predictive values for the f/V_T ratio, ranging from 0.27 to 0.66 [5, 15, 16]. In a prospective study of 94 patients with an f/V_T measured at the onset of a weaning trial that resulted in extubation, Epstein [5] found a negative predictive value of 0.40 (4 of 10 patients with an $f/V_T > 100$ failed extubation), and, in a subsequent study, a negative predictive value of 0.27 (8 of 29 patients with an f/V_T ratio > 100 failed extubation) [16].

The value of a diagnostic test depends not only on its sensitivity and specificity, but also on the prevalence of the disease in the population being tested. The "pretest probability of weaning failure" in a population like ours is 0.25. The "posttest probability of weaning failure" in patients with an f/V_T ratio > 11 breaths/min per ml per kg would be 0.53. The precision of the weaning failure prediction improves when that threshold value of the f/V_T ratio is used; however, our opinion is that the addition of such a weaning index to the other weaning criteria used in our study population is not an aid in the decision-making process to start weaning, because almost 50% of patients who might have a chance of weaning success would not be considered for weaning if the decision to start weaning was based on values of an f/V_T ratio < 11 breaths/min per ml per kg.

In the light of our results and those reported by others [5, 6, 15, 16], it seems that an elevated f/V_T ratio is not an indication for delaying trials of weaning or extubation after a successful trial of spontaneous breathing. It is our contention that a trial of spontaneous breathing lasting up to 2 h should be attempted in every patient who is clinically stable with resolution of the underlying cause of acute respiratory failure and adequate gas exchange, irrespective of values of weaning parameters such as the f/V_T ratio or tidal volume. If a patient does not show signs of respiratory distress during the trial or a deterioration in gas exchange, the probability of successful extubation will range from 0.60 to 0.80.

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