

Original article

Weaning from invasive respiratory support in newborn: is there just one strategy?

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Abstract. Despite a even more frequent use to non-invasive respiratory support, mechanical ventilation is still often necessary for supporting premature infants with lung disease. Protracted mechanical ventilation is associated with increased morbidity and mortality and thus the earliest weaning from invasive respiratory support is desirable. Weaning protocols may be helpful in achieving more rapid reduction in support. However, no consensus has been reached on criteria to identify when patients are ready to wean or how to achieve it. In this article, available evidence is reviewed and reasonable evidence-based recommendations for weaning and extubation are provided. (www.actabiomedica.it)

Key words: weaning, extubation, premature infants

Introduction

Although non-invasive respiratory support is increasingly employed, mechanical ventilation (MV) remains an essential tool in the care of critically ill newborns.

According to the Vermont Oxford Database, about 60% of Very Low Birth Weight Infants (VLBW) and 95% of Extremely Low Birth Weight Infants (ELBW) are subjected to MV during hospitalization (1). Therefore, most of the infants who now receive mechanical ventilation are smaller and more immature than those ventilated only 10 years ago. Particularly, they have serious lung immaturity, inconsistent respiratory drive and a weak respiratory pump.

Moreover, infants who are subjected to MV need an analgosedative theraphy to avoid discomfort and pain.

Despite its crucial role in reducing mortality rate, MV is associated with morbidity, risks and complications, including bronchopulmonary dysplasia and periventricular hemorrhage (2-5).

To minimize risks and complications, it is recommended to discontinue MV as soon as infants are able to maintain spontaneous breathing and achieve appropriate gas exchange with minimal respiratory effort.

The ideal time for weaning from MV is frequently established on clinical and laboratory parameters which at least are not very standardised.

The extubation failure may expose to hypoxia and hypercapnia. The subsequent reintubation procedure may exacerbate blood gas alterations with an unknown impact on cerebral function (6). Based on the damage associated with the inappropriate duration of MV in newborns and since the rate of extubation failure is higher the lower the gestational age (30-40% in ELBW) there is necessity to establish objective criteria for extubation (7-9).

Weaning ventilator setting

Conventional Mechanical Ventilation

Weaning is the gradual reduction of ventilatory support and the transfer of respiratory control back to the patient.

The first requirement for weaning is the improvement of the underlying disease as suggested by the decreasing of oxygen requirement. Weaning from MV is usually achieved by the gradual reduction of ventilatory support until the settings are judged to be low enough to remove the endotracheal tube. In conventional MV settings, the peak inspiratory pressure (PIP) is one of the most important parameters used for weaning to avoid the risk of overdistention. Reduction in PIP must be based on chest movement and $PaCO_2$ levels. When tidal volume (V_T) is the primary control variable, reduction in PIP occurs automatically with the improvement of lung compliance and spontaneous inspiratory effort. PIP is only adjusted by clinician to achieve adequate V_T in the range of 4-6 mL per kg body weight (11). According to Patel et al., reduction of VT below the normal physiological value increases the work of breathing (13). On the other hand, despite Wheeler et coll. reported in a meta-analysis that V_T strategies reduce the duration of MV (12), optimal V_T values to perform weaning are not well established.

Infants treated with MV for a long period need a progressive increase in V_T over time as a result of increasing anatomical intrathoracic dead space (14). Therefore, monitoring of V_T facilitates weaning of PIP and is also helpful for detecting hypoventilation if the reduction in PIP is too large. This is important to prevent a gradual alveolar collapse.

Regardless of the specific modality of ventilation, with triggered ventilation (PTV) V_T is combination of respiratory effort of the newborn (negative intrapleural pressure on inspiration) and the positive pressure generated by ventilator. This results in the transpulmonary pressure which determine V_T in addition to compliance of the respiratory system (16).

Moreover, the positive end expiratory pressure (PEEP), usually kept between 4 and 8 cm H_2O to maintain the end-expiratory lung volume, can be gradually decreased during weaning as oxygenation improves. Further reductions may be associated with alveolar collapse.

Although it is established that it is better to wean using triggered ventilation (PTV) (15), studies have not indicated consistent differences in weaning from mechanical ventilation when using assist control (A/C) or pressure support (PSV) compared to synchronized intermittent mandatory ventilation (SIMV) in premature infants. During SIMV the weaning is accomplished by gradual reduction of the mechanical rate allowing the patient to increase his contribution to minute ventilation. During A/C or PSV the reduction of the ventilator rate does not have any effect except for reducing the backup rate when the infant becomes apneic.

Given the difficulty with precise measurement of the transpulmonary pressure at the bedside of newborn, monitoring the respiratory dynamics through specific scores (eg Silverman score) could help in the early diagnosis of exhaustion of the respiratory pump.

As alternative strategy, a randomized trial revealed faster weaning and shorter duration of ventilation in infants who were ventilated with SIMV in combination with PSV (17).

High frequency ventilation

High-frequency oscillatory ventilation (HFOV) is increasingly used in preterm infants, but data on weaning and extubation are limited.

To prevent alveolar collapse, some Authors suggested that mean airway pressure (MAP) is not reduced if fraction of inspired oxygen (FIO_2) is still >0.30. Reduction in pressure amplitude must be based on V_T and $PaCO_2$ levels. Targeting V_T below anatomical dead space could be an useful tool to maintain $PaCO_2$ in the normal range (18). Frequency is not usually changed during weaning although Venegas et al. speculated that improvements in respiratory compliance require a lower optimal frequency (19).

Some clinicians switch from HFOV to conventional MV once the acute lung disease has improved and subsequently wean and extubate from this ventilation mode. However, this combined use of HFOV and conventional MV may be less effective compared with a strategy using HFOV alone. Others studies reported that weaning and extubating directly from HFOV might be an alternative approach and can be successful in preterm infants (20-23).

Extubation readiness

In the last two decades, many studies have investigated different tools to predict successful extubation in newborns (24). They have included pulmonary function testing and the ability to breathe during a period when ventilator cycling is stopped (spontaneous breathing trial, SBT). Although none of these predictive tests has been confirmed in randomized trials some of them are simple and associated with earlier extubation (25, 26).

Postextubation management

Preterm infants that are not supported after extubation by continuous distending pressure are more prone to failure. This is mainly due to the inability of the immature rib cage to maintain adequate functional residual capacity and also to the edema of vocal cords unable to sustain effective grunting, a mechanism normally used by preterms to maintain internal distending pressure.

Currently the gold standard is nasal continuous positive airway pressure (nCPAP); this approach reduces the deterioration that frequently occurs in these infants after extubation and reduces the need for reintubation.

Although nasal CPAP has been used for many years, there are no data on the most effective level of pressure to use. At present, a level of 4-6 cm H_2O is the gold standard (27), although a recent study indicates that higher pressures (7-9 cm H_2O) reduce extubation failure, especially in more immature newborns who are still oxygen dependent (28).

Nasal intermittent positive pressure ventilation (NIPPV or SNIPPV if synchronized) was proposed as alternative strategy but only in small trials.

Heated humidified high flow nasal cannula (HHHFNC) has recently been introduced as an effective alternative to nCPAP after extubation (29). nCPAP is certainly an effective mode of NIV but traumatic nasal complications and intolerance of the nasal interface are common. HHHFNC could allow better access to the baby's face, which may improve nursing, feeding and bonding. However, further larger randomized trials are required before being able to recommend HHHFNC as first line therapy during weaning from MV.

More recently, nasal high frequency oscillatory ventilation (NHFOV) has been proposed to overcome the problem that high pressure, normally used in NIPPV, can lead to an active, inspiratory laryngeal closure that limits lung ventilation and diverts gas into the digestive system (30). If this strategy will be confirmed, it could be a valuable tool during weaning, especially when glottis is particularly fragile and sensitive.

Drug therapies during the process of weaning

A recent Cochrane review has indicated that infants exposed to methylxantine have a lower risk of failed extubation (31). Caffeine is generally preferred for its longer half-life and fewer side effect. The optimal dose to prevent extubation failure could be higher than that normally used to treat apnea of prematurity (32).

Systemic steroids were also suggested to facilitate weaning from the ventilator but their administration is associated with many complications. Nevertheless, *Doyle et al*. reported that use of systemic steroids is not recommend in infants with mild disease but the risk/benefit ratio is favourable in more immature and severely ill newborns (33).

In addiction, inhaled dexamethasone or racemic epinephrine to prevent post-extubation stridor have also been used but data on effectiveness are not conclusive enough to recommend their routine use (34, 35).

Conclusions

In summary, weaning from mechanical ventilation is a complex process that may be characterized as a series of interrelated and codependent steps. Given the range of existing weaning modes and parameters available, these require explanation and clarification in the context of current evidence. As mechanical ventilation is associated with severe complications in premature infants it is important to limit its duration as much as possible. There is frequently some inertia to wean infants from mechanical ventilation; for this reason it is useful to have written criteria to guide weaning from the ventilator and extubation.

An improved ability to predict when a preterm infant has a high likelihood of successful extubation is highly desirable.

This approach could allow to customize weaning from MV by targeting for respiratory strategy and pharmacological therapy.

References

1. Vermont Oxford Network Database available at http://www.vtoxford.org/
2. Miller JD, Carlo WA. Pulmonary complications of mechanical ventilation in neonates. Clin Perinatol 2008; 35 (1): 273-81.
3. Garland JS. Strategies to prevent ventilator-associated pneumonia in neonates. Clin Perinatol 2010; 37 (3): 629-43.
4. Walsh MC, Morris BH, Wrage LA, et al. Extremely low birthweight neonates with protracted ventilation: mortality and 18-month neurodevelopmental outcomes. J Pediatr 2005; 146 (6): 798-804
5. Venkatesh V, Ponnusamy V, Anandaraj J, et al. Endotracheal intubation in a neonatal population remains associated with a high risk of adverse events. Eur J Pediatr 2011; 170 (2): 223-7.
6. Shangle CE, Haas RH, Vaida F, et al. Effects of endotracheal intubation and surfactant on a 3-channel neonatal electroencephalogram. J Pediatr 2012; 161 (2): 252-7
7. Stefanescu BM, Murphy WP, Hansell BJ, et al. A randomized, controlled trial comparing two different continuous positive airway pressure systems for the successful extubation of extremely low birth weight infants. Pediatrics 2003; 112 (5): 1031-8.
8. Vento G, Tortorolo L, Zecca E, et al. Spontaneous minute ventilation is a predictor of extubation failure in extremely-low-birth-weight infants. J Matern Fetal Neonatal Med 2004; 15 (3): 147-54.
9. Dimitriou G, Fouzas S, Vervenioti A, et al. Prediction of extubation outcome in preterm infants by composite extubation indices. Pediatr Crit Care Med 2011; 12 (6): e242-9.
10. Bancalari E, Claure N. Weaning preterm infants from mechanical ventilation. Neonatology 2008; 94 (3): 197-202.
11. Wheeler K, Klingenberg C, McCallion N, et al. Volume-targeted versus pressure-limited ventilation in the neonate. Cochrane Database Syst Rev 2010; (11).
12. Patel DS, Sharma A, Prendergast M, et al. Work of breathing and different levels of volume-targeted ventilation. Pediatrics 2009; 123 (4).
13. Keszler M, Nassabeh-Montazami S, Abubakar K. Evolution of tidal volume requirement during the first 3 weeks of life in infants <800 g ventilated with volume guarantee. Arch Dis Child Fetal Neonatal Ed 2009; 94 (4): F279-82.
14. Greenough A, Dimitriou G, Prendergast M, et al. Synchronized mechanical ventilation for respiratory support in newborn infants. Cochrane Database Syst Rev 2008; (1).
15. Sant'Anna GM, Keszler M. Weaning infants from mechanical ventilation. Clin Perinatol. 2012;39(3):543-62
16. Reyes ZC, Claure N, Tauscher MK, et al. Randomized, controlled trial comparing synchronized intermittent mandatory ventilation and synchronized intermittent mandatory ventilation plus pressure support in preterm infants. Pediatrics 2006; 118 (4): 1409-17.
17. Pillow JJ. Tidal volume, recruitment and compliance in HFOV: same principles, different frequency. Eur Respir J 2012; 40 (2): 291-3
18. Sánchez Luna M, Santos González M, Tendillo Cortijo F. High-frequency oscillatory ventilation combined with volume guarantee in a neonatal animal model of respiratory distress syndrome. Crit Care Res Pract 2013; 2013.
19. Venegas JG, Fredberg JJ. Understanding the pressure cost of ventilation: why does high-frequency ventilation work? Crit Care Med 1994; 22(9 Suppl).
20. van Velzen A, De Jaegere A, van der Lee J, et al. Feasibility of weaning and direct extubation from open lung high-frequency ventilation in preterm infants. Pediatr Crit Care Med 2009; 10 (1): 71-5.
21. Clark RH, Gerstmann DR, Null DM Jr, et al. Prospective randomized comparison of high-frequency oscillatory and conventional ventilation in respiratory distress syndrome. Pediatrics 1992; 89 (1): 5-12.
22. Courtney SE, Durand DJ, Asselin JM, et al. High-frequency oscillatory ventilation versus conventional mechanical ventilation for very-low-birth-weight infants. N Engl J Med 2002; 347 (9): 643-52.
23. Johnson AH, Peacock JL, Greenough A, et al. High-frequency oscillatory ventilation for the prevention of chronic lung disease of prematurity. N Engl J Med 2002; 347 (9): 633-42.
24. Kamlin CO, Davis PG, Morley CJ. Predicting successful extubation of very low birthweight infants. Arch Dis Child Fetal Neonatal Ed 2006; 91 (3): F180-3.
25. Kamlin CO, Davis PG, Argus B, et al. 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): F305-6.
26. Davis PG, Henderson-Smart DJ. Nasal continuous positive airways pressure immediately after extubation for preventing morbidity in preterm infants. Cochrane Database Syst Rev 2003; (2): CD000143.
27. Buzzella B, Claure N, D'Ugard C, et al. A randomized controlled trial of two nasal continuous positive airway pressure levels after extubation in preterm infants. J Pediatr 2014; 164 (1): 46-51.
28. Barrington KJ, Bull D, Finer NN. Randomized trial of nasal synchronized intermittent mandatory ventilation compared with continuous positive airway pressure after extubation of very low birth weight infants. Pediatrics 2001; 107 (4): 638-41.
29. Collins CL, Holberton JR, Barfield C, et al. A randomized controlled trial to compare heated humidified high-flow nasal cannulae with nasal continuous positive airway pressure postextubation in premature infants. J Pediatr 2013; 162 (5): 949-52
30. Roy B, Samson N, Moreau-Bussiere F, et al. Mechanisms of active laryngeal closure during noninvasive intermittent positive pressure ventilation in nonsedated lambs. J Appl Physiol 2008; 105 (5): 1406-12.
31. Henderson-Smart DJ, Davis PG. Prophylactic methylxanthines for endotracheal extubation in preterm infants. Cochrane Database Syst Rev 2010; (12): CD000139.

32. Steer P, Flenady V, Shearman A, et al. High dose caffeine citrate for extubation of preterm infants: a randomised controlled trial. Arch Dis Child Fetal Neonatal Ed 2004; 89 (6): F499-503.
33. Doyle LW, Halliday HL, Ehrenkranz RA, et al. Impact of postnatal systemic corticosteroids on mortality and cerebral palsy in preterm infants: effect modification by risk for chronic lung disease. Pediatrics 2005;115 (3): 655-61.
34. Davies MW, Davis PG. Nebulized racemic epinephrine for extubation of newborn infants. Cochrane Database Syst Rev 2002; (1): CD000506.
35. Khemani RG, Randolph A, Markovitz B. Corticosteroids for the prevention and treatment of post-extubation stridor in neonates, children and adults. Cochrane Database Syst Rev 2009; (3): CD001000

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