The impact of daily evaluation and spontaneous breathing test on the duration of pediatric mechanical ventilation: A randomized controlled trial*

Flávia K. Foronda, MD; Eduardo J. Troster, MD, PhD; Julio A. Farias, MD; Carmen S. Barbas, MD, PhD; Alexandre A. Ferraro, MD, PhD; Lucília S. Faria, MD; Albert Bousso, MD, PhD; Flávia F. Panico, MD; Artur F. Delgado, MD, PhD

Objectives: **To assess whether the combination of daily evaluation and use of a spontaneous breathing test could shorten the duration of mechanical ventilation as compared with weaning based on our standard of care. Secondary outcome measures included extubation failure rate and the need for noninvasive ventilation.**

Design: **A prospective, randomized controlled trial.**

Setting: **Two pediatric intensive care units at university hospitals in Brazil.**

Patients: **The trial involved children between 28 days and 15 yrs of age who were receiving mechanical ventilation for at least 24 hrs.**

Interventions: **Patients were randomly assigned to one of two weaning protocols. In the test group, the children underwent a daily evaluation to check readiness for weaning with a spontaneous breathing test with 10 cm H_2O pressure support and a positive end-expiratory pressure of 5 cm H_2O for 2 hrs. The spontaneous breathing test was repeated the next day for children who failed it. In the control group, weaning was performed according to standard care procedures.**

Measurements and Main Results: **A total of 294 eligible children were randomized, with 155 to the test group and 139 to the control group. The time to extubation was shorter in the test group, where the median mechanical ventilation duration was 3.5 days (95% confidence interval, 3.0 to 4.0) as compared to 4.7 days (95% confidence interval, 4.1 to 5.3) in the control group (p = .0127). This significant reduction in the mechanical ventilation duration for the intervention group was not associated with increased rates of extubation failure or noninvasive ventilation. It represents a 30% reduction in the risk of remaining on mechanical ventilation (hazard ratio: 0.70).**

Conclusions: **A daily evaluation to check readiness for weaning combined with a spontaneous breathing test reduced the mechanical ventilation duration for children on mechanical ventilation for >24 hrs, without increasing the extubation failure rate or the need for noninvasive ventilation. (Crit Care Med 2011; 39:2526–2533)**

Key Words: artificial, respiration; intensive care units; pediatrics; randomized controlled trial; respiratory insufficiency; ventilator weaning

Acute respiratory insufficiency is common in the pediatric population. It is estimated that two to three million children a year worldwide die of respiratory causes (1).

Undoubtedly, mechanical ventilation (MV) is an important medical intervention capable of reducing morbidity and mortality in this population, especially among severe cases (2). However, it remains a practical challenge to accurately predict when a patient is ready to sustain spontaneous breathing and successfully discontinue MV (2–5).

Extubation failure, which is defined as the need for reintubation and reestablishment of MV within 48 to 72 hrs after the tracheal cannula is removed (6–10), is associated with a poor prognosis and an increased mortality rate (11, 12). In the pediatric population, extubation failure rates vary between 16% and 19% (6–9). Nevertheless, ventilation times are often extended unnecessarily. In a previous study in which 136 children underwent unplanned extubation, most of the patients did not require reintubation (12).

Extended MV periods are associated with an increased risk of complications, such as nosocomial pneumonia (13–16), ventilator-induced lung injury (17, 18), airway injuries (19), and an increased need for sedatives. Thus, MV should be discontinued as soon as possible.

However, successful early extubation is difficult because extubation criteria may vary. Thus, the continued search for criteria to indicate the correct time to end MV is a priority. Several previous studies conducted in the pediatric population have tried to define predictors of successful extubation. However, it has not been possible to determine which set of parameters accurately predicts successful extubation (6, 8, 9, 20).

The spontaneous breathing test (SBT) was developed as an attempt to identify patients who are ready to discontinue ventilation (21, 22). The test aims at monitoring signs of respiratory muscle fatigue while the patient is still intubated. A previous study showed that SBT performed with a T-piece was able to predict successful extubation in 70% of intubated children (20). In a subsequent work, the

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From the Intensive Care Unit (FKF, LSF), Hospital Sírio Libanês, São Paulo, Brazil; Pediatric Department (FKF, EJT, AAF, LSF, FFP, AFD), and Pneumology Department (CSB), Hospital das Clínicas, Medical School of São Paulo University, São Paulo, Brazil; Intensive Care Unit (EJT, AB, FFP), Hospital Albert Einstein, São Paulo, Brazil; Intensive Care Unit (JAF), Hospital de Niños R Gutiérrez, Buenos Aires University, Buenos Aires, Argentina; and Intensive Care Unit (AB), Hospital Universitário, Medical School of São Paulo University, São Paulo, Brazil.

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For information regarding this article, E-mail: flikrepel@foronda.com.br

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same research team showed that SBT performed with a T-piece or pressure support was equally effective in identifying these patients, with both predicting the same extubation failure rates (11).

In adults, the use of daily evaluation combined with an SBT has been shown to reduce MV duration, treatment costs, and treatment-associated complications (23).

Some authors (2, 24, 25) have proposed a combination of daily evaluation and SBT use as a possible way to reduce ventilation times. However, to our knowledge, this strategy has not been formally investigated in the pediatric population. We conducted a randomized controlled trial to determine whether the combination of a daily evaluation and SBT use could shorten the MV duration as compared with weaning based on standard care procedures in a pediatric population. We also determined the extubation failure rate, the need for postextubation noninvasive ventilation (NIV), the occurrence of ventilator-associated pneumonia and accidental extubation, and the factors associated with MV duration.

METHODS

Patients

This study was approved by the institutional review boards of the participating hospitals, and written informed consent was obtained from the parents or guardians of all patients before enrollment.

Eligible patients were children of both genders, aged between 28 days and 15 yrs, who were admitted to the pediatric intensive care units (ICUs) of the Hospital das Clínicas da Universidade de São Paulo and Hospital Universitário in Sao Paulo, Brazil, between July 2007 and July 2009, and who had been receiving MV for >24 hrs. The exclusion criteria were as follows: intubation due to upper airway obstruction (UAO); the presence of diaphragmatic hernia or paralysis; chronic MV use; cyanotic congenital heart disease; primary pulmonary hypertension; neuromuscular disease; or tracheostomy. Patients on chronic MV were defined as those who were dependent on invasive or noninvasive ventilation before ICU admission, including children from other units at the same hospital, other hospitals, or home-care units. Patients could be enrolled in the study only once during their hospital stay, and only the first intubation was considered for analysis in patients who required reintubation. The study is registered in the International Standard Randomized Controlled Trial Number Register (ISRCTN37806223).

Overall Study Design

The design of this study is illustrated in Figure 1. Patients were randomly assigned to weaning following a protocol that combined the daily screening of SBT (test group), or weaning based on standard care procedures (control group). In the test group, the SBT was performed on patients after they fulfilled predetermined criteria on the daily evaluation. This procedure was performed every morning until the patient was extubated by fellows who were specifically trained for this task before study initiation, and then every 3 months; these fellows were not involved in the decision to extubate patients. In addition, new cases from both participating institutions were evaluated once a week to check whether the eligibility criteria had been followed at enrollment and whether the daily evaluations were being performed appropriately. The two study groups were treated by the same medical team, and team members were unaware of the group to which the patients had been randomized until the patients passed the daily evaluation and the SBT was indicated. In the control group, weaning was performed at the

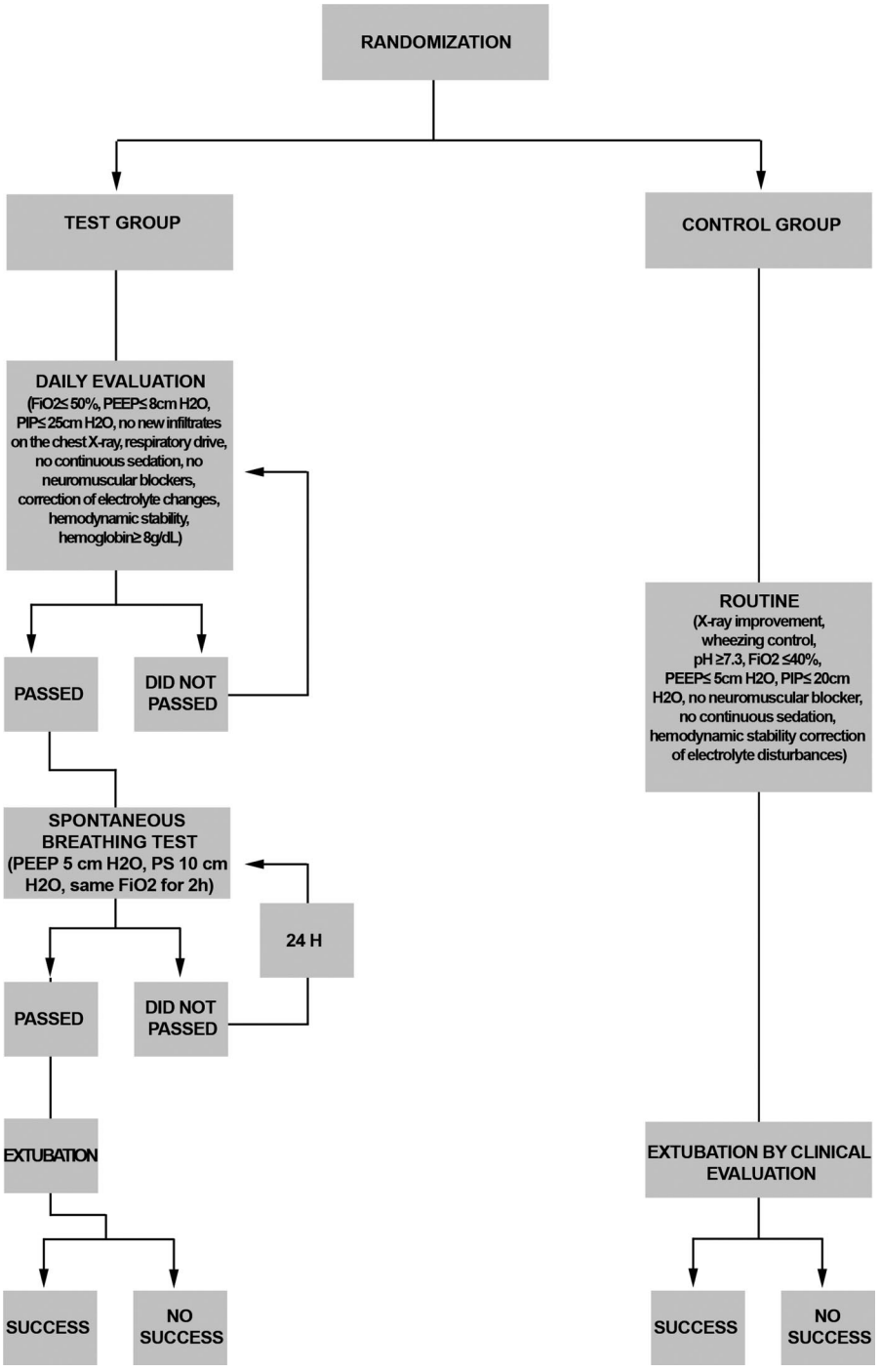

Figure 1. Study design. *PEEP*, positive end-expiratory pressure; *PIP*, peak inspiratory pressure; *PS*, pressure support.

discretion of the attending physician in charge of the medical team, with no influence from study protocols. The ventilators used in the study were the Newport E500 (Newport Medical Instruments, Newport Beach, CA), Servoi (Siemens, Elema, Solna, Sweden), and Evita 4 (Dräger, Lübeck, Germany).

To control for the differences between routine procedures at each ICU, randomization was stratified according to hospital and carried out using opaque plastic bags containing varying numbers (i.e., six, 12, or 20) of sealed envelopes prepared by staff who were not involved with patient care. The same fellow in charge of the daily evaluations, with no knowledge from the medical team, randomized patients in a 1:1 ratio.

Study Procedures

To pass the daily evaluation and undergo the SBT, patients had to meet the following criteria: F_{IO_2} ≤50%; positive end-expiratory pressure (PEEP) ≤8 cm H_2O; peak inspiratory pressure (PIP) ≤25 cm H_2O; an absence of new infiltrates on the chest radiograph; the presence of respiratory drive; no continuous sedation; no use of neuromuscular blockers in the last 24 hrs; correction of electrolyte changes (calcium, magnesium, phosphorus, and potassium); hemodynamic stability (doses of sodium nitroprusside, dopamine, or dobutamine <10 μg/kg/min); and hemoglobin ≥8 g/dL. Patients who met these criteria underwent SBT with a PEEP of 5 cm H_2O, pressure support ventilation of 10 cm H_2O, and the F_{IO_2} that was used before the test for a period of 2 hrs. The test was interrupted in the presence of any signs of intolerance, including respiratory or heart rate increase 20% above the initial values, signs of increased respiratory work (i.e., use of accessory muscles or paradoxic respiration), changes in the level of consciousness, blood pressure <fifth percentile for patient's age, arterial blood oxygen saturation <90%, or P_{aCO_2} >50 mm Hg (or an increase >10 mm Hg in 1 hr in patients with chronic lung disease). Arterial blood gas samples were collected before the SBT and in the first hour of the test. Extubation was performed in patients who did not meet any criteria for a failed test. Otherwise, MV was reestablished using the previous parameters, and the test was repeated 24 hrs later (Fig. 1).

In the control group, weaning was performed according to the routine procedures of each ICU, with no SBT. Briefly, the ventilator mode and settings were at the discretion of the attending physician. Pressure-based ventilatory modes were more frequently used in our institution, although other modes were available. The most frequently used modes were pressure support, synchronized intermittent mandatory ventilation, and pressure-controlled ventilation, the latter of which was used more often in severe cases (26). Respiratory frequency and PIP reductions were performed according to the presence of ventilatory parameters, including increased chest cage expansion, increased exhaled tidal volume, and reduced P_{aCO_2} or end-tidal CO_2. F_{IO_2} and PEEP were reduced according to patient oxygenation to maintain arterial oxygen saturation between 92% and 98%.

Weaning and Extubation

Until patients in the test group met the criteria for the SBT, weaning was similar to that of the control group and was initiated according to clinical and blood-gas criteria. The criteria routinely used in the two ICUs for extubating patients from MV included the following: resolution of the cause that led to intubation, pharmacologic control of wheezing, absence of respiratory acidosis (pH <7.3), F_{IO_2} ≤40%, PEEP ≤5 cm H_2O, PIP <20 cm H_2O, body temperature <38.5°C, no need for continuous sedation, hemodynamic stability, correction of electrolyte disturbances, and the absence of a neuromuscular blocker in the last 24 hrs.

After extubation, patient progress was monitored for 48 hrs. A failed extubation was defined as the need for reintubation within this period. Reintubation was indicated when patients met two or more clinical criteria (i.e., increase in respiratory rate ≥40% of the normal rate for age, apnea >20 secs, subdiaphragmatic or suprasternal retractions, or cyanosis) or blood-gas criteria (P_{aO_2}/F_{IO_2} ratio <200 or P_{aCO_2} >50 mm Hg with pH <7.35). NIV was indicated in cases of respiratory distress, hypoxemia (pulse oxygen saturation <90%), and decreased level of consciousness leading to inadequate respiratory effort, UAO, or cardiovascular insufficiency. Patients were reintubated and placed on MV if they were unable to maintain P_{aO_2} ≥80 mm Hg with F_{IO_2} ≤60% after an attempt at NIV with two different levels of pressure.

Data Collection and Statistical Analysis

For all patients, the following variables were collected and analyzed: age, gender, primary diagnosis, comorbidities, indication for MV, Pediatric Risk of Mortality II score, Pediatric Index of Mortality 2, respiratory complications, duration of MV, ventilatory parameters, medication use, extubation failure, and use of NIV.

For sample size calculation, given our previous experience at the participating ICUs, the inclusion of 133 patients per group would give the study a power of 80% in detecting an increase in the proportion of patients successfully extubated at 4 days, from 35% in the control group to 50% in the test group based on a one-sided Type I error of 5%. The study was analyzed on an intention-to-treat basis.

The Kolmogorov-Smirnov test was used to assess whether continuous variables were normally distributed. Continuous variables with non-normal distribution were summarized as medians and interquartile ranges, and comparisons between groups were conducted using the Mann-Whitney *U* test. For categorical data, percentages and their 95% confidence intervals were calculated, and comparisons between groups were conducted using Pearson's chi-squared test or Fisher's exact test, as appropriate.

Kaplan-Meier survival curves were used to estimate the time to extubation in both groups, with comparisons based on the log-rank test. Time to extubation was defined as the elapsed time between the initiation of ventilation and the first extubation. Only patients who were extubated were considered for the analysis of MV duration and for the analysis of the secondary outcomes. Those who died without ever being weaned from the ventilator were not considered for the analysis of these outcomes. A 30-day follow-up period was considered for analysis. Patients on MV for >30 days were considered as weaning failures and thus censored in the analysis. The Cox proportional-hazards regression model was used to investigate the predictive role of variables with $p < .20$ using univariate analyses.

Statistical analysis was conducted by a professional research organization and performed using SPSS software, version 17. Two-sided *p* values <.05 were considered significant.

RESULTS

Patient Characteristics

A total of 776 patients were screened, but 464 were considered ineligible for the study before randomization (Fig. 2). Of the 312 children who were randomized to the study, 18 were not eligible to participate; 11 patients were on ventilation for <24 hrs, three had neuromuscular disease, two had UAO, a single patient was older than 15 yrs, and for another patient, the index intubation was the second intubation. Eight of these protocol violations occurred in the test group and ten in the control group (Fig. 2). These ineligible patients were therefore not included in the analysis.

Of the 294 eligible children randomized to the study, 155 were assigned to the test group and 139 were assigned to the control group. Patients had a median age of 11 months, and 54.8% were male. Table 1 summarizes demographic and clinical baseline characteristics of these patients. The groups did not differ in terms of age, gender, Pediatric Risk of Mortality II and Pediatric Index of Mortality 2 scores, or primary diagnoses, with the exception of

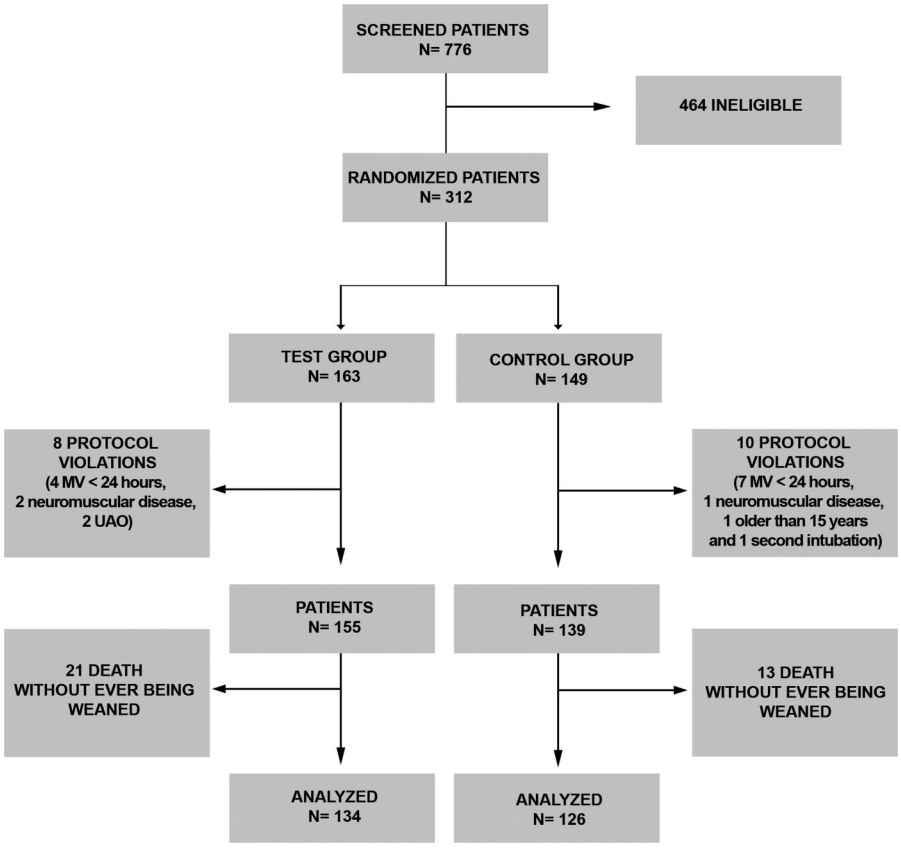

Figure 2. Patient flow. *MV,* mechanical ventilation; *UAO,* upper airway obstruction.

Table 1. Demographic and clinical baseline characteristics of the patients enrolled according to the study group

Characteristics	Test Group (n = 155)	Control Group (n = 139)	*p*
Age (yrs)[a]	0.922 [0.303; 3.483]	0.933 [0.344; 3.399]	.918
Pediatric Risk of Mortality II[a]	0.050 [0.025; 0.118]	0.051 [0.128; 0.275]	.756
Pediatric Index of Mortality 2[a]	0.098 [0.040; 0.244]	0.080 [0.036; 0.177]	.148
Male[b]	86 (55.5%)	75 (54%)	.793
Immunodeficiency[b]	7 (4.5%)	6 (4.3%)	.934
Congenital Heart Disease[b]	9 (5.8%)	8 (5.8%)	.985
Genetic Disorders[b]	7 (4.5%)	7 (5%)	.834
Malignant Tumors[b]	12 (7.7%)	3 (2.2%)	.030
Neurologic Disorders[b]	17 (11%)	9 (6.5%)	.176
Liver Disease[b]	13 (8.4%)	20 (14.4%)	.104
Chronic Lung Disease[b]	20 (12.9%)	19 (13.7%)	.847
Leukemia[b]	5 (3.2%)	6 (4.3%)	.623
Main Indications for Mechanical Ventilation			
Congestive heart failure[b]	4 (2.6%)	9 (6.5%)	.105
Wheezing[b]	34 (21.9%)	31 (22.3%)	.940
Septic shock[b]	35 (22.6%)	20 (14.4%)	.072
Coma[b]	24 (15.5%)	14 (10.1%)	.167
Pneumonia[b]	60 (38.7%)	60 (43.2%)	.576
Bronchiolitis[b]	27 (17.4%)	34 (24.5%)	.200
Acute respiratory distress syndrome[b]	13 (8.4%)	8 (5.7%)	.382

Values are median [25th percentile and 75th percentile] or numbers (percent).
[a]Mann-Whitney *U* test; [b]Chi-square test.

malignant tumors, which showed a higher frequency in the intervention group. In addition, we found no significant differences between the test and control groups regarding the main indications for MV. Finally, there were no significant differences between the two groups regarding the mortality rate observed during the study course (14.8% in the test group vs. 10.8% in the control group; $p = .302$).

As the primary and secondary objectives of the study were focused on patients that had been extubated or were still on MV during the 30-day follow-up period, 34 patients who died without ever being weaned from the ventilator were not considered for the following analysis; 21 were in the test group and 13 were in the control group (Fig. 2).

In the test group, five patients were extubated without undergoing a complete SBT, including three due to the physician's decision, one due to psychomotor agitation during the test, and one due to accidental extubation. In the control group, 17 patients were extubated after a SBT; most cases occurred within the last 2 months of the study, but all patients were analyzed on an intention-to-treat basis. Table 2 shows the demographic and clinical baseline characteristics of the patients who were considered for the analysis of the primary and secondary outcomes.

In both groups, ICU admission was mostly due to medical reasons (92.9% in the control group vs. 96.3% in the test group; $p = .223$). The main indications for initiating MV were pneumonia (42.3%), wheezing (24.6%), bronchiolitis (23.0%), septic shock (16.9%), and coma (12.3%). Acute respiratory distress syndrome (ARDS) was present in 5% of the patients. We found no significant differences between the test and control groups regarding these main indications for MV (Table 2).

Comparing the occurrence of complications in both groups, the frequency of shock during MV was higher in the test group than in the control group (12.7% vs. 5.6%; $p = .047$). For the rates of all other complications analyzed, namely ARDS ($p = .585$), sepsis ($p = .218$), acute renal failure (ARF) ($p = .190$), and coagulopathy ($p = .806$), no significant between-group differences were found. The two groups were also similar with respect to MV modes. Pressure-controlled modes (i.e., pressure-controlled ventilation or synchronized intermittent mandatory ventilation + pressure support) were used in most cases in both ICUs, but 21 patients were ventilated in the pressure-regulated volume control mode, with 12 in the test group and nine in the control group. The volume-controlled mode was not used. Finally, groups were similar in their use of drugs, including benzodiazepines, opioids, dobutamine, dopamine, noradrenaline, milrinone, and adrenaline (all p values $>.05$).

Table 2. Demographic and clinical baseline characteristics of the patients analyzed according to the study group

Characteristics	Test Group (n = 134)	Control Group (n = 126)	p
Age (yrs)[a]	1.160 [0.371; 3.506]	0.712 [0.254; 2.172]	.070
Pediatric Risk of Mortality II[a]	0.042 [0.023; 0.097]	0.051 [0.028; 0.128]	.419
Pediatric Index of Mortality 2[a]	0.091 [0.033; 0.188]	0.081 [0.036; 0.180]	.598
Male[b]	71 (53.0%)	72 (57.1%)	.501
Immunodeficiency[b]	4 (3.0%)	3 (2.4%)	.764
Congenital Heart Disease[b]	6 (4.5%)	8 (6.3%)	.504
Genetic Disorders[b]	7 (5.2%)	6 (4.8%)	.864
Malignant Tumors[b]	8 (6.0%)	3 (2.4%)	.151
Neurologic Disorder[b]	15 (11.2%)	9 (7.1%)	.259
Liver Disease[b]	7 (5.2%)	15 (11.9%)	.053
Chronic Lung Disease[b]	20 (14.9%)	17 (13.5%)	.741
Leukemia[b]	4 (3.0%)	5 (4.0%)	.665
Main Indications for Mechanical Ventilation			
Congestive heart failure[b]	3 (2.2%)	6 (4.8%)	.266
Wheezing[b]	34 (25.4%)	30 (23.8%)	.770
Septic shock[b]	26 (19.4%)	18 (14.3%)	.271
Coma[b]	19 (14.2%)	13 (10.3%)	.344
Pneumonia[b]	55 (41.0%)	55 (43.7%)	.671
Bronchiolitis[b]	28 (20.9%)	32 (25.4%)	.389
Acute respiratory distress syndrome[b]	7 (5.2%)	6 (4.8%)	.864

Values are median [25th percentile and 75th percentile] or numbers (percent).
[a]Student's *t* test; [b]Chi-square test.

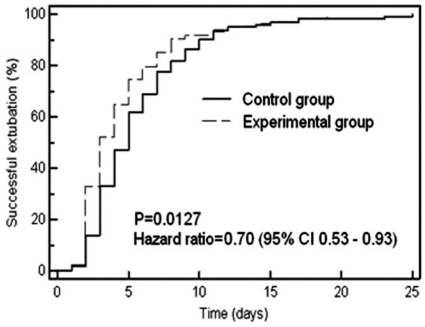

Figure 3. Comparison of the extubation time between groups.

Time to Extubation

Twenty-one patients in the test group passed the daily evaluation but failed their first SBT. Among these patients, 20 passed on a second SBT and one passed after a third SBT. A Kaplan-Meier analysis of the time to extubation showed that the median duration of MV was 3.5 days (95% confidence interval, 2.95–4.02) in the test group, as compared with 4.7 days (95% confidence interval, 4.08–5.34) in the control group (Fig. 3). Within the 30-day follow-up period, there was a statistically significant 30% reduction in the risk of remaining on MV in the test group vs. the control group (hazard ratio = 0.70; 95% confidence interval, 0.53–0.93; $p = .0127$).

In the univariate analysis, being assigned to the test group ($p = .004$), Pediatric Risk of Mortality II score ($p = .042$), Pediatric Index of Mortality 2 score ($p = .024$), liver disease ($p = .024$), having ARDS as an indication for MV ($p = .003$), barotrauma ($p = .006$), and developing ARDS ($p = .002$) or ventilator-associated pneumonia ($p < .001$) during MV were all factors significantly associated with the MV duration. In addition to these variables, genetic disorders ($p = .085$), pneumonia as an indication for MV ($p = .164$), developing shock ($p = .077$), ARF ($p = .067$), and accidental extubation ($p = .129$) showed *p* values <.20 and were also included in the multivariate analysis.

In a multivariate analysis adjusting for covariates, being assigned to the test group was identified as an independent factor associated with shorter MV duration ($p < .001$), whereas the presence of ARDS as an indication for MV ($p < .001$), and the development of ARF ($p = .018$), ventilator-associated pneumonia ($p < .001$), and ARDS during the MV ($p = .001$) were identified as factors independently associated with longer MV duration (Table 3).

Secondary Outcomes and Exploratory Analyses

The significant reduction in the MV duration in the test group was not associated with an increase in the extubation failure rate. As presented in Table 4, an analysis of the secondary outcomes showed similar rates of reintubation, ventilator-associated pneumonia, and accidental extubation between groups. Although there was a less frequent need for NIV in the test group than in the control group, this difference was not statistically significant ($p = .088$). Importantly, comparisons between test and control groups regarding the parameters present before extubation showed no significant difference in F_{IO_2} ($p = .4$), PIP ($p = .71$), PEEP ($p = .35$), or tidal volume ($p = .26$), as shown in Table 5.

Regarding the 21 patients that required more than one SBT, median F_{IO_2}, PIP, and PEEP values present at the first SBT were 0.30, 20 cm H_2O, and 6 cm H_2O, respectively. In most cases, no significant changes in ventilatory parameters were observed when the first and the second SBT were compared, and the ventilatory parameters of these patients were similar to parameters shown by the rest of the sample (data not shown).

Among the 22 cases of protocol deviations, none of the five patients in the test group that were extubated without undergoing a complete SBT failed extubation and required a reintubation; of the 17 patients in the control group that were extubated after a SBT, only one failed extubation and required reintubation (5.9%). Ventilatory parameters of these 22 patients were similar to the parameters present by the rest of the patients (F_{IO_2}, $p = .675$; PIP, $p = .895$; PEEP, $p = .855$). Furthermore, the analysis of time to extubation excluding the 22 patients who violated the protocol confirmed the overall results of the study.

In an exploratory investigation, we found that a total of 20 patients underwent the first SBT with a PEEP of 8 cm H_2O, which was one of the predetermined criteria. Among these patients, only two required a second SBT. Of the 18 patients that were extubated after the first SBT, 16 were successfully extubated and only two required reintubation (11.1%). None of the patients that performed the first SBT with PEEP of 8 cm H_2O died during the study course.

DISCUSSION

Although we currently have a better understanding of how to avoid MV-induced pulmonary lesions, challenges remain in reducing patient MV duration and extubating patients as early as possible (2, 16, 27–29). Thus, it is crucial to establish strategies that can predict whether a patient is ready to be extubated. Here we show that a weaning protocol that combines a daily evaluation using pre-

Table 3. Multivariate analysis of factors predicting time to extubation

Variable	Relative Risk	[95% Confidence Interval]	p
Group (test)	0.60	[0.47; 0.78]	<.001
Acute Respiratory Distress Syndrome (as indication)	3.86	[2.13; 6.99]	<.001
Presence of Acute Renal Failure	1.99	[1.12; 3.52]	.018
Ventilator-Associated Pneumonia	3.32	[2.02; 5.45]	<.001
Acute Respiratory Distress Syndrome (as complication)	3.73	[1.77; 7.86]	.001

Table 4. Respiratory complications in the two groups

Variable	Test Group (n = 134)	Control Group (n = 126)	p
Need for Noninvasive Mechanical Ventilation[a]	29 (21.6%)	39 (31.0%)	.088
Reintubation[a]	15 (11.2%)	18 (14.3%)	.454
Ventilator-Associated Pneumonia[a]	9 (6.7%)	12 (9.5%)	.406
Accidental Extubation[a]	3 (2.2%)	8 (6.3%)	.100

[a]Chi-square test.

Table 5. Comparison of parameters present before the extubation

Parameter	Test Group	Control Group	p
Fio_2[a]			
Mean ± SD	0.33 ± 0.06	0.34 ± 0.08	.40
Median	0.3	0.3	
Peak Inspiratory Pressure (cm H_2O)[a]			
Mean ± SD	18.67 ± 2.83	18.36 ± 2.44	.71
Median	18.0	18.0	
Positive End-Expiratory Pressure (cm H_2O)[a]			
Mean ± SD	6.38 ± 0.93	6.24 ± 0.66	.35
Median	6.0	6.0	
Tidal Volume (mL/kg)[a]			
Mean ± SD	7.36 ± 1.94	6.91 ± 1.40	.26
Median	7.0	7.0	

[a]Mann-Whitney *U* test.

determined criteria with a 2-hr SBT to assess readiness for extubation was associated with a shortened MV duration. This implies a reduction in the median MV duration by about 1 day as compared with standard care procedures.

Adult studies have shown that most patients do not need gradual weaning; when assessed with a daily evaluation and SBT, approximately 75% of patients are ready to be extubated (21, 23). Pediatric studies have shown similar results (11, 20). However, although the introduction of weaning protocols has resulted in decreased ventilation times in adult patients (22, 23), it is still unknown whether similar protocols can benefit the pediatric population. In a study conducted by Randolph et al (24), the use of a defined protocol produced no significant differences between groups with regard to the time required for weaning. The authors found no significant differences in ventilator weaning times among the three groups (i.e., pressure support, volume support, or no protocol). They concluded that most children are weaned from MV over a short period of time and that protocols may not further shorten this brief duration. However, approximately one-third of intubated children eligible for a weaning trial actually passed an extubation readiness test, and most remained successfully extubated at 24 hrs. Thus, the question remained whether protocol-dependent weaning may indicate an earlier readiness for extubation. In our study, we showed that the application of a weaning protocol significantly shortened MV duration. Although our main finding contrasts with those presented by Randolph et al, it should be noted that both studies differ in important aspects relating to goals, study design, and methodology. One of the major differences is that in the Randolph study, only patients who failed a test for extubation readiness were randomized to one of the study groups, and therefore the test was used as a screening strategy to identify patients with more difficult weaning (24).

The MV reduction of approximately one day that was achieved with the use of the weaning protocol may not seem especially compelling at first. However, the median MV time was reduced from 4.7 to 3.5 days, which represents a reduction of almost 25% in the total time on MV. Toward that, it is also important to emphasize that although the criteria that we initially set for performing the SBT were different from those used in conventional weaning, comparative analysis showed no differences between the groups regarding the levels of PEEP, Fio_2, PIP, or tidal volume before extubation. Therefore, we cannot affirm from the present study that higher ventilatory parameters can be adopted to extubate a patient earlier. On the other hand, 80% of the 20 patients that underwent a SBT with the predefined parameter originally proposed in the protocol were successfully extubated after a single SBT, thus suggesting that higher ventilatory parameters cannot be considered a risk factor for extubation failure and for the need of a second SBT. We speculate that children in the control group were probably kept under MV longer than necessary, and if the daily evaluation had been less conservative and the SBT had been performed with higher parameters we could have reduced the duration of MV even more. Importantly, all the analyses in the present study were performed on an intention-to-treat basis, and therefore the results were analyzed according to the intervention to which patients were randomized, irrespective of the treatment they had actually received during the study. One may thus speculate that the exclusion from analysis of the 22 patients that were treated differently from the group to which they were randomized could result in an even higher benefit of the test protocol. It also should be noted that subgroup analysis was not planned in our study, and therefore, we

decided not to investigate whether our combined protocol was more successful in specific groups of children defined by age, diagnosis, or other baseline factors. Although speculative in nature, our view is that the positive results obtained in our study, in which the median age was close to 1 yr, as well as previous results in the adult population, are evidence against a treatment-by-age interaction, at least when age is considered as a possible determinant of treatment effect. In the multivariate analysis (Table 3), we observed that the development of ARF, ventilator-associated pneumonia, or ARDS during the ICU stay were associated with increased MV duration. However, the proportion of patients with these conditions in the two groups was similar. The association of ARF and the duration of MV contrasts with a previous study, where the cumulative fluid intake minus output was not associated with MV duration, and highlights the importance of new prospective studies in this field (30).

In the test group, there was a higher frequency of shock, which could conceivably be associated with extending times under ventilation because one of the criteria for daily evaluation was the presence of hemodynamic stability. Nevertheless, this condition was not associated with increased ventilation times in the multivariate analysis. Reassuringly, both the reintubation rate and the need for NIV were lower in the test group, albeit with no statistically significant findings.

The daily evaluations and the SBT can be easily incorporated into patient treatment routines. In our study, the SBT was applied using the pressure-support mode, which requires less time than assembling the T-piece system. We would like to stress, however, that the use of the T-piece may be preferred in places where resources are scarce.

Regardless of the system adopted for conducting the SBT, the protocol presented here remains an easy and efficient strategy to reduce pediatric patient MV duration. To our knowledge, this is the first study in which an SBT was used in pediatric intensive care patients as a weaning strategy and was performed daily until extubation. This contrasts with previous studies in which SBT was performed only in patients whose physician judged them ready to undergo a breathing trial or extubation (6, 11, 20, 31), or before randomization as in the prospective study conducted by Randolph et al (24).

The results presented above are encouraging, but our protocol has some limitations. First, we did not assess the children's upper airways because the SBT was conducted while the patients were still intubated. In addition, the open-label study design may have influenced our results, despite our attempts to minimize bias. Regarding the first limitation, it is well known that UAO is the main cause of pediatric extubation failure. In our study, 33 children failed extubation, and 57.5% had an UAO. The fact that the weaning protocol tested here was effective at shortening the MV duration but was not able to reduce the extubation failure rate highlights the importance of developing new studies in this field.

CONCLUSION

In children who received MV for >24 hrs, a daily evaluation to check readiness for weaning and the use of an SBT reduced MV duration without increasing the extubation failure rate or the need for NIV.

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