Journal of Cardiovascular Disease Research

ISSN:0975-3583,0976-2833 VOL12,ISSUE 06,2021

Predictors of Extubation Failure in Preterm Infants With Respiratory Distress: The Role of Spontaneous Breathing Trial

Mohamed Elsayed Elsetouhi , Lotfy Mohamed Elsayed, Ali Abd El-Hameed Abdo , M. M. Shehab

Pediatrics Department, Faculty of Medicine, Zagazig University, Egypt.

Corresponding author: Mohamed E. Elsetouhi, Email: mohamadelsotohy@gmail.com

ABSTRACT

Background: Mechanical ventilation is a common therapy in the neonatal intensive care unit (NICU), especially in low birth weight (LBW) infants. The decision to extubate is usually based on a clinical subjective assessment, which takes into account personal experience, analysis of blood gas, and ventilator settings. The aim of the present study was to evaluate the efficacy of spontaneous breathing trial as an accurate indicator for the success of extubation in mechanically ventilated preterm infants.

Patients and methods: Our study was prospective cohort study conducted on62 preterm infants born less than 37 weeks of gestation and maintained on mechanical ventilation. divided in two groups: First group (32 infants): infants for whom a spontaneous breathing trial will be carried out for 5 minutes.Second group (30 infants): infants for whom a spontaneous breathing test will be carried out for 3 minutes. Then, rapid Shallow Breathing Index (RSBI) will be calculated for each patient.

Results: There is statistically non-significant difference between the studied groups regarding RSBI. There is statistically non-significant difference between the studied groups regarding pre-extubation parameters including respiratory rate, MAP, PO2, PCO2 or PH.There is significant association between fate of weaning and all of age at extubation, gestational age, birth weight, APGAR at 5 minutes<6, history of maternal PIH, pre-extubation MAP, PO2, and PCO2. Failure of weaning associated with younger age, younger gestational age, lower birth weight, history of maternal PIH, higher pre-extubation MAP, lower PO2, and PCO2. **Conclusion:** Actual outcome of weaning has strong agreement with predicted outcome on RSBI (less or more than 8 breaths ml/kg). Failure of weaning associated with younger age, younger gestational age, lower birth weight, history of maternal PIH, higher pre-extubation MAP, lower PO2, and PCO2.

Keywords: Extubation , Preterm Infants ; Respiratory Distress

INTRODUCTION

Mechanical ventilation is a common therapy in the neonatal intensive care unit (NICU), especially in low birth weight (LBW) infants, even in the current era of noninvasive respiratory support. Invasive respiratory support is associated with risk and complications including mortality and neurological impairments. Consequently, extubation of a ventilated infant should be as early as possible **(2)**.

Hence, extubation of ventilated infants as early as possible is a clinical goal to reduce unwarranted pulmonary morbidities. The decision to extubate premature neonates usually is based on clinical assessment of infant's spontaneous respiratory effort, adequacy of ventilation and oxygenation as judged by blood gas parameters, oxygen saturations, and ventilator settings. Up to 40% of mechanically ventilated infants weighing <1,000 g at birth require re-intubation following extubation. Failure of extubation has been associated with higher mortality, increased length of hospital stay and more ventilator days in adult and pediatric population **(2)**.

The adverse effects of reintubation such as trauma, bradycardia, hypercapnia, alteration of cerebral blood flow, ventilator associated pneumonia, and sepsis are common(**3**).A predictor to assess extubation readiness in LBW infants may reduce the morbidity**(1)**. Several strategies to assess extubation readiness in preterm infants have been investigated, none of which have demonstrate significant improvement over clinical decision making **(4).** Therefore, this study aimed to evaluate the efficacy of spontaneous breathing trial as an accurate indicator for the success of extubation in mechanically ventilated preterm infant.

ISSN:0975-3583,0976-2833 VOL12,ISSUE 06,2021

PATIENTS AND METHODS

The current study was a prospective cohort study performed on 62 preterm mechanically ventilated infants (All enrolled preterm infants were less than 37 weeks of gestation and were fit for extubation). Approval from Zagazig university institutional review board (IRB) was obtained prior starting the study.

The patients were classified into two groups:

- First group (32 infants): infants for whom a spontaneous breathing trial were carried out for 5 minutes.
- Second group (30 infants): infants for whom a spontaneous breathing test were carried out for 3 minutes.

Inclusion criteria:

Preterm infants less than 37 weeks of gestation, Mechanically ventilated infants Fit for extubation.

Exclusion criteria:

Preterm infants more than 37 weeks of gestation, Non-mechanically ventilated infants and Unfit for extubation.

Study design:

Rapid Shallow Breathing Index (RSBI) was calculated for each patient, so the 2 groups were further subdivided into 4 groups:

- The first group comprised the patients who had a SBT for 5 minutes and result of RSBI more than 8 breaths/ml/kg.
- The second group comprised patients who had a SBT for 5 minutes and result of RSBI less than 8 breaths/ml/kg.
- The third group comprised the patients who had a SBT for 3 minutes and result of RSBI more than 8 breaths/ml/kg.
- The forth group comprised the patients who had a SBT for 3 minutes and result of RSBI less than 8 breaths/ml/kg.

Extubation was carried out for all patients as recommended by their treating physician.Patients were followed up regarding failure of extubation.Failure of extubation is defined as the need for re-intubation within 72 hours after extubation.

Spontaneous breathing trial were performed under continued positive airway pressure (CPAP) with 5 cmH2O end-expiratory pressure (PEEP), inspiratory flow 10 L/min for 5 minutes for patients of the first group, and for 3 minutes for patients of the second group. The mean airways pressure and the inspired oxygen fraction were directly collected from the mechanical ventilator monitor before the SBT.

A SBT failure was recorded if the infant had either a bradycardia lasting longer than 15 s, defined as a drop in heart rate below 100 beats per minute, and/or a fall in oxygen saturation below 85% despite a 15% absolute increase in the fraction of inspired oxygen. Physician responsible for the care of the infant who were not be present at the time of SBT. The RSBI is defined as the ratio of respiratory frequency to tidal volume (f/VT). At the end of the test, the newborns were extubated and placed on CPAP or just oxygen, as needed, according to the unit's routine protocol.

Statistical analysis:

IBM's SPSS statistics (Statistical Package for the Social Sciences) for windows (version 25, 2017) was used for statistical analysis of the collected data. Shapiro-Wilk test was used to check the normality of the data distribution. All tests were conducted with 95% confidence interval. P (probability) value < 0.05 was considered statistically significant. Charts were generated using SPSS' chart builder and Microsoft Excel for windows 2019. Quantitative variables were expressed as mean and standard deviation, median, inter-quartile range, minimum and maximum as appropriate while categorical variables were expressed as frequency and percentage. Fisher exact and Chi square tests were used for inter-group comparison of nominal data using the crosstabs function.

ISSN:0975-3583,0976-2833 VOL12,ISSUE 06,2021

RESULTS

The present study showed a statistically non-significant difference between the studied groups regarding RSBI **(Table 1)**.

There is statistically non-significant difference between the studied groups regarding gestational age, birth weight, APGAR score at 1 or 5 minutes, mode of delivery, history of maternal PIH or birth weight **(Table 2)**.

There is statistically non-significant difference between the studied groups regarding pre-extubation parameters including respiratory rate, MAP, PO2, PCO2 or PH **(Table 3)**.

There is statistically non-significant difference between the studied groups regarding fate of weaning **(Figure 1).**

There is significant association between fate of weaning and all of age at extubation, gestational age, birth weight, APGAR at 5 minutes<6, history of maternal PIH, pre-extubation MAP, PO2, and PCO2. Failure o weaning associated with younger age, younger gestational age, lower birth weight, history of maternal PIH, higher pre-extubation MAP, lower PO2, and PCO2 **(Table 4)**.

There is statistically significant strong agreement between actual outcome of weaning and predicted outcome on RSBI **(Table 5)**.

Table (1) Comparison between the studied groups regarding RSBI:

Parameters	Groups		Test	
	5 min SBT group	3 min SBT group	χ^2	p
	N=32(%)	N=30 (%)		
RSBI:				
<8	14 (43.7)	17 (56.7)	1.033	0.309
>8	18 (56.3)	13 (43.3)		

χ^2 chi square test

Table (2) Comparison between the studied groups regarding antenatal and natal history:

Parameter	Groups				Test	
	5 min SBT+RSBI>8 group	5 min SBT+RSBI<8 group	3 min SBT+RSBI>8 group	3 min SBT+RSBI<8 group	F/χ^2	p
	N=18 (%)	N=14 (%)	N=13 (%)	N=17 (%)		
Gestational age: Mean ± SD	33.0 ± 2.14	33±2.72	34.32±1.88	33.59±2.35	0.932	0.431
APGAR 1min: Mean ± SD	5.5 ± 0.62	5.57 ± 0.51	6 ± 0.82	6 ± 0.71	2.567	0.063
APGAR 5min: Mean ± SD	6.5 ± 0.99	6.29 ± 0.83	7 ± 0.91	6.82 ± 1.01	1.629	0.193
Birth weight: Mean ± SD	1356.11±123.25	1417.86±92.25	1402.31±66.73	1438.82±100.55	2.134	0.106
Delivery mode:						
NVD	3 (16.7)	3 (21.4)	7 (53.8)	8 (47.1)	6.89	0.075
CS	15 (83.3)	11 (78.6)	6 (46.2)	9 (52.9)		
Maternal PIH:						
Absent	12 (66.7)	10 (71.4)	11 (84.6)	13 (76.5)	1.372	0.765
Present	6 (33.3)	4 (28.6)	2 (15.4)	4 (23.5)		

F One way ANOVA χ^2 chi square test

ISSN:0975-3583,0976-2833 VOL12,ISSUE 06,2021

Table (3) Comparison between the studied groups regarding parameters on extubation:

Parameter	Groups				Test	
	5 min SBT+RSBI>8 group	5 min SBT+RSBI<8 group	3 min SBT+RSBI>8 group	3 min SBT+RSBI<8 group	F	p
	N=18 (%)	N=14 (%)	N=13 (%)	N=17 (%)		
Respiratory rate: Mean ± SD	15.0 ± 0.84	15.29±0.99	14.77±0.83	14.82±0.83	1.068	0.37
MAP: Mean ± SD	5.69 ± 0.38	5.53 ± 0.12	5.69 ± 0.12	5.7 ± 0.33	1.28	0.29
PO2: Mean ± SD	26.17 ± 3.54	27.71 ± 1.98	27.62 ± 2.79	27.59 ± 2.85	1.102	0.356
PCO2: Mean ± SD	36.78±4.83	37.29±3.05	37.92±1.38	38.59±1.46	1.058	0.374
PH: Mean ± SD	6.88 ±0.32	7.1±0.11	6.94±0.27	6.92±0.49	1.143	0.34

F One way ANOVA χ^2 chi square test

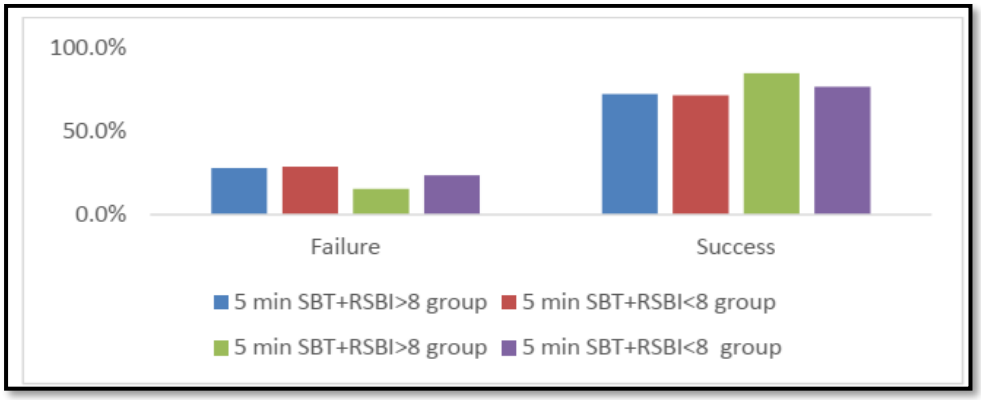

Figure (1) Multiple bar chart showing fate of weaning among the studied groups

Table (4) relation between fate of weaning and the studied parameters:

ISSN:0975-3583,0976-2833 VOL12,ISSUE 06,2021

Parameter	Fate		Test	
	Fail	Success	t/χ^2	p
	N=15(%)	N=47(%)		
Age (days): Mean ± SD	6.73 ± 1.28	8.04 ± 1.47	-2.748	0.008*
Gender: Male Female	7 (46.7) 8 (53.3)	33 (70.2) 17 (29.8)	2.754	0.097
Gestational age: Mean ± SD	30.27 ± 1.28	34.43 ± 1.47	-9.818	<0.001**
Birth weight: Mean ± SD	1332.67 ± 142.35	1424.68 ± 76.41	-2.396	0.029*
APGAR at 5 minutes<6	8 (53.3)	1 (2.1)	Fisher	<0.001**
Delivery mode: NVD CS	6 (40) 9 (60)	15 (31.9) 32 (68.1)	0.332	0.565
Maternal PIH: Absent Present	8 (53.3) 7 (46.7)	38 (80.9) 9 (19.1)	4.497	0.034*
Respiratory rate: Mean ± SD	14.87 ± 0.92	15 ± 0.83	-0.527	0.6
MAP: Mean ± SD	5.93 ± 0.43	5.57 ± 0.14	3.253	0.005*
PO2: Mean ± SD	23.13 ± 2.61	28.51± 1.4	-7.625	<0.001**
PCO2: Mean ± SD	35.07 ± 3.53	38.45 ± 2.56	-3.428	0.003*
PH: Mean ± SD	7.06 ± 0.3	6.92 ± 0.35	1.406	0.165

t Independent sample t test χ^2 chi square test

Table (5) validity of outcome predicted by and actual outcome on weaning:

Outcome regarding RSBI	Outcome on weaning		Total	K	p
	Fail	Succeed			
Fail	11	1	12	0.764	<0.001**
Succeed	4	46	50		
Total	15	47	62		

Kappa agreement **p≤0.001 is statistically highly significant

DISCUSSION

Mechanical ventilation is common in preterm infants in the treatment of respiratory distress and respiratory failure. Although essential and lifesaving, prolonged mechanical ventilation is associated with increased morbidities. Nevertheless, untimely extubation may also be harmful, as failure and subsequent reintubation is associated with increased morbidity and mortality as well **(5).**

It is imperative that a timely and safe extubation be undertaken to shorten the duration of mechanical ventilation after the resolution of respiratory distress. However, there are no standardized processes to assess for extubation readiness and marked variation among neonatal intensive care units (NICUs) persists. Multiple strategies have been investigated, such as use of minute ventilation, spontaneous breathing tests **(6)**.

The objective of this study was to evaluate the efficacy of spontaneous breathing trial as an accurate indicator for the success of extubation in mechanically ventilated preterm infant.

ISSN:0975-3583,0976-2833 VOL12,ISSUE 06,2021

Before treating the patients, we had to decide which duration of SBT should be decided in our study. Both SBT for 3 minutes and for 5 minutes were in our study as in a previous study, Kamlin et al. performed a 3-min SBT using endotracheal CPAP of 5–6 cmH2O in preterm infants with birth weights (BW) < 1250 g who were deemed 'ready' for extubation (Kamlin et al., 2006). The SBT showed a sensitivity of 97% and a specificity of 73% at predicting extubation success, thus it was adopted as standard of care in that institution. However, a follow-up prospective audit of this practice found that routine use of SBTs did not improve weaning times or extubation success rates **(7).** In the latest prospective observational study, the validity of a 5-min SBT was evaluated in 49 infants with GA < 32 weeks **(2).** Therefore, we compared 3 and 5 minutes SBT in our study.

To our best of knowledge, the present study is one of the first study comparing 3 and 5 minutes SBT.

The present study revealed that there is statistically non-significant difference between the studied groups regarding age, gender, RSBI ,gestational age, birth weight, APGAR score at 1 or 5 minutes, mode of delivery, history of maternal PIH or birth weight. Also, non-significant difference between the studied groups regarding pre-extubation parameters including respiratory rate, MAP, PO2, PCO2 or PH or fate of weaning. And thus indicating that no clinical need for increased time of spontaneous breathing trial.

In the present study it was found that there is statistically non-significant difference between fate of weaning and either gender, mode of delivery, pre-extubation respiratory rate or PH. In agreement with our resuts **Kaczmarek et al., (4)** studied a total of 47 infants; 36 were successfully extubated and 11 reintubated. There were no differences in patient demographics, ventilator settings, blood gases or post-extubation management between the groups. All components of the HRV analysis were significantly decreased in infants who failed, gen erating high areas under the receiver operating characteristic curve. The specificity and positive predictive values were 100, but with limited sensitivity and negative predictive values.

In agreement with our results previous studies have noted gestational age to be associated with extubation success, however they disagreed with our results in higher postmenstrual age, lower PO2, lower PCO2, lower oxygenation index, and higher **(8,9).**

Gupta et al found that extubation succeeded in 73% and failed in 27%. Adjusted factors associated with successful extubation included greater gestational age, chronologic age and lower preextubation PO2, along with lower "peak" respiratory severity score in the first 6 h of age **(10).**

Chavez et al conducted Prospective, blinded, clinical study in Pediatric intensive care unit (ICU) of a university hospital. Logistic regression analysis revealed no significant association between extubation outcome and any of the following: gender, indication for ventilation, cause of acute respiratory failure, secretion quantity and quality, and presence or absence of a cuffed endotracheal tube. There was a significant association between passing the SBT and extubation success. Duration of intubation was significantly associated with extubation failure. Patients failing extubation had almost twice the duration of intubation. Increased diastolic blood pressure at 5 mins from baseline also was significantly associated with extubation failure **(11)**.

Also, Mueller et al Studied 486 premature infants on mechanical ventilation was used to develop predictive models, birth weight for infants who failed their first extubation attempt was lower (929 ± 326 grams) compared to infants who were extubated successfully. depicts distributions of birth weight for infants who were extubated successfully versus those who failed. Among ventilator settings, tidal volume (VT) immediately prior to extubation was statistically significantly higher in infants who succeeded their first extubation attempt than in infants who failed. PaCO2 and SaO2 were statistically significantly different between the two groups: SaO2 was higher, while PaCO2 was lower for infants succeeding their first extubation compared to those who failed. Infants who failed extubation received more dosages of surfactant prior to extubation compared to infants who did not fail. Time between last blood gas analysis and extubation was statistically significantly shorter in the group that was extubated successfully compared to the group that failed extubationhowevere **(12).**

The present study proved that there is statistically significant strong agreement between actual outcome of weaning and predicted outcome on RSBI.

In agreement with our results Saikia et al. conducted a prospective cohort study in PICU and NICU of a multispecialty tertiary care institute. All consecutive newborns, infants and children, who remained on the ventilator for more than 12 h, were included. They observed RSBI as a potentially useful index that can predict EF-the higher the value, the higher the chances of EF **(13).**

ISSN:0975-3583,0976-2833 VOL12,ISSUE 06,2021

Also, **Munshi et al. (14)** conducted a retrospective cohort study was conducted at King Faisal Cardiac Center on all extubated children, pediatric patients who suffer extubation failure usually have a higher RSBI measurement compared to the patients who have a successful extubation. The most significant RSBI measurements to predict the extubation outcome were recorded earlier two hours prior to extubation.

CONCLUSION

Actual outcome of weaning has strong agreement with predicted outcome on RSBI (less or more than 8 breaths ml/kg). Failure of weaning associated with younger age, younger gestational age, lower birth weight, history of maternal PIH, higher pre-extubation MAP, lower PO2, and PCO2.

No Conflict of interest.

REFRERNCES

1- **Janjindamai W, Pasee S, Thatrimontrichai A.(2017).** The Optimal Predictors of Readiness for Extubation in Low Birth Weight Infants. Journal Of The Medical Association Of Thailand. 1;100(4):427.
2- **Chawla, S., Natarajan, G., Gelmini, M. (2013).** "Role of spontaneous breathing trial in predicting successful extubation in premature infants." Pediatric pulmonology 48(5): 443-448.
3- **Sant'Anna, G. M. and Keszler, M. (2012).** "Weaning infants from mechanical ventilation." Clinics in perinatology 39(3): 543-562.
4- **Kacmarek S., Villar J.& Sulemanji N. et al., (2016).** Open lung approach for the acute respiratory distress syndrome: a pilot, randomized controlled trial. Critical care medicine, 44(1), 32-42
5- **Parke R.(2016).** High-Flow Nasal Cannula Oxygen in Acute Respiratory Failure After Extubation: Key Practical Topics and Clinical Implications. In Noninvasive Mechanical Ventilation and Difficult Weaning in Critical Care (pp. 139-146). Springer, Cham.
6- **Shalish I., Kanbar H.& Rao M. et al., (2017).** Prediction of Extubation readiness in extremely preterm infants by the automated analysis of cardiorespiratory behavior: study protocol. BMC pediatrics, 17(1), 167
7- **Kamlin F., Davis G., Argus B., et al. (2008).** "A trial of spontaneous breathing to determine the readiness for extubation in very low birth weight infants: a prospective evaluation." Archives of Disease in Childhood-Fetal and Neonatal Edition 93(4): F305-F306.
8- **Manley J., Doyle W., Owen S. et al. (2016).** "Extubating extremely preterm infants: predictors of success and outcomes following failure." The Journal of pediatrics 173: 45-49.
9- **Chawla S., Natarajan G., Shankaran S. et al. (2017).** "Markers of successful extubation in extremely preterm infants, and morbidity after failed extubation." The Journal of pediatrics 189: 113-119. e112.
10- **Gupta, D., Greenberg, R. G., Sharma, A., et al. (2019).** "A predictive model for extubation readiness in extremely preterm infants." Journal of Perinatology 39(12): 1663-1669.
11- **Chavez, A., dela Cruz, R. and Zaritsky, A. (2006).** "Spontaneous breathing trial predicts successful extubation in infants and children." Pediatric Critical Care Medicine 7(4): 324-328.
12- **Mueller, M., Almeida, J. S., Stanislaus, R., et al. (2013).** "Can Machine Learning Methods Predict Extubation Outcome in Premature Infants as well as Clinicians?" Journal of neonatal biology 2: 1000118.
13- **Saikia, B., Kumar, N. and Sreenivas, V. (2015).** "Prediction of extubation failure in newborns, infants and children: brief report of a prospective (blinded) cohort study at a tertiary care paediatric centre in India." SpringerPlus 4(1): 827.
14- **Munshi, F. A., Bukhari, Z. M., Alshaikh, H., et al. (2020).** "Rapid Shallow Breathing Index as a Predictor of Extubation Outcomes in Pediatric Patients Underwent Cardiac Surgeries at King Faisal Cardiac Center." Cureus 12(6): e8754-e8754.