Extubating Failure in The Preterm Infant

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Abstract

Background: Preterm infants usually have multiple complications, mainly due to their low birth weight. Multiple factors may lead to the need for intubating preterm infants. However, some infants may suffer from difficult extubation and failure to extubate from ventilation. This failure can result in increased morbidity or mortality.

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1. INTRODUCTION

Many very preterm infants require assisted ventilation. After resolution of their initial pulmonary dysfunction, when extubated they are at risk of failure due to poor respiratory drive, atelectasis, residual pulmonary function abnormalities, or intercurrent illness. Keeping such infants extubated will decrease lung injury and improve long-term pulmonary and perhaps even neurologic outcomes. On the other hand, if failure of extubation could be accurately predicted, then extubation could be deferred and the trauma of reintubation after a brief failed extubation, with increased work of breathing, hypoventilation, and respiratory acidosis, could be avoided **(1).**

Lower GA (<26 weeks)
Prolonged ventilation (>10–14 days)
History of previous extubation failure
Use of sedatives (eg, morphine, fentanyl)
Multiple reintubations: upper airway problems
Evidence of residual lung injury: BPD, pulmonary interstitial emphysema
Extubation from high ventilatory settings
Extubation from high FiO_2
Hemodynamically significant PDA

Abbreviation: PDA, patent ductus arteriosus.

Figure (1): Risk factors for extubation failure (2).

Table (1): Causes of extubation failure (3)

Severe or multiple episodes of apnea
Hypoxemia
Hypercapnia
Upper airway obstruction
• Edema of the epiglottic area
• Subglottic edema/stenosis

Prediction of extubation failure

Several studies have examined factors associated with failure of extubation. The contribution in this issue of Jornal de Pediatria from **Hermeto et al. (4), Michael et al. (5) and Sarafidis et al. (6)** confirms that infants with lower gestational ages are more likely to fail extubation; other factors which they investigated did not independently predict extubation failure. They also showed an association between extubation failure and both severe intracranial hemorrhage and patent ductus arteriosus. As the authors point out, the causal relationship between these findings is uncertain; in both cases the abnormal finding could be caused by, or could cause, failure of extubation. Their finding confirms that attempts to prevent extubation failure should be focused on the most immature infants. Other studies have examined physiologic or clinical measurements as a means of predicting successful extubation in individual infants, unfortunately there is no clear evidence that any specific test or physiologic measurement can adequately predict a successful extubation.

The maximal inspiratory force, that is, the most negative pressure that an infant can generate during an airway occlusion, has been suggested as a way of determining the capacity of an infant to tolerate extubation. However, this measure, like many others, is very dependent on the state of arousal of the infant, thus it varies from one minute to the next and has not proved helpful in predicting extubation failure **(7, 8).**

More sophisticated measurements, such as a low post-extubation functional respiratory capacity, have been shown to be statistically associated with extubation failure but in that study low gestational age was in fact a better predictor **(9).**

The test which appears to have the greatest potential currently is the minute ventilation test of **Gillespie et al. (10)** a measurement of minute ventilation during complete ventilator support followed by a repeat during 10 minutes of continuous positive airway pressure (CPAP). If the infant is capable of maintaining a minute ventilation at least 50% as high during CPAP, then successful extubation is likely.

A randomized controlled trial showed that the use of this test significantly decreased the duration of assisted ventilation, although the very early extubations were associated with a higher rate of extubation failure (**11).**

Dekker et al. (12) evaluated another test of the ability to breathe spontaneously, the spontaneous breathing test, in which there is a short trial period of endotracheal CPAP. A failed test is defined as a bradycardia (< 100/min) for > 15 seconds or SpO_2 below 85% despite a 15% increase in FiO_2.

Barrington, (1) also demonstrated that minute ventilation falls by a greater amount during this 3-minute test for infants who fail extubation than among those who succeed. Further confirmation of the utility of this test will probably require a randomized controlled trial.

Prevention of extubation failure:

An evidence-based review of strategies to reduce extubation failure shows the following (**13):**

Immature infants are more likely to be successfully extubated if they are not weaned to endotracheal CPAP prior to extubation, but extubated from low ventilator settings.

- It is uncertain whether weaning using synchronized intermittent mandatory ventilation (SIMV) and reducing the rate, or using assist control and weaning the pressure is preferable. Similarly, it is unclear whether newer modes of volume ventilation or pressure support ventilation improve the chances of successful extubation.
- Nasal CPAP after extubation is preferable to no pressure support.
- The method for generating the positive pressure appears to be unimportant, specifically the infant flow device is no better than other means of generating a positive pressure, it is possible that bubble CPAP is preferable to the infant flow device **(14),** but this requires confirmation.
- Nasal ventilation using the Infant Star® ventilator with peak inspiratory pressures greater than 14 cmH_2O is preferable to CPAP**,** in contrast, bi-level positive airway pressure (BiPAP) using the infant flow device is no better than CPAP **(15, 16).**
- The infant should probably have binasal prongs rather than a single nasal prong.
- Immature infants receiving methylxanthines prior to extubation have reduced extubation failure; more specifically, caffeine has been shown to decrease bronchopulmonary dysplasia and to improve long-term outcomes and should probably be the methylxanthine of choice **(17)**
- Additional respiratory stimulants, such as doxapram, do not further improve extubation success **(18).**

Extubating the very immature infant:

These considerations lead to the following recommendations: very preterm infants should be extubated as early as possible, since the maneuver is likely to be successful, perhaps using the minute ventilation test, with infants receiving more than 40% oxygen, and those who already have a low lung volume prior to extubation are unlikely to be successful. Apart from these limitations, most infants deserve an attempt to extubate as long as a reintubation can be achieved with little trauma, with experienced intubators and good premedication. Infants should receive a loading dose of 20 mg/kg of caffeine citrate prior to extubation, followed by a maintenance dose of 5 mg/kg/day and should be extubated from low ventilator settings. After extubation, they should be supported with nasal ventilation. As the Infant Star® ventilator is no longer available, and there is no other method of reliably synchronizing nasal ventilation, non- synchronized nasal ventilation with pressures of at least 14 cmH O peak and 6 cmH O positive end-expiratory pressure (PEEP) and a rate of 20 per minute should be initiated. In general, 72 hours of nasal ventilation would be a minimum, followed by CPAP or a trial of unsupported breathing depending on the clinical condition (19, 20).

Role of Sponatneous Breathing Trials:

In Chawla et al. (21) 's study, their objectives, were

(a) To evaluate the validity of respiratory compliance (Crs) and SBT in predicting successful extubation in premature neonates with planned extubation attempt within the first 3 weeks of life,

(b) To identify clinical determinants of successful extubation,

(c) To compare ventilator parameters before extubation and 24 hr after re-intubation among infants who fail extubation attempts, and (22).

(d) To compare hospital outcomes between infants who fail and those who successfully remain extubated 72 hr later. They hypothesized that Crs and SBT prior to planned extubation within the first 3 weeks of life can independently predict successful extubation >72 hr in preterm infants < 32 weeks gestation (21).

Further hypothesized that a failed extubation attempt would be associated with higher ventilator support 24 hr later and worse clinical outcomes at hospital discharge (23).

In a cohort of mechanically ventilated premature infants, **Chawla et al., (21)** were able to demonstrate that SBT performed up to 6 hr of elective extubation, within the first 3 weeks of life, was able to predict success of extubation with 92% sensitivity and 88% PPV. Respiratory compliance prior to extubation was not helpful in predicting success of extubation. As expected, successfully extubated infants had a higher GA and weighed more at extubation, compared to infants who required re-intubation. Multivariate logistic regression analysis with GA as covariate revealed that passing SBT remained an independent predictor of successful extubation. Infants who passed the SBT were 6.6 times more likely to be successfully extubated, compared to infants who failed the SBT. Finally, rates of BPD, days on oxygen, mechanical ventilation, and hospital stay were significantly increased in infants who failed their first extubation attempts.

Chawla et al. (21) data on the usefulness of SBT in neonates were comparable to previously reported literature on the SBT in premature infants by Kamlin et al. who found a sensitivity of 97%, and a positive predictive value for extubation success of 93%. In a further prospective audit, the same investigators found that VLBW infants (<1,250g) were extubated at significantly higher support compared to historic controls. There was no difference in the rate of BPD or proportion of infants who were successfully extubated for 72 hr. Chawla et al., arbitrarily selected 5 min for duration of SBT, because they speculated that a longer duration of SBT (15–120 min) as used among children and adults may precipitate atelectasis and increase the work of breathing in premature infants. Low negative predictive value of SBT may be due to increased work of breathing through a small diameter ETT without pressure support, precipitating failure of SBT.

In **Kamlin's** study, SBT was performed for 3 min and most neonates who failed SBT did so in the first 90 sec, compared to 3–4 min in Chawla et al.'s study. Infants in Kamlin's study were on higher ventilator support prior to elective extubation, compared to those in the Chawla et al.'s study (ventilator rate of 20–30 breaths/min, MAP of 7.2 mmHg vs. 16 breaths/min and 5.8 mmHg). In addition, in the study by **Kamlin,** the mode of ventilation was either assist control or SIMV, in contrast to SIMV in all Chawla et al.'s infants. These differences may explain the difference in the timing of failed SBT in the two studies. Having a shorter time (3 min vs. 5 min) for SBT may miss some patients who would fail the trial after 3 min. Therefore, a 5-min SBT may be a reasonable time period to identify extubation-readiness in the majority of infants, whereas failure of 5-min SBT may suggest reassessment of clinical condition of the patient, prior to extubation **(24).**

Previous studies in premature infants have found spontaneous minute ventilation to be a useful predictor of successful extubation. Veness-Meeham et al. in a study of 50 premature infants with RDS, found that dynamic lung compliance and minute ventilation were poor predictors of successful extubation. In contrast, Szymankiewicz et al. and Balsan et al. demonstrated that higher lung compliance and low airway resistance measured prior to extubation among very low birth weight infants were predictive of successful extubation **(24).**

In Chawla et al. (21) study, Crs measurement prior to extubation was not predictive of successful extubation. One possible explanation could be the high use of antenatal steroids and postnatal surfactant therapy which might have improved Crs in their infant population. Their extubation failure rate of 20% is consistent with previous reported rates of 20–22% in the premature infant population. Ventilator parameters 24 hr after re-intubation were significantly higher than pre-extubation parameters among infants who failed extubation. Timing of elective extubation is crucial and needs a balanced approach of avoiding adverse effects of prolonged intubation and potential risks associated with hasty failed extubation in premature neonates.

The need for higher ventilator support after a failed extubation attempt may be due to periods of ineffective spontaneous breathing, associated sub-segmental lung atelectasis, and/or underlying co-morbidity (such as PDA). Higher morbidities at discharge among infants who failed extubation may also be due to younger GA and other inherent differences in baseline characteristics of these infants. Chawla et al.'s findings of higher mortality, increased length of hospital stay and number of days on mechanical ventilation among infants who failed extubation is comparable to those reported among adult and older pediatric patients (**21).**

In summary, SBT prior to elective extubation may be used in predicting successful extubation in premature infants. Guidelines for extubation among premature infants are needed in order to reduce unnecessary exposure to adverse effects of mechanical ventilation, while maintaining successful spontaneous breathing efforts **(25).**

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