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Volume 1 • Issue 2 • 2017

Research Article

Pulmonary Research and Respiratory Care

ISSN: 2575-9779

Predictors of Successful Extubation in a Pediatric Intensive Care Unit

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Received: December 09, 2017; **Published:** December 15, 2017

Abstract

Introduction: A number of useful predictors have been proposed for the weaning process in adults, evaluating oxygenation, inspiratory muscle strength, lung function, minute ventilation, and ventilatory reserve, but no objective criteria have been established for predicting successful extubation in children, and previous studies indicate that weaning rates in adults were not predictive of successful extubation in children (1). The aim of this study was identify predictors of successful extubation in patients undergoing invasive mechanical ventilation in the pediatric intensive care unit.

Methods: Observational analytic study of a prospective cohort, with a duration of one year, a single-center in the cardiovascular pediatric intensive critical unit (PICU). Analysis: A receiver operating characteristic (ROC) curve was constructed in order to establish sensitivity cut-off points as predictors of successful extubation

Result: We included 121 patients. Failure of extubation was seen in 17% (28) of patients. The most frequent cause of extubation failure was obstruction of the upper airway, in 42% of the patients. 53% of the patients that experienced a failed extubation were less than 3 months old 3 (2-10), in contrast to the patients with a successful extubation, where only 26% were less than 3 months old 12 (3-60). We found that having IO < 3.3, $PaCO_2$ < 27, $PvCO_2$ < 34, and HCO_3 > 16.3 had a sensitivity greater than 80 with a value of p =< 0.05, for predicting a successful extubation

Conclusion: The present study shows a percentage of failed extubation of 17%. The variables that significantly predict successful extubation were arteriovenous CO_2, bicarbonate, IO, and PAFI for children without cyanosis and SAFI for children with cyanosis.

Keywords: *Weaning; Failure of extubation; Mechanical ventilation; Reintubation; Invasive mechanical ventilation; Prediction of success*

Abbreviations: FIO_2: Fraction of Inspired oxygen; SaO_2: Arterial blood oxygen saturation; SpO_2: Arterial saturation by pulse oximetry; IMV: Invasive mechanical ventilation; PICU: Pediatric intensive critical unit; PCO_2: Partial pressure of carbon dioxide; PaO_2: Partial pressure of oxygen; PvO_2: Partial venous pressure of oxygen; ISO: Saturation index; IO: Oxygenation index; IV: Ventilation index; PaFi: oxygen blood pressure/inspired fraction of oxygen; SaFi: Oxygen saturation/inspired fraction of oxygen; APA: average pressure of the airway; PIM: Maximum inspiratory pressure; Vt: Tidal volume; PEEP: Expiratory pressure at the end of expiration; HCO_3: Bicarbonate; ROC: Receiver operating characteristic curve

Volume 1 Issue 2 December 2017

Introduction

Invasive mechanical ventilation (IMV) is a life-saving measure that is widely used in pediatric intensive critical units (PICU). In developed countries, it is employed in approximately 30% of the patients that are admitted to the PICU, with a length of 6 days [1]. Ventilatory support has been associated with an increase in the use of sedating agents and their undesired effects, as well as with direct harm to the airway produced by the endotracheal tube [2]. Early withdrawal of mechanical ventilation with a requirement of reintubation has been associated with increases in mortality, in adults as well as in children [3,4].

It is important to determine the optimum moment for extubation, since doing it early or prolonging the ventilation unnecessarily is associated with major complications. Although multiple studies have been carried out in adults and in the pediatric population [5] for evaluating predictors of successful extubation, the prevalence of failed extubation continues to be high, between 4.9% and 29%, without having determined which of these predictors has a significant impact on predicting successful extubation [5].

The aim of this study was to establish what clinical and paraclinical factors best predict successful extubation in patients hospitalized in a pediatric intensive care unit, in order to be able optimize the length of time of invasive mechanical ventilation.

Materials and Methods

Design: Observational analytic study of a prospective cohort without a proof of hypothesis, with a duration of one year (between October, 2015 and October, 2016), in the cardiovascular PICU of Soacha, Colombia, which is a mixed PICU (medical and cardiovascular pathologies are attended, with a 12-bed capacity, located 2,600 meters above sea level).

Inclusion Criteria: Patients that were admitted to the PICU and required IMV and were candidates for programmed extubation.

Exclusion Criteria: Patients that required tracheostomy, patients in a protocol of reorientation of therapeutic objectives, and patients that had non-programmed extubation. The study was approved by the Ethics Committee on Human Research of the Children's Cardiovascular Hospital of Cundinamarca.

Data Collection: The data collection method was non-participant direct observation, and a database was created where the processing of the collection form and data storage were performed on an Excel® spreadsheet (Microsoft Corporation, Redmond, WA) that contained epidemiological, demographic, clinical, and paraclinical data (ventilatory parameters, prior history of intubation, chronic disease at baseline, diagnosis that caused the ventilation, length of stay PICU, days of mechanical ventilation, accumulated balance de liquids/kg, failed extubation, hours of reintubation, causes de failed extubation, death, ISO: saturation index ((FIO_2 x MAP x 100)/$SatO_2$); IO: oxygenation index ((FIO_2 x MAP x 100)/PaO_2); IV: ventilation index ($PaCO_2$ (mmHg) x Pimax (cmH_2O) x FR/1000); PaFi: arterial oxygen pressure/fraction of inspired oxygen; SaFi: oxygen saturation/fraction of inspired oxygen; tobin index (spontaneous respiratory frequency/current vol. normalized for the weight of the patient)).

Extubation Protocol: All of the patients with IMV were evaluated by a treating physician in order to determine if they were candidates for a test of spontaneous ventilation. A check list was carried out, including: a) resolution of the pathology that necessitated the IMV; b) neurological (without the presence of an abstinence syndrome and/or delirium), hemodynamic, and respiratory stability; c) ventilator parameters $fio_2 < 50\%$, PIP < 20 cmde H_2O (for 22 a programmed current volume between 6 and 7 ml/kg), PEEP below or equal to 5 cm H_2O, programmed respiratory frequency less than 10 per minute. When the patients met these requirements, a spontaneous ventilation test was carried out.

Spontaneous Ventilation Test: Programming of the ventilator in support pressure mode of 10 cm of water in patients with an ore-tracheal tube greater than or equal to 4.5. After 30 minutes of the test, an evaluation of the neurological stability was carried out (to assure that the patient did not present an abstinence syndrome), hemodynamic (lactate levels and vital signs with the normal range for the age), respiratory (lack of signs of respiratory difficulty), ventilatory mechanics (current volume > 6cc/kg; PEEP < 6; FIO_2: < 50%; PMVA > 10, the ventilator monitoring was recorded that the patient had at that time) and arterial and/or venous gases that would indicate an acid-base equilibrium.

Initial measurements were carried out on the patient, consisting of ; ISO: saturation index ((FIO_2 x MAP x 100)/$SatO_2$); IO: oxygenation index ((FIO_2 x MAP x 100)/PaO_2); IV: ventilation index ($PaCO_2$ (mmHg) x Pimax (cmH_2O) x FR/1000); PaFi: arterial oxygen pressure/fraction of inspired oxygen; SaFi: oxygen saturation/fraction of inspired oxygen; tobin index (spontaneous respiratory frequency/current vol. normalized for the weight of the patient).

The patients that met the extubation criteria were given an amount of oxygen according to the necessities of the patient, as follows: low-flow cannula, high-flow cannula, nitric oxide, non-invasive ventilation (NIV), and oxygen-helium mixture. A pilot test was carried out for one week after the beginning of the project for the training of the personnel in charge of the data collection.

Outcome

Extubation failure: Every patient that required reintubation during the 48 hours following the withdrawal of the orotracheal tube (OTT).

Statistical Analysis

Sample Size: For the estimation of the size of the sample, established parameters for cohort studies were followed; 0.42 as a proportion of exposed subjects with an outcome and 0.07 as a proportion of non-exposed ones with an outcome were taken as parameters. A maximum permissible error of 0.05 and reliability of 95% were established. With respect to the estimation of the sample, an additional 10% of losses was calculated for a total of 130 events [6].

Analysis: The descriptive statistics were carried out using estimations of proportions and relative frequencies for the categorical variables; for the continuous variables, measurements of central tendency were used. A Kolmogorov-Smirnov normality test and the Wilcoxon tests for related samples and Mann-Whitey for independent samples were carried out. The differences between the categorical variables according to the presence or lack thereof failed extubation were analyzed by means of the Chi squared test. A bivariate analysis was carried out on subgroups among patients with non-cyanotic pathologies and those with cyanotic cardiopathies and each of the predictor variables, and the outcome variable (extubation successful yes or no). A receiver operating characteristic (ROC) curve was used to determine the best cut-off point for estimating the predictive capacity of the clinical and para clinical extubation variables, using the continuous variables with statistically significant differences. All of the analyses were carried out using the IBM SPSS ® 20.0 (IBM) package.

Results

121 patients and 159 mechanical ventilation events that met the inclusion criteria were included. The general characteristics of the patients are reported in Table 1. Failed extubation was seen in 28 patients, corresponding to 17.6% of the sample. 53% of the patients that experienced a failed extubation were less than 3 months old and 18% less than 1 month old, in contrast to the patients with a successful extubation, where only 26% were less than 3 months old. Of the patients with a failed extubation, 60% corresponded to patients with congenital cardiopathies.

86% of the patients had some chronic illness at baseline, the causes that led to mechanical ventilation are described in Table 1, cardiovascular patients, with 41.3%(66 patients), being the principal cause of intubations in our hospital, followed by respiratory illnesses 33,3% (53 patients) and neurological illnesses 14,4% (23 patients).

Characteristic	Failed extubation n = 28 (17,6%)	successful extubation n = 131 (82,3%)	p
Age (months)	3 (2-10)	12 (3-60)	0,001
Female gender (n)%	(10) 35,7	(49) 37,4	0,867
Weight (kg)**	5,2 (4,2-7,3)	9 (5,6-16)	0,0001
antecedent OTI (n)%	(16) 57,1	(55) 41,9	0,143
Mechanical ventilation time (days)	5 (3-10)	3 (1-6)	0,004
Length of stay PICU (IQR)	4 (0-13)	6 (2-13)	0,254
Dynamic Compliance***	0,8 (0,6-0,9)	0,8 (0,6-1,2)	0,27
Static Distensibility***	0,9 (0,7-1,2)	1 (0,8-1,5)	0,097
Dynamic Distensibility Kg***	0,9 (0,8-1,1)	0,9 (0,7-1,1)	0,734
PMVA	9,6 (9-10)	10 (9-11)	0,226
Hydric Balance ml/kg++	-60,9 (-182, -6)	-19 (-106, 10)	0,099
Vt**	8,4 (7,1-9,4)	8,7 (7,5-10,1)	0,97
Tobin Index**	4,1 (3,2-6,8)	3,8 (2,7-5,6)	0,35
$PaCo_2$ mmHg**	39 (32-44)	32 (29-37,5)	0,047
$PvCO_2$ mmHg**	43,5 (41-46)	40 (35-45)	0,004
lactate mmol/L**	1,5 (1,1-1,8)	1,5 (1,1-2)	0,93
HCO_3**	25,7 (23,7-28,2)	21,8 (19,3-25)	0,001
Mortality (n)%	(6) 21	(5) 3,8	0,001
Diagnostic Cause of Mechanical Ventilation (n)%			
Cardiovascular	(10) 6,2	(56) 35,1	0.0025
Respiratory	(14) 8,8	(39) 24,5	0.0684
Neurological	(2) 1,25	(21) 13,19	0.0686
Others	(2) 1,25	(15) 9,4	0.1495

Table 1: *Demographic Description*

D. Dynamic: Dynamic Distensibility, FiO_2: Fraction inspired oxygen, TOI: Tracheal Oral intubation, PVE: Spontaneous ventilation test, PMVA: Average airway pressure, PImax: Maximum inspiratory pressure, PICU: Pediatric intensive care unit, VT: volume tidal, ** Continuous variables expressed in medians and interquartile ranges (IQR 25 - 75). *** Period of controlled ventilation.

The average time of reintubation was 19 hours, with a maximum time of 48 hours. The most frequent cause of failure of extubation was obstruction of the upper airway in 42% of the patients, followed by pulmonary edema and apnea, which was seen in 25%. There were only two events of atelectasis, which corresponded to 8%. 25% of the patients received ventilator support for 24 hours of less.

The accumulated hydraulic balance adjusted for the weight of the patient was more negative in those patients with successful extubation -19(-106, -10) vs. -60, 9(-182, 6); however, no statistically significant association was found (P => 0.05).

Bivariate Analysis

A bivariate analysis was carried out on subgroups among patients with non-cyanotic pathologies and those with cyanotic cardiopathies described in Table 2. A statistical significance was found in the values of PAFI, IO, arteriovenous CO_2, and bicarbonate in the group of patients without cyanotic pathologies (P = > 0.05), and in patients with cyanotic cardiopathy a significant association was found only in the value of SAFI (P = < 0.05).

Diagnostic	Variable	Failed extubation	successful extubation	p
Other pathologies n = 142	$PaCO_2$	39 (36-43)	32 (29-37)	0,007
	$PvCO_2$	45 (41-47)	40 (35-45)	0,012
	HCO_3	26 (23-28)	21 (19,3-25)	0,001
	$PAFIO_2$	143 (122-197)	228 (173-280)	0,007
	$SAFIO_2$	233 (184-313)	240 (196-306)	0,7
	OI	7 (5-8)	4 (3-6)	0,03
	OSI	3,8 (3,1-5,3)	3,4 (2,7-5)	0,3
	IV	24 (18-29)	16 (11-23)	0,052
cyanosis cardiopathy N = 17	$PaCO_2$	44 (37-47)	38 (34-45)	0,61
	$PvCO_2$	46 (43-49)	40 (32-46)	0,1
	HCO_3	25 (20,28,9)	21,4 (18-25)	0,3
	$PAFIO_2$	85 (67-115)	128 (104-148)	0,17
	$SAFIO_2$	150 (105-166)	247 (163-263)	0,01
	OI	11 (10-15)	8 (6-9)	0,067
	OSI	5,9 (4,7-7)	4 (3,2-5,1)	0,09
	VI	24 (11-32)	28 (20-37)	0,6

Table 2: *Bivariate analysis oxygenation and ventilation indices in patients diagnosed with cyanozantes cardiopathies and other pathologies*

*Values expressed in medians and interquartile ranges (IQR 25-75). Statistical significance value P < 0,05; ISO: Saturation index, OI: Oxygenation index, VI: Ventilation index, PaFi: Blood pressure oxygen/Inspired oxygen fraction, SaFi: Oxygen saturation/Inspired oxygen fraction

ROC Curve

An ROC curve was constructed in order to establish sensitivity cut-off points as predictors of successful extubation in patients with cyanotic cardiopathy and other non-cyanotic pathologies. We found that having IO < 3.3, $PaCO_2$ < 27, $PvCO_2$ < 34, and HCO_3 > 16.3 had a sensitivity greater than 80 with a value of p = < 0.05, for predicting a successful extubation. See Table 3.

Diagnostic	Variable	Cut-off points	Sensitivity	p
Pathologies not cyanozantes	OI	<3.3	80	<0.05
	$PaCO_2$	<27	86.5	<0.05
	$PvCO_2$	<34	84.1	<0.05
	HCO_3	>16.3	85.3	<0.05
Cyanosizing pathologies	OI	<3.95	100	<0.05
	$PaCO_2$	<27	86.5	<0.05
	$PvCO_2$	<34	84.1	<0.05
	HCO_3	>19	70	<0.05

Table 3: *Sensitivity cut-off points for successful extubation COR curve*

PCO_2: Partial pressure of carbon dioxide; PaO_2: Partial pressure of Oxygen; PvO_2: Partial pressure venous of Oxygen; IO: Oxygenation index; HCO_3:bicarbonate; ROC: receiver operating characteristic curve

Discussion

The present study shows a percentage of failed extubation of 17%, being within the documented range in the literature of 4.9% to 29% [7]. As is described in the results, an age of less than 3 months is a determining factor for failed extubation, associated with a greater time of ventilation and greater complexity of the pathology at baseline. These are factors frequently described in the literature [7]. Among the measurements of gaseous interchange and the parameters of tissue perfusion of all of the study population, it was found that the patients with the largest values of arteriovenous CO_2 and lower values of bicarbonate were at greater risk of failed extubation. As for the indexes of oxygenation and ventilation, we show that patients with the lowest values of PAFI and highest IO are at greater risk of failed extubation.

Analyzing the subgroup of patients with cyanotic cardiopathies, those that did not tolerate extubation exhibited the lowest SAFI values, which could be considered as a predictor of extubation in this group of patients. The ventilation index had a tendency to be a significant parameter in patients without cyanotic pathology. Nevertheless, we noted that this is a factor for confusion that is influenced by the age of the patients, since in the group of patients without cyanosis, the median age is significantly higher and is influenced because there are adolescent and young adult patients, whose respiratory frequency is lower, and in this group of patients a lower rate of failed extubation is seen.

On analyzing the patients with cyanotic pathologies whose age is lower, there exists no association between the ventilation index and a failed extubation or lack thereof. This can be explained because the ventilation index has as a variable the respiratory frequency and was not normalized for age. Finally, failed extubation was significantly associated with an outcome of mortality. Although it has been written in the literature that failed extubation increases the risk of mortality, we consider that in our population the high rate of mortality in patients with failed extubation can be explained by the age and the high degree of complexity of the cardiopathies included in the present study.

There exists a relationship that has been described between PAFI and SAFI that allows interchanging these measures of oxygenation for evaluating oxygenation disorders and their severity [8, 9]. However, our study shows that this relation doesn't obtain, finding a significant association for the PAFI in patients with non-cyanotic pathologies but not for SAFI (failed extubation median PAFI 143 and SAFI 233, and successful extubation PAFI 228 and SAFI 240). This difference is also maintained in patients with cyanotic pathologies, where the SAFI was found to be significant and the PAFI not. This lack of correlation between the two measures of oxygenation could be explained by the high altitude above sea level (2,600 m) that exists in the city where the study was carried out.

We found no studies that analyzed this difference in children, but these findings could suggest that we should not use these measures interchangeably in cities that are located at high altitudes. According to the data obtained for patients with successful extubation in our study, the values of PAFI and SAFI that were associated with successful extubation were 200 and 240, respectively, values that could be taken into account at the time of a programmed extubation.

Our findings agree with those reported in the literature, in that at a younger age and therefore smaller diameter of the upper airway there is a greater risk of failure for extubation [10]. Likewise, we found that a prolonged time of mechanical ventilation is associated with failed extubation [11]. In the study by Venkata Raman [12], an association was found between the oxygenation index and the risk of failed extubation, being low with indexes below 1.5 and high with indexes above 4.5. In the present study, between 80% and 100% of the patients with an oxygenation index lower than 3.3 (without cyanosis) and lower than 3.95 (cyanotics) were successfully extubated. In the study by Farias [13], it was found that a PAFI lower than 200, as in this study, is associated with failure of extubation.

The variables that were found to be significant for the prediction of failed extubation do not have a clear correlation with obstruction of the upper airway, which was the principal cause for which the extubation was unsuccessful. New studies should be undertaken in order to search for measurements that allow evaluating the stability of the upper airway, since even measurements like the leak test [14] do not consistently predict the development of post-extubation stridency and the requirement of reintubation.

The strengths of the present investigation lie in that it is a prospective study. It proposes cut-off points for some variables of daily use in intensive care units, in patients with and without cyanotic pathologies that allow evaluating respiratory and hemodynamic stability and the integrity of the respiratory center, conditions that should be met in patients for whom withdrawal of invasive ventilator support is proposed.

These variables have been little studied in protocols of extubation for the pediatric population in general, and much less in those patients with cyanotic cardiopathies. Although the number of patients with cyanotic cardiopathies is low, finding a significant association between the SAFI and a risk of failed extubation allows this measurement to be taken into account when considering a programmed extubation, since this is a simple, low-cost, widely-used measurement.

We found a small number of patients with cyanotic cardiopathies, which possibly would not be consistently found in later studies. In this study, variables that allowed evaluating the stability of the upper airway at the time of extubation were not included. Another limitation found is that the ventilation index is not validated according to the age and the respiratory frequency, so in populations like ours that include patients with diverse ages (newborns to young adults), this index becomes a systemic bias, due to the variation in the respiratory frequency with age, although it has been reported as being useful for predicting mortality in newborns with diaphragmatic hernia [15]. It should be taken into account that respiratory frequencies of this population are similar. Nevertheless, as a predictor index for extubation, it does not seem to be useful, according to the data presented in our study. There was no significant association found between the ventilation index and failed extubation in patients with cyanotic pathologies that were of similar ages.

Conclusions

The frequency of failed extubation was 17%, obstruction of the upper airway being the principal cause. The variables that significantly predict successful extubation were arteriovenous CO_2, bicarbonate, oxygenation index, and PAFI for children without cyanotic pathologies and SAFI for children with cyanotic pathologies.

Finding measurements that allow predicting possible successful extubation is very important, keeping in mind that early and delayed extubation constitute risk factors for an increase in morbidity and mortality for critically ill children. This fact underlines the importance of continuing to explore different predictors of extubation that would allow making decisions more objectively and predictably.

Conflict of Interest: The authors declare no conflict of interest.

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