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Lack of accuracy of ventilatory indexes in predicting extubation success in children submitted to mechanical ventilation

Falta de acurácia dos índices ventilatórios para predizer sucesso de extubação em crianças submetidas a ventilação mecânica

ABSTRACT

Objectives: Between 10% and 20% of children submitted to mechanical ventilation in the pediatric intensive care unit present extubation failure. Several ventilatory indexes have been proposed to predict extubation failure. The aim of this study was to analyze the accuracy of these indices in predicting successful extubation in children and to evaluate these variables according to the age of the patient and the specific disease.

Methods: A prospective observational study including all children submitted to mechanical ventilation in a Brazilian referral pediatric intensive care unit was conducted between August 2007 and August 2008. The tidal volume, maximal negative inspiratory pressure, rapid shallow breathing index and other ventilatory indexes were measured before extubation. These variables were analyzed according to the extubation outcome (success or failure) as well as age and specific disease (post cardiac surgery and acute viral bronchiolitis).

Results: A total of 100 patients were included (median age of 2.1 years old). Extubation failure was observed in 13% and was associated with lower weight (10.3+8.1 Kg vs. 5.5+2.4 Kg; p=0.01). We also evaluated the relationship between extubation failure and the main cause indicating mechanical ventilation: children who had received cardiac surgery (n=17) presented an extubation failure rate of 29.4% with a relative risk of 4.6 (1.2-17.2) when compared to children with acute viral bronchiolitis (n=47, extubation failure rate of 6.4%). The maximal inspiratory pressure was the only physiologic variable independently associated with the outcome. However, this variable showed a wide dispersion and lack of accuracy for predicting extubation success (sensitivity of 82% and specificity of 55% for a cut point of -37.5 cmH_2O predicting successful extubation). The same wide dispersion was observed with other ventilatory indexes.

Conclusion: The indexes for predicting extubation success in children submitted to mechanical ventilation are not accurate; they vary widely depending on age, main disease and other clinical aspects. New formulas including clinical variables should be developed for better prediction of extubation success in children submitted to mechanical ventilation.

Keywords: Pediatric intensive care; Respiration, artificial; Intubation/adverse effects; Respiratory insufficiency; Ventilator weaning

This study was conducted at Hospital São Lucas, Pontifícia Universidade Católica do Rio Grande do Sul – PUC/RS, Porto Alegre (RS), Brazil.

Conflicts of interest: None.

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INTRODUCTION

Between 40% and 60% of children admitted to the pediatric intensive care unit (PICU) are submitted to mechanical ventilation (MV). Extubation failure (EF) is observed in 10% to 20% of these patients.[1-3] EF is defined as the need for reinsertion of the tracheal tube and resumption of MV in the first 48 hours after the tracheal tube has been removed.[3-5] EF has been associated with poor outcomes, such as cardiopulmonary arrest, prolonged length of stay in the PICU, predisposition to hospital infections and increased mortality rates.[6-10] Risk factors associated with EF include lower age (less than 24 months old), dysgenetic condition, chronic respiratory disorders, chronic neurologic conditions, prolonged hypoxia (shock or cardiopulmonary arrest) and the number of tracheal tube changes during the period on MV.[11-14]

EF in children occurs as a consequence of upper airway obstruction in a quarter of the cases. The leading causes of EF in pediatric patients comprise a heterogeneous group, which includes deterioration of pulmonary condition, cardiovascular failure, ventilatory musculature failure (fatigue), neurologic impairment and residual effects of sedatives.[1,5,6,8,11,12,14]

There are no specific clinical signs that can accurately predict EF in children prior to withdrawing the tracheal tube. Several adult indexes have been proposed for predicting extubation success in children, including rapid shallow breathing index (RSBI), Compliance/rate/oxigenation/pressure index CROP [dynamic compliance x maximal negative inspiratory pressure x (PaO_2/PAO_2) / respiratory rate] and maximum inspiratory pressure (MIP).[11,15-21] However, the exact cutoff points of each of these different indices to predict extubation success in children have not been clearly defined.[9,10,12]

The goals of this study were to analyze the accuracy of ventilatory indexes in predicting extubation success in children submitted to MV and to evaluate these variables according to age and specific disease.

METHODS

Between August 2007 and August 2008, a prospective observational study was conducted in a PICU located in a referral and university-affiliated Brazilian hospital (Hospital São Lucas, Pontificia Universidade Católica do Rio Grande do Sul, Porto Alegre (RS), Brazil). On average, 450 children are annually admitted to the 13 pediatric intensive care beds, with a mortality rate of 9%.[22] Close to 60% of children admitted to the PICU are submitted to MV, and 50-60% of these are submitted to MV for longer than 24 hours.[11,22] This PICU is a regional referral center for kidney transplants, neurosurgery and cardiac surgery. The local institutional Ethics and Research Committee approved this study and required that parents (or the legal guardian) signed the informed consent.

All infants and children (1 month old to 15 years old) admitted to the PICU during this period and submitted to MV for more than 24 h were eligible for the study. Patients with tracheostomy were excluded. During the study, three models of ventilators were available: Siemens Servo 300, Siemens Servo i and Engströn GE Healthcare ventilator.

In this PICU, the preferred mode of ventilation is based on pressure control with synchronized intermittent mandatory ventilation coupled with pressure support. The weaning process and the precise moment of tracheal extubation were at the discretion of the medical staff without any interference from the main researcher (SG). The required general conditions for extubation were (a) that the patient be alert and awake (Ramsay 1-2) without (or minimal) sedatives and analgesic infusion; (b) improvement or resolution of the underlying cause of acute respiratory failure; (c) adequate gas exchange as indicated by a partial pressure of arterial oxygen (P_aO_2) higher than 60 mmHg while breathing with a fractional inspired oxygen (F_IO2) of 0.40 or less, (d) a positive end-expiratory pressure (PEEP) less than 7 cmH_2O, and (e) good response to the spontaneous breathing trial (SBT) on pressure support of 7 cmH_2O for 30-60 minutes.[5,6,10,12]

Immediately after the medical staff determined that a child was ready to be extubated, the patient was maintained on mechanical ventilation with the same parameters previous to the spontaneous breathing trial, and the respiratory therapist was contacted to collect the following variables: a) MV parameters; b) relative risk (RR); c) minute volume (V_E) through a ventilometer for one minute; d) tidal volume (V_T), calculated by dividing V_E by RR; e) RSBI, calculated by dividing RR by V_T and indexed to the body weight [RSBI= (RR/V_T)/ weight];[23] f) maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), measured with a digital manovacuometer. The most negative values of all five parameters were used. After all measurements and regardless of index values, the tracheal tube was withdrawn, and the MV was stopped.

After removing the tracheal tube, the child continued receiving oxygen (2-4 liters/min) through nasal prongs. In this study, EF was defined as the requirement for tracheal tube reinsertion within 48 hrs after extubation. Based on the medical staff information and data obtained from the medical chart, the reasons for EF were classified as a) upper airway obstruction and b) respiratory failure.

The end point of this study was successful tracheal extubation. Specific cases were analyzed for evaluating the different indexes regarding successful extubation, including children under a year old, children with acute viral bronchiolitis and children in the post-cardiac surgery period.

Sample size: based on our previous studies,[11,23] we assumed an extubation failure rate of 15%. Adopting an alpha error of 5% and a 1-beta of 80%, it was estimated that a minimum number of 13 children in the extubation failure group would be appropriate for evaluating respiratory indexes regarding successful extubation. Considering our previous studies and the inclusion criteria, we estimate that a one-year period of study would be necessary to obtain the necessary number of children in both groups.

Student´s *t* test was used for comparing continuous variables with normal distribution, and the Mann-Whitney U test was used for variables with abnormal distribution. Possible associated factors related to extubation failure were measured using the univariate analysis (relative risk with the respective 95% confidence interval). The significant factors were selected and analyzed using the multivariate analysis, which was expressed as the odds ratio with the respective 95% confidence interval. The receiver operating characteristic (ROC) curve was used to verify the cutoff point with better sensitivity and specificity to predict extubation success.

The study was approved by the Ethics and Research committee of the São Lucas Hospital - PUCRS University (CEP 271/04)

RESULTS

During the study period, one hundred children submitted to MV [mean age= 25.8 + 41.9 years old; median = 6.5 ($IQ_{25-75\%}$ 3.0-27.3) years old] met the inclusion criteria and were prospectively evaluated. All candidates were evaluated without any loses. EF was observed in 13 children (13%), and 6 of them (46%) required that MV be reinstituted in the first hour after tracheal withdrawal. The mean length of MV for the whole group was 7.3 +0.8 days (only 2 cases over 1 month on MV). Acute viral bronchiolitis was the main clinical diagnosis (47%).

The rate of EF varied according to the main cause indicating MV. Children with acute viral bronchiolitis (AVB; n=47) had an EF rate of 6.4%, while children who had received cardiac surgery (n=17) had an EF rate of 29.4% [RR 4.6 (1.2-17.2); p=0.02]. EF was associated with lower weight (10.3+8.1 Kg vs. 5.5+2.4 Kg; p=0.01), but there was no difference regarding the mean age, height and duration of MV. The mean maximal inspiratory pressure measured immediately before extubation was much more negative in children who were successfully extubated than in the EF group (-60 + 28.5 cmH_2O *vs.* -40.9 + 19.5 cmH_2O; p=0.02). In a regression model analysis, we observed that MIP and age were independent factors associated with extubation failure (p=0.015 and 0.012; respectively). Otherwise, we did not find significant correlation between maximal inspiratory pressure and age (r^2= 0.59; p=0.07).

The MV parameters (Peak Inspiratory Pressure -PIP; PEEP, F_iO_2 and Inspiratory Time iT) evaluated immediately before extubation did not show any difference between the two groups (Table 1).

Table 1 - Characteristics and physiologic respiratory measurements obtained immediately before extubation

	Success (N=87)	Extubation failure (N=13)	Difference (IC95%)	p value
Age (months)	28.7 $\pm$ 44.2	6.4 $\pm$ 6.1	22.3 (12.3_32.2)	0.1
Height (cm)	74.1 $\pm$ 27.3	61.3 $\pm$ 12.5	12.7 (-6.9_32.3)	0.2
Weight (Kg)	10.3 $\pm$ 8.1	5.5 $\pm$ 2.4	4.9 (2.7_7.2)	0.01
Length of MV (days)	6.3 $\pm$ 4.6	14.1 $\pm$ 17.2	-7.8 (-18.3_2.5)	0.07
MIP (cmH_2O)	-60 $\pm$ 28.5	-40.9 $\pm$ 19.5	16.9 (-0.09_33.8)	0.02
MEP (cmH_2O)	56.2 $\pm$ 43.02	42.1 $\pm$ 27.3	11.9 (-13.3_37.3)	0.4
V_T (ml/Kg)	7.9 $\pm$ 4.4	9.5 $\pm$ 6.3	-1.9 (-6.1_2.2)	0.6
V_E (ml/Kg/min)	2.6 $\pm$ 1.9	1.5 $\pm$ 1.1	1.05 (0.2_1.8)	0,07
RSBI (RR/min/ml/Kg)	6.2 $\pm$ 4.9	8,1 $\pm$ 10.8	1,7 (-8.3_.8)	0.5
PIP (cmH2O)	26.1 + 4.6	27.2 + 3.7	-1.33 (-4.18_1.5)	0.42
PEEP(cmH2O)	5.4 + 1.2	6.1 + 1.2	-0.76 (-1.4_-0.02)	0.06
FiO2 (%)	0.3 + 0.04	0.3 + 0.05	-0.05 (-0.3_0.02)	0.76
Ti (s)	0.8 + 0.1	0.7 + 0.1	0.01 (-0.6_0.8)	0.61

Data are expressed as mean + standard deviation (SD) and compared using Student *t* test for those with normal distribution or with the Mann Whitney U test for those variables without normal distribution. MIP - maximal inspiratory pressure; MEP - maximal expiratory pressure; V_T - tidal volume; V_E - expiratory minute volume; RSBI - rapid shallow breathing index; MV - mechanical ventilation; Ti - inspiratory time; PIP - peak inspiratory pressure; PEEP - positive and expiratory pressure; F_iO_2 - oxygen inspired fraction.

When the group with AVB (n=47) was analyzed exclusively, it was observed that even though this was a homogenous group with respect to age and clinical diagnosis, the results obtained for the physiologic respiratory measurements showed remarkable dispersion. The mean MIP was -66.2 +29.9 cmH_2O (Figure 1A), and the rapid shallow breathing index showed the same high level of variability, making any prediction regarding extubation outcome difficult (Figure 1B).

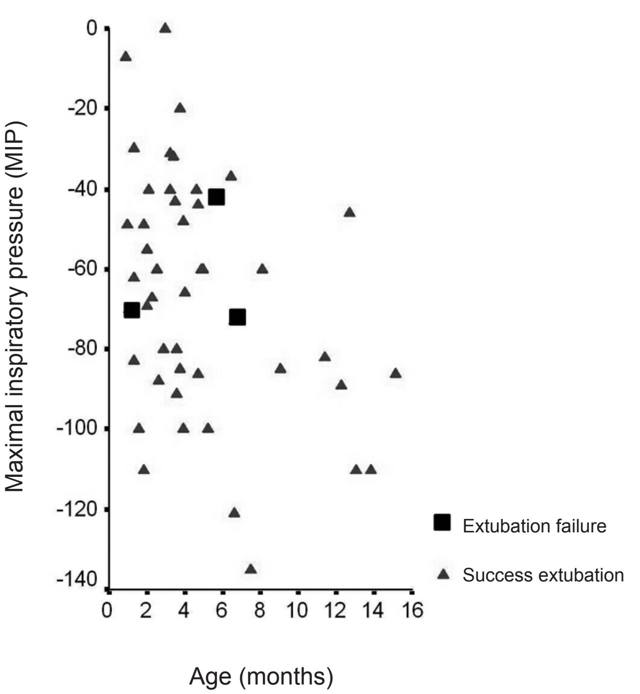
There were 61 children under a year old who were extubated (70% male) with a mean duration of MV of 8.5 days. AVB was the main diagnosis in 42 (69%) patients, followed by post-cardiac surgery (8%), a group with different clinical diagnoses (15%) and another group with diverse post-surgery conditions (8%). The rate of EF in this group was 18% (11 children), and all cases of EF were due to worsening respiratory distress without any case of upper airway obstruction (according to the clinical diagnosis of the medical staff).

The maximal inspiratory pressure was the only ventilatory index in children under a year old that showed difference between children successfully extubated and those with EF (-62.6±29 cmH_2O *vs.* -42.7±20.2 cmH_2O; p=0.03) (Table 2). The area under the ROC curve for MIP was 0.7 with a sensitivity of 82% and specificity of 55% for a cutoff point of -37.5 cmH_2O in predicting successful extubation (Figure 2).

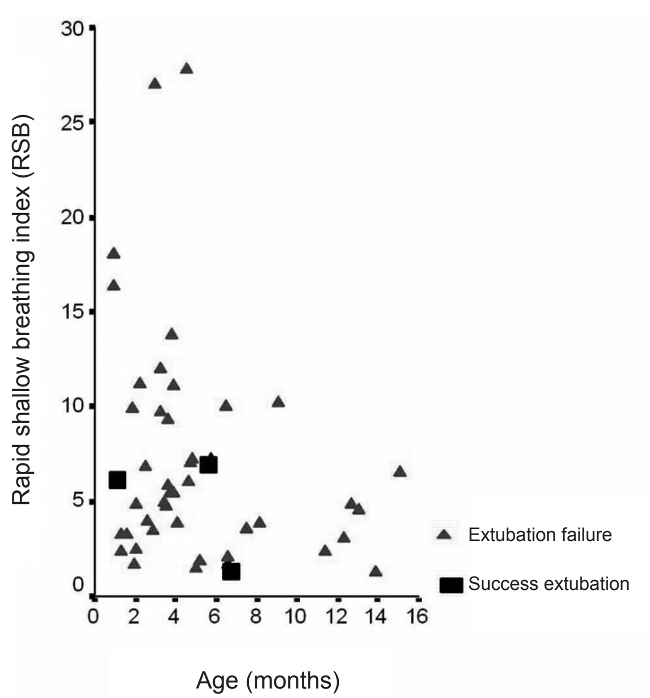
Table 2 - Characteristics and physiologic ventilatory variables observed in children under a year old before tracheal extubation

	Whole group (N=61)	Extubation success (N=50)	Extubation failure (N=11)	p value
Gender: male	43	36	7	
Age (months)	4 ± 2.4	3.9 ± 2.4	4.2 ± 2.6	0.7
Height (cm)	43:18	60.9 ± 10	58.5 ± 10.4	0.5
Weight (Kg)	5.3 ± 1.96	5.4 ± 1.9	4.9 ± 2.1	0.4
Lenght of MV (days)	8.5 ± 8.3	7.4 ± 4	13.6 ± 17.3	0.2
V_T (ml/Kg)	7.6 ± 4.8	7.2 ± 4.3	9.5 ± 6.6	0.4
V_E (ml/Kg/min)	1.49 ± 1.1	1.4 ± 1.1	1.5 ± 1.1	0.97
RSBI (RR/min/ ml/Kg)	7.1 ± 5.7	7.5 ± 5.9	5.4 ± 5.2	0.3
MIP (cmH_2O)		-62.6 ± 29	-42.7 ± 20.2	0.04
MEP (cmH_2O)		59.5 ± 44	45.3 ± 28.6	0.4

Data are expressed as mean + standard deviation (SD) and compared using Student *t* test for those with normal distribution or with the Mann Whitney U test for those variables without normal distribution. MV - mechanical ventilation; MIP - maximal inspiratory pressure; V_T - tidal volume; V_E - expiratory minute volume; RSBI - rapid shallow breathing index; Ti - inspiratory time.



1-A) The maximal inspiratory pressure (MIP) before extubation



1-B) The rapid shallow breathing index (RSBI) before extubation

Figure 1 - Maximal inspiratory pressure and rapid shallow breathing index before extubation in children with acute viral bronchiolitis (N=47).

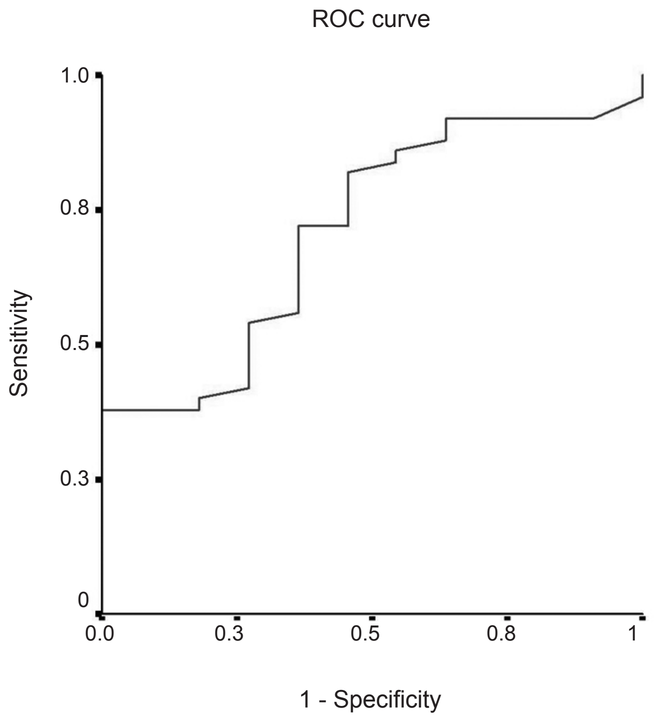


Figure 2 - The maximal inspiratory pressure ROC curve for predicting extubation success in children under a year old.

DISCUSSION

In this study, the rate of EF (13%) was comparable to what has been reported in similar studies involving children submitted to mechanical ventilation.(3,5,6,11,22) In the present study, EF was associated with lower weight. With respect to the primary diagnosis, children submitted to cardiac surgery showed a significantly higher EF rate than children with AVB [29.4% versus 6.4%, RR 4.6 (1.2-17.2)] as reported in several studies.(3,6,24,25) When comparing the success and the failure groups, only one physiologic respiratory variable showed statistical significance: the mean maximal inspiratory pressure (MIP), which was much more negative in the success group than in the failure group. However, the non-uniform and wide dispersion of this variable affected its accuracy for predicting extubation success (sensitivity of 82% and specificity of 55% for a cut point of -37.5 cmH_2O in predicting successful extubation).

Accurate identification of children on MV with a high risk for EF is one of the most pressing challenges in the field of pediatric intensive care.(1-15) Removing tracheal tubes from children who are not ready to sustain their own respiratory demands has been associated with several life threatening problems, including sudden cardiorespiratory arrest, the need for an emergency tracheal intubation, a higher rate of acquired hospital infection, prolonged PICU stay, prolonged hospital stay and an increased mortality rate.(3,5,6,12,13)

As demonstrated in several studies, the EF is a result of several interacting factors, such as the child's age, the duration of MV, the number of changes of the tracheal tube, heavy use of sedatives and cardiac and neurologic dysfunction.(5-8,11,13,14,25,26) Consequently, it is intriguing that even though these variables are known to be associated with the worst prognosis of tracheal tube withdrawal, they are not taken in account in the various formulas and indexes used to predict extubation success/failure in children. Furthermore, it is unlikely that only one variable or index could accurately predict extubation success in a heterogeneous group of children submitted to MV.

To better evaluate the limitations of these indexes, we present in figure 3 the tidal volume of our patients measured immediately before extubation along with information regarding the cutoff point indicated by different authors as accurate for predicting extubation success.(7,11,16,17) Using a tidal volume cutoff point of 4 ml/Kg,(4,7,12,17) as a predictor of successful extubation in children, its sensitivity and specificity would be 16% and 85%, respectively. If a cutoff point of V_T<5,5ml/Kg(16) is adopted, its sensitivity would be 31%, and its specificity would 69%; however, if the tidal volume cutoff point is set at 6 ml/Kg,(5) the sensitivity and specificity would be 39% and 54%, respectively (Figure 3).

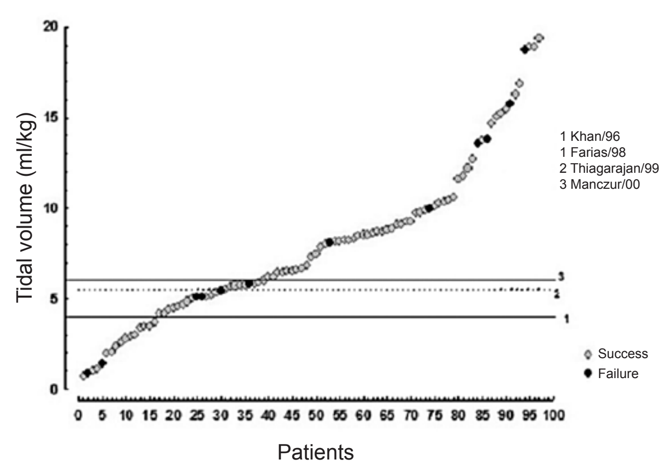


Figure 3 - The tidal volume measured in one hundred children in the moment before tracheal extubation.
The three horizontal lines represent the cutoff points defined by different authors as accurate for predicting extubation success/ failure in children.

The limitations described above were also observed when different cutoff points for two other indices were adopted. Assuming a cutoff point of 8 rpm/ml/Kg[7,8,11,16] using the rapid shallow breathing index as predictor of successful extubation would result in a sensitivity of 72% and specificity of 23%. Adopting the cutoff point of MIP ≤-50 cmH_2O[9] to predict successful extubation would result in a sensitivity of 57% and a specificity of 69%.

It is well known that physiological parameters vary widely in children. Depending on their physiologic reserve and host defenses, as well as the impact of the disease process, the variability of these parameters can be even higher. Thus, it is not surprising that these indices are inaccurate and insensible in predicting extubation success in a pediatric population.

We are aware that our study presents some limitations. A) The weaning process and the tracheal tube withdrawal were based on medical indication rather than a strict protocol. However, it should be noted that in this case, the possible bias would result in an excessive number of extubation failures. Nevertheless, it did not occur in our study, where the rate of EF (13%) was in accordance with the lower acceptable number of EF reported in previous studies.[3,11,14] B) The sample size was not calculated for comparison subgroups, such as just children with AVB, children under a year old, or the cardiac surgery group; obviously, these comparisons should be evaluated with caution; C) The restricted number of children with EF is also a limitation of this study. The small number of children with EF makes it difficult to calculate the accuracy of these indices in predicting extubation failure. Nevertheless, it is not an obstacle for calculating the sensitivity and specificity for extubation success or for analyzing the wide variability of these parameters.

Considering the multiple aspects involved in tracheal extubation, it is unlikely that only one or two respiratory physiological variables would be able to predict the success or failure after tracheal tube removal.[14-18,26-28] As M. Tobin stated, "As a practicing intensivist, nothing taxes my intellect more than the difficult-to-wean patient".[26] If this is true for adult patients, we might infer that withdrawing the tracheal tube from children submitted to mechanical ventilation represents an even greater challenge.

Recently, Harikumar demonstrated that the Tension-Time Index (TTI) is an accurate predictor of extubation outcome in a group of 80 ventilated children.[29] In this study, TTI was measured simultaneously using two approaches: the (traditional) invasive measurement and a non-invasive method. Both measurements demonstrated good agreement and excellent capacity to predict the extubation outcome in ventilated children. However, these results must be validated in other similar populations of children submitted to mechanical ventilation.

In conclusion, the actual formulas and indexes for predicting extubation success or extubation failure in children submitted to MV are not accurate. They have a wide variability depending on age, primary disease and other clinical aspects. We suggest that the next step in this field should be the development of indexes or formulas for predicting extubation success in children that include some of the variables considered here, such as weight, age, primary disease, nutritional status, neurologic disability, and the dose of neuromuscular blockers and analgesics/sedatives used.

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RESUMO

Objetivos: Entre 10% e 20% das crianças submetidas a ventilação mecânica na unidade de terapia intensiva terão falha da extubação. Foram discutidos diversos índices ventilatórios para prever falha da extubação. O objetivo deste estudo foi analisar a acurácia destes índices para prever extubação bem sucedida em crianças e avaliar estas variáveis segundo a idade e doença específica.

Métodos: Este foi um estudo prospectivo observacional que incluiu todas as crianças submetidas a ventilação mecânica em uma unidade de terapia intensiva pediátrica de referência no Brasil realizado entre agosto de 2007 e agosto de 2008. Foram medidos antes da extubação o volume corrente, máxima pressão inspiratória negativa, índice de respiração rápida e superficial e outros índices ventilatórios. Estas variáveis foram analisadas segundo o desfecho da extubação (sucesso ou falha) assim como em relação à idade e doença específica (pós-cirurgia cardíaca e bronquiolite viral aguda).

Resultados: Foram incluídos 100 pacientes (idade mediana de 2,1 anos). Foi observada falha da extubação em 13%, que foi associada a baixo peso (10,3 ± 8,1 kg versus 5,5 ± 2,4 kg; p=0,01) e com a principal causa para indicação de ventilação mecânica: crianças em pós-operatório de cirurgia cardíaca (n=17) tiveram um índice de falha da extubação de 29,4%, com um risco relativo de 4,6 (1,2-17,2) em comparação com crianças com bronquiolite aguda (n=47; taxa de falha da extubação de 6,4%). A pressão inspiratória máxima foi a única variável fisiológica independentemente associada com o desfecho. Entretanto, esta variável demonstrou uma ampla dispersão e falta de acurácia para prever o sucesso da extubação (sensibilidade de 82% e especificidade de 55% para um ponto de corte de -37,5 cmH_2O para prever sucesso). A mesma ampla dispersão foi observada para os demais índices ventilatórios.

Conclusão: Os índices disponíveis para prever o sucesso da extubação em crianças submetidas a ventilação mecânica não são acurados; eles têm uma ampla variabilidade que depende da idade, doença de base e outros aspectos clínicos. Devem ser desenvolvidas novas fórmulas que incluam variáveis clínicas para melhor previsão da extubação em crianças submetidas a ventilação mecânica.

Descritores: Unidades de terapia intensiva pediátrica; Respiração artificial; Intubação/efeitos adversos; Insuficiência respiratória; Desmame do respirador

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