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ORIGINAL RESEARCH

The FiO_2 is associated with the successful extubation of mechanically ventilated neonates

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Abstract: Early extubation may be beneficial in preventing or attenuating the development of bronchopulmonary dysplasia (BPD). We tested the hypothesis that patients extubated from higher ventilator pressures would be more likely to fail extubation. To determine the relationship between peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), and fraction of inspired oxygen (FiO_2) at the time of extubation and success of extubation, we reviewed the charts of all patients extubated in our neonatal intensive care unit (NICU) over two time periods; April 4, 2005–May 7, 2005 and November 14, 2005–January 7, 2006. Successful extubation was defined as not requiring re-intubation within 36 hours of extubation. There were 67 patients extubated during the study periods, and 58 patients (88%) were successfully extubated. There was no difference in the ventilator settings (PIP, PEEP, mean airway pressure, ventilator rate, or inspiratory time) between the patients with successful vs unsuccessful extubations. However, the FiO_2 was significantly ($P = 0.011$) lower in the successful extubations (median 24, intraquartile range 21–31) than in the unsuccessful extubations (median 33, intraquartile range 28–43). The median PIP was 22 cm H_2O (intraquartile range 20–24) in the patients successfully extubated. Our data suggest that the FiO_2 may be the only ventilator setting associated with successful extubations in this patient population. Randomized control trials are needed to determine if extubating neonatal patients from relatively high PIP using FiO_2 will shorten the duration of mechanical ventilation.

Keywords: extubation, neonates, FiO_2, bronchopulmonary dysplasia

Introduction

Mechanical ventilation is central in the pathogenesis of bronchopulmonary dysplasia (BPD).[1] Institutions that successfully limit or avoid exposure to mechanical ventilation have reported relatively low rates of BPD.[2,3] In a primate model, prolonged exposure to mechanical ventilation resulted in BPD, while short periods of ventilation followed by nasal continuous positive airway pressure (nCPAP) did not result in BPD.[4] While there is consensus that avoiding or limiting the duration of mechanical ventilation is likely to improve outcomes, there is concern that subjecting patients to unsuccessful extubation attempts also may carry risks including increased length of stay and mortality.[5,6] There is little agreement among neonatologists on the best means of predicting successful extubation in neonates. Various trials have used specific ventilator settings, including mean airway pressure (MAP), ventilator rate, peak inspiratory pressure (PIP), fraction of inspired oxygen (FiO_2), or various combinations of these parameters as criteria for extubation.[7] However, extubation criteria range widely from study to study with little evidence presented to support them. There have been attempts to examine

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objective criteria by which to predict successful extubation, with varying rates of success reported,[7,8] and many of these studies use techniques and methodologies, such as pulmonary function measurement, that are not widely available to the clinician.[9] The aim of this study is to determine the relationship between PIP, positive end expiratory pressure (PEEP), ventilator rate, and/or FiO_2 at the time of extubation and success of extubation. We speculated that patients extubated from higher PIP would be more likely to fail extubation.

Methods

This study was approved by the Nationwide Children's Hospital Institutional Review Board. The charts for all patients extubated in the all-referral level IIIc neonatal intensive care unit (NICU) at Nationwide Children's Hospital (Columbus, OH) during two different time periods, April 4, 2005–May 7, 2005 and November 14, 2005–January 7, 2006 were reviewed. There are three different neonatology attending groups that admit patients to the Nationwide Children's NICU, and thus distinct periods were examined to minimize the likelihood of data being disproportionately influenced by individual decision making. Clinical information, including gestational age at birth (GA), birth weight in g, days of ventilation, weight at extubation, and ventilator settings at extubation were collected. Successful extubation was defined as not being reintubated within 36 hours of extubation. The decisions to either extubate or reintubate the patients were entirely at the discretion of the attending physician. These decisions are typically based on available clinical, radiological, and laboratory data. In our NICU there is no specific, laboratory-based reintubation protocol. This is due in part to concerns regarding the accuracy of capillary gases in this patient population, as well as the possibility that obtaining such gases negatively affects the infant's respiratory status.[10,11] Furthermore, there is a lack of consensus among the neonatology practices regarding the exact target PCO_2 and pH levels in these patients.

Those patients who were successfully extubated were compared with those that were not successfully extubated using one-way analysis of variance (ANOVA). Differences were identified using the Student Newman–Keuls post-hoc test for normally distributed data and a Kruskal–Wallis ANOVA on Ranks for nonparametric data (SigmaStat, Jandel Scientific, Carlsbad, CA). Multiple logistic regression was done to determine the various contributions of the measured parameters on successful or unsuccessful extubation (SigmaStat). Comparisons were considered statistically significant if $P < 0.05$.

Results

During the periods studied, there were 67 patients who had extubation attempts, of which 59 (88%) were successful. These patients had a mean GA of 31 ± 5 weeks and a birth weight of 1741 ± 1081 g. At the time of extubation the mean body weight was 2194 ± 990 g and the average time on mechanical ventilation was a median of 5 days with an intraquartile range of 2–8 days. There was no difference in either birth weight or weight at extubation between the patients extubated successfully and those that were not extubated successfully (Table 1). Upon extubation, 37 patients were placed on nCPAP (mean nCPAP 7.9 ± 0.7 cm H_2O; median CPAP 8 cmH_2O, range 6–10 cm H_2O), 13 patients were placed on room air, and 17 patients were placed on supplemental oxygen either by nasal cannula or oxyhood. The patients that were extubated successfully had a greater GA and fewer ventilator days than those patients who were not successfully

Table 1 All patients

	Overall	Successful	Unsuccessful	*P* value
Number	67	59 (88%)	8 (12%)	–
Birth weight (g)	1489 (870–2635)	1635 (918–2707)	870 (800–1260)	0.087
GA (completed weeks)	31 ± 5	32 ± 5	27 ± 6	**0.021**
Ventilator days	5 (2–8)	5 (2–7)	20 (7–33)	**0.002**
Extubation weight (g)	2194 ± 990	2278 ± 942	1575 ± 1182	0.06
PIP (cm H_2O)	22 (20–24)	22 (20–24)	24 (21–26)	0.20
PEEP (cm H_2O)	6 (5–6)	6 (5–6)	6 (5.5–6.5)	0.30
Ventilator rate (per minute)	18 (15–20)	18 (15–20)	18 (17.5–21.5)	0.48
Ti (seconds)	0.40 (0.36–0.40)	0.40 (0.40–0.40)	0.45 (0.35–0.50)	0.47
MAP (cm H_2O)	7.8 ± 1.3	7.8 ± 1.3	8.4 ± 0.8	0.17
FiO_2 (%)	25 (21–32)	24 (21–31)	33 (28–43)	**0.011**

Notes: Mean ± SD for normally distributed data; median (25th percentile–75th percentile) for nonparametric data. Numbers in bold are significant at the 0.05 level.
Abbreviations: EGA, estimated gestational age; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; Ti, inspiratory time; MAP, mean airway pressure; FiO_2, fraction of inspired oxygen.

extubated (Table 1). The ventilator settings, including PIP, PEEP, ventilator rate, inspiratory time (Ti), and MAP, were not different between the two groups (Table 1). However, the patients who were successfully extubated had a significantly lower FiO_2 than did those patients who were not successfully extubated (Table 1).

Since the patients who were extubated successfully had a greater GA we decided to do a subgroup analysis on the extremely low birth weight (ELBW) patients even though the numbers were relatively small. In the ELBW subgroup, there were 23 patients who had extubation attempts and 18 (78%) were successful. These patients had a mean GA of 25 ± 2 weeks and a birth weight of 763 ± 161 g. All of these patients were placed on nCPAP following extubation. At the time of extubation the mean body weight was 1398 ± 572 g and the average time on mechanical ventilation was 17 ± 20 days. There was no difference in birth weight, GA, or weight at extubation between the patients extubated successfully and those who were not extubated successfully (Table 2). The patients who were extubated successfully had fewer ventilator days than those patients who were not extubated successfully (Table 2). The ventilator settings (PIP, PEEP, ventilator rate, Ti, and MAP) were not different between the patients with successful and unsuccessful extubations (Table 2). In this subgroup analysis of ELBW patients, those patients who were successfully extubated also had a significantly lower FiO_2 than did those patients who were not successfully extubated (Table 2).

We employed multiple logistic regression to identify the relative contribution of the various measured variables for successful extubation. When PIP, ventilator rate, mean airway pressure, FiO_2, birth weight, gestational age, extubation weight, and ventilator days were used in the multiple logistic regression model, none of the eight variables were significant. We then used the ventilator-related variables: PIP; rate; MAP; and FiO_2, and found that only FiO_2 was significant (Table 3), with an odds ratio of 0.87 [95% CI: 0.79–0.97]. We also performed multiple logistic regression using the nonventilator parameters, birth weight (OR: 0.998, 95% CI: 0.995–1.001), gestational age (OR: 1.52, 95% CI: 0.82–2.85), weight at time of extubation (OR: 1.73, 95% CI: 0.27–11.14), and days on ventilator (OR: 0.95, 95% CI: 0.89–1.01), and none of these variables were significant. Although the numbers were small, we also performed the logistic regression on patients <1001 g. Given the small numbers the logistic regression with all eight variables failed to converge. When just the four respiratory variables were used in the model, the logistic regression converged but none of the four variables were significant, with FiO_2 having a *P*-value of 0.09 (Table 3). Although, the multiple logistic regression even for the full data set is somewhat limited by the absolute numbers in this study, this analysis also suggests that FiO_2 may be a predictor of successful extubation in the NICU.

Discussion

Our data do not support our belief that patients extubated from a higher PIP would be more likely to fail extubation. Furthermore, our results suggest that patients can be successfully extubated from ventilator settings that are generally higher than those reported in the literature with similar rates of success.[9,12,13] For example, in the successfully extubated infants the average MAP was ~8 cm H_2O, the average PIP was ~22 cm H_2O, ventilator rates were ~20 breaths per minute, and the average PEEP was ~6 cm H_2O. We found in this population of patients that the only ventilator setting that was associated with successful

Table 2 Patients with birth weight <1001 g

	Overall	Successful	Unsuccessful	*P* value
Number	23	18 (78%)	5 (22%)	–
Birth weight (grams)	763 ± 161	754 ± 174	793 ± 112	0.65
GA (completed weeks)	25 ± 2	25 ± 2	24 ± 0	0.21
Ventilator days	17 ± 20	11 ± 12	35 ± 30	**0.01**
Extubation weight (grams)	1398 ± 572	1460 ± 570	1190 ± 570	0.36
PIP (cm H_2O)	23 ± 3	23 ± 2	23 ± 4	0.88
PEEP (cm H_2O)	6 ± 1	6 ± 1	6 ± 1	0.91
Ventilator rate (per minute)	19 ± 4	19 ± 2	21 ± 8	0.24
Ti (seconds)	0.43 ± 0.08	0.41 ± 0.08	0.47 ± 0.07	0.18
MAP (cm H_2O)	8.3 ± 1.2	8.1 ± 1.3	8.7 ± 0.8	0.42
FiO_2 (%)	32 ± 10	30 ± 8	42 ± 11	**0.01**

Notes: Data presented as mean ± SD; *P* value for one-way ANOVA comparing successful and unsuccessful. Numbers in bold are significant at the 0.05 level.
Abbreviations: EGA, estimated gestational age; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; Ti, inspiratory time; MAP, mean airway pressure; FiO_2, fraction of inspired oxygen.

Table 3 Logistic regression

	Entire cohort			Patients <1001 g		
	OR	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
PIP	0.72	0.47–1.09	0.12	0.45	0.13–1.54	0.20
RR	0.87	0.73–1.03	0.11	0.67	0.39–1.18	0.16
MAP	1.20	0.53–2.70	0.66	1.10	0.30–4.08	0.89
FiO_2	**0.87**	**0.79–0.97**	**0.009**	0.75	0.53–1.05	0.09

Notes: Odds ratio (OR), 95% confidence interval (95% CI), and *P*-value from the logistic regression model using PIP, RR, MAP and FiO_2 as independent variables and successful extubation as the dependent variable. Numbers in bold are significant at the 0.05 level.

Abbreviations: PIP, peak inspiratory pressure; RR, set rate on ventilator; MAP, mean airway pressure; FiO_2, fraction of inspired oxygen.

extubation was the FiO_2 at the time of extubation. As perhaps expected, nonventilator parameters that were associated with successful extubation included the GA at birth as well as time on the ventilator. However, it should be pointed out that the vast majority of neonates (88%) in this study were successfully extubated from ventilator settings that might be considered relatively high by many neonatologists and neonatal nurse practitioners. Our results suggest that a large randomized control trial should be considered to determine if extubating neonates from higher pressures will decrease length of time on mechanical ventilation and bronchopulmonary dysplasia.

One possible concern regarding our study is the lack of "objective" criteria for extubation and/or reintubation. For example, we do not uniformly utilize a specific blood gas-based protocol. This may add bias, but in general as suggested by the data, the decisions to extubate and reintubate are made using a relatively standard approach to patient care. However, we support the notion that the use of a specific protocol for extubation and reintubation would decrease practice variability and likely improve outcomes as well. There are a few additional limitations to this study that should be considered. For example, this is a single center study in a relatively small and specialized population, therefore the results may not be generalizable to all NICUs, particularly those with large inborn populations. Another potential limitation is that perhaps our relatively high success rate was secondary to waiting too long to extubate these patients. However, we wish to emphasize that our findings support the notion that extubation can be done successfully from relatively high ventilator settings, and we propose that similar criteria should be used in a multi-center randomized controlled trial of extubation.

Numerous strategies to predict extubation success in neonates have been proposed; some have used measures of pulmonary function in combination with baseline ventilator criteria. In one such study,[9] the use of pulmonary function to predict extubation success resulted in an ~60% success rate. Recently, Smith, et al[13] reported an 81% success rate, predicted by a compliance of ≥0.5 mL/cm H_2O. More recently, Kamlin et al[12] have reported on the prospective use of a 3-minute spontaneous breathing trial in infants with birth weight ≤1250 g during endotracheal tube CPAP with a reported subsequent extubation success rate of 83%. Furthermore, their data also suggested that infants could be extubated from higher MAP (7.2 cm H_2O vs 6.5 cm H_2O) and rates (42 breaths per minute vs 27 breaths per minute) than previously described, with no discernable differences in the rate of successful extubation or the number of ventilator days.[12]

Our data suggest that neonates can be successfully weaned from mechanical ventilation at relatively high PIP, and that more mature infants who have been ventilated for shorter periods of time are more likely to be successfully extubated. We speculate that extubating neonatal patients from relatively high PIP may result in a shortened duration of mechanical ventilation, which may lead to a decrease in the incidence of BPD. It remains difficult to predict which patients are ready for extubation. Based on our findings and those of Kamlin et al[12] we believe that a large randomized controlled multi-center study should be considered to evaluate the utility of the FiO_2 to actually predict extubation success in NICU patients.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Chess PR, D'Angio CT, Pryhuber GS, Maniscalco WM. Pathogenesis of bronchopulmonary dysplasia. *Semin Perinatol*. 2006;30(4):171–178.
2. De Klerk AM, De Klerk RK. Nasal continuous positive airway pressure and outcomes of preterm infants. *J Paediatr Child Health*. 2001; 37(2):161–167.
3. Verder H, Bohlin K, Kamper J, Lindwall R, Jonsson B. Nasal CPAP and surfactant for treatment of respiratory distress syndrome and prevention of bronchopulmonary dysplasia. *Acta Paediatr*. 2009;98(9):1400–1408.

4. Coalson JJ. Pathology of bronchopulmonary dysplasia. *Semin Perinatol*. 2006;30(4):179–184.
5. Farias JA, Retta A, Alia I, et al. A comparison of two methods to perform a breathing trial before extubation in pediatric intensive care patients. *Intensive Care Med*. 2001;27(10):1649–1654.
6. Seymour CW, Martinez A, Christie JD, Fuchs BD. The outcome of extubation failure in a community hospital intensive care unit: a cohort study. *Crit Care*. 2004;8(5):R322–R327.
7. Dimitriou G, Greenough A, Endo A, Cherian S, Rafferty GF. Prediction of extubation failure in preterm infants. *Arch Dis Child*. 2002;86(1): F32–F35.
8. Kamlin COF, Davis PG, Morley CJ. Predicting successful extubation of very low birthweight infants. *Arch Dis Child Fetal Neonatal Ed*. 2006; 91(3):F180–F183.
9. Szymankiewicz M, Vidyasagar D, Gadzinowski J. Predictors of successful extubation of preterm low-birth-weight infants with respiratory distress syndrome. *Pediatr Crit Care Med*. 2005;6(1):44–49.
10. Courtney SE, Weber KR, Breakie LA, et al. Capillary blood gases in the neonate. A reassessment and review of the literature. *Am J Dis Child*. 1990;144(2):168–172.
11. Kim EH, Cohen RS, Ramachandran P. Effect of vascular puncture on blood gases in the newborn. *Pediatr Pulmonol*. 1991;10(4):287–290.
12. Kamlin COF, Davis PG, Argus B, Mills B, Morley CJ. A trial of spontaneous breathing to determine the readiness for extubation in very low birth weight infants: a prospective evaluation. *Arch Dis Child Fetal Neonatal Ed*. 2008;93(4):F305–F306.
13. Smith J, Pieper CH, Maree D, Gie RP. Compliance of the respiratory system as a predictor for successful extubation in very-low-birth-weight infants recovering from respiratory distress syndrome. *S Afr Med J*. 1999;89(10):1097–1102.