EC MICROBIOLOGY
Review Article

Basics of Mechanical Ventilation in Neonatal Care: Types, Modes, and Modalities

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Received: January 11, 2021; **Published:** January 20, 2021

Abstract

Introduction: Mechanical ventilation provided lifesaving support for infants with respiratory failure and improved neonatal survival, especially for preterm infants with immature lung function. There are many concepts, modes and modalities that render MV a tricky and sophisticated tool, especially for residents and physicians early in their careers. Adequate use of MV requires an understanding of basic physiologic and pathophysiologic features of respiration, gas exchange, ventilation, and lung disease as long as the available modes and modalities.

Aim of the Work: This review focuses on the indication of MV in neonate, available modes and modalities of mechanical ventilation, and the advantages and disadvantages of these modes and modalities.

Methods: We have conducted a thorough search of medical literature databases regarding mechanical ventilation in neonates. All studies until November 2020 were screened and included, when relevant.

Conclusion: There is two broad types of ventilator used in the neonatal intensive care unit (NICU): conventional mechanical ventilation (CMV) and high-frequency ventilation (HFV). Conventional mechanical ventilation could be classified by modalities to pressure-control or volume-control ventilation, and by modes to mandatory or synchronized ventilation. Either of the modalities can be used with either of modes. Pressure-limited ventilators are associated with instability in tidal volume that may harm the immature lungs of preterm. Volume-targeted ventilators is considered more advanced and safe. They are able to provide more consistent tidal volume during neonatal mechanical ventilation, which is associated with lower risk of lung injury compared with pressure-limited ventilation.

Keywords: *Mechanical Ventilation; Neonate; NICU*

Introduction

Mechanical ventilation (MV) remains one of the greatest inventions in medicine. In the sixties, MV was introduced in neonatal care and provided lifesaving support for infants with respiratory failure. This, among other technologic advancements, has improved neonatal survival, especially for preterm infants with immature lung function. Mechanical ventilation provides many benefits in adults and neonate, the main benefits in neonates suffering respiratory failure include: improving gas exchange; decreasing work of breathing; providing adequate minute ventilation essential in the setting of respiratory depression or apnea.

Respiratory failure is the principal indication of MV in neonatal intensive care unit (NICU). The presence of hypoxia, respiratory acidosis, or severe apnea denotes respiratory failure. Hypoxia is evident by an arterial PaO_2 < 50 mmHg despite oxygen supplementation, whereas an arterial pH < 7.2 and partial pressure of arterial carbon dioxide ($PaCO_2$) > 60 mmHg verify respiratory acidosis. Accordingly, assisted ventilation is commonly used with conditions causing respiratory failures such as respiratory distress syndrome (RDS), apnea, infection, postoperative recovery, persistent pulmonary hypertension, meconium aspiration syndrome, congenital pulmonary and heart anomalies, and hypoxic-ischemic encephalopathy.

Mechanical ventilation is still an invasive procedure; associated with chronic lung injury such as in bronchopulmonary dysplasia (BPD) [1]. Hence, new modalities and technology have been developing to reduce the risks without compromising adequate gas exchange [2]. There are many concepts, modes and modalities that render MV a tricky and sophisticated tool, especially for residents and physicians early in their careers. Adequate use of MV requires an understanding of basic physiologic and pathophysiologic features of respiration, gas exchange, ventilation, and lung disease as long as the available modes and modalities. Such understanding is essential to achieve desired outcomes and to minimize the risk associated with MV.

This review focuses on the indication of MV in neonate, available modes and modalities of mechanical ventilation, and the advantages and disadvantages of these modes and modalities. The basic respiratory physiology and pathophysiology of lung diseases in neonate will not be discussed. Similarly, less invasive methods of oxygen delivery such as continuous positive airway pressure (CPAP) will not be discussed here.

Methods

We have conducted a thorough search on medical literature databases regarding mechanical ventilation in neonates. The main databases were PubMed and Google scholar search engine. All studies were screened and included when relevant. Medical Subject Heading (MeSH) terms were used on PubMed for precise search results. The terms used in the search include mechanical ventilation, NICU, respiratory failure, and neonates.

Types, modes, and modalities of mechanical ventilation

There are two broad types of ventilators used in the neonatal intensive care unit (NICU) according to the method of providing minute ventilation: conventional mechanical ventilation (CMV) and high-frequency ventilation (HFV). In CMV, the principle is intermittent exchange of gas volume similar to physiologic tidal volume and hence the minute ventilation is resulted by frequency of breaths and tidal volume. Conventional mechanical ventilation could be classified by modalities to pressure-control or volume-control ventilation, and by modes to mandatory or synchronized ventilation. A hybrid of pressure-control and volume-control also exists [3].

High-frequency ventilation (HFV) is based upon the delivery of small gas volumes at an extremely rapid rate as rapid as 300 to 1500 breaths per minute. The amount of gas is equal to or smaller than the anatomic dead space. Hence, the minute ventilation is the product of frequency of breaths and the square of the tidal volume. According to available evidence, HFV is not routinely used in NICU, because this mode of ventilation does not add any significant benefit over the less-costly and easier-to-operate conventional ventilators. This evidence is concluded by several systematic reviews [4-6]. Thus, types and characteristics of HFV will not be furtherly discussed in this article.

Conventional mechanical ventilation

The time-cycled, pressure-limited (TCPL) assisted ventilators are the most common type used ventilator in NICU. These ventilators work by providing a continuous flow of gas (warmed and humidified) through the breathing circuit, allowing the patient to breathe spontaneously at any time. Initially, when first used in neonate, the TCPL provided only pressure-limited ventilation with a mandatory ventilation rate. Advancement in understanding respiratory physiology and risk factors for neonatal lung injury, new modes and modalities have been invented and led to safer and more effective generation of TCPL ventilator. This is caused by the ability of controlling the delivered tidal volume.

Nowadays, different settings are available in TCPL ventilator to control the way of gas delivery to neonate patient. Conventional mechanical ventilation settings include the ability to control the initiation of the breath (ventilatory modes) either a mandatory or synchronized breath, and the ability to regulate the gas flow either by pressure or volume control (ventilator modalities). Synchronized breath simply means that it is triggered by the spontaneous breath of the patient. Either of the modalities can be used with either of modes, so the ventilator could be set as mandatory pressure/volume control, or synchronized pressure/volume control. Pressure-control setting basically means that the delivered tidal volume will fluctuate depending on the lung compliance of the patient; volume-control option regulates the delivered tidal volume and the pressure needed to deliver that volume will vary depending on lung compliance. Other important settings include the ability to set the time of inspiration and expiration, and control positive end-expiratory pressure (PEEP). The latter is the positive pressure maintained at the end of expiration to preserve lung residual volume and prevent alveolar collapse.

Ventilator modes

The choice of initiation of breath in neonate was limited to intermittent mandatory ventilation (IMV) mode. In IMV, a mandatory rate of breaths is provided at regular intervals that is not influenced by spontaneous breathing of the infant. Nowadays, synchronization option allows delivery of breath to be triggered by the infant spontaneous breathing. Settings of synchronization could be adjusted to match all or some of infant's spontaneous breathing. The benefits of synchronization include improving comfort, reducing the need for sedation, and lowering mean airway pressure (MAP) [7]. Other suggested benefits of synchronization versus non-synchronized ventilation in neonates include fewer periods of low oxygen saturation and less variability in exhaled tidal volume [8,9]. However, one meta-analysis has found that synchronized breath does not appear to reduce the mortality rate or the incidence of bronchopulmonary dysplasia (BPD) [9]. Compared with conventional old methods, patient-triggered mode carries similar rates of air leaks, severe intraventricular hemorrhage (IVH), BPD, or extubation failure. Although death rate was higher in the synchronized MIV group, the results were not statistically significant. On the other hand, the analysis found a shorter duration of ventilation with synchronized delivery. In spite of this results, some experts believe that patient-triggered breath may be beneficial in a subgroup of preterm infants below 28 weeks of age, as it shortens the period of ventilation in this population of patients who are more susceptible to mechanical ventilatory lung injury [10]. When the synchronization mode is chosen, different modalities could be further set to produce variable methods of ventilation. In this ventilators, a preset value of inspiratory flow, pressure change, or movement can be adjusted to initiate the breath when reached.

Synchronized intermittent mandatory ventilation (SIMV) mode

Synchronized intermittent mandatory ventilation (SIMV) provides mechanical breaths in synchrony with infant's spontaneous breaths. The breath is delivered at the onset of spontaneous breath that meet the preset inspiratory flow within a timing window. Typically, the rate of mechanical breath is set lower than the spontaneous rate so some spontaneous breaths occur without ventilator support. PEEP is provided for every breath.

Assist/control (AC) or synchronized intermittent positive pressure ventilation (SIPPV)

In assist control (AC) mode, the ventilator will deliver mechanical breath with each infant's spontaneous breath that exceed a preset threshold measure. Inspiratory time, peak inflation pressure, or target tidal volume are preset. In addition, mandatory breathing rate could be provided should the infant respiratory drive becomes limited. Compared with SIMV mode, AC (or SIPPV) provides consistent tidal volume and ensures lower work of breath by the infant.

Pressure support ventilation (PSV)

Similar to AC mode, PSV mode ensures ventilator support of each infant's spontaneous breath that exceeds a preset measure and is usually used with a preset mandatory breathing. The difference is the mechanical breath is terminated when inspiratory flow falls below certain proportion of peak flow as well as by expiration. The proportion is usually 10 to 20 percent of the peak flow, which could be adjusted in many ventilators. This technique is basically a flow cycled ventilation, which means the inspiratory time and pattern are determined by the infants themselves rather than by a preset time. The operator only sets the pressure parameter, and the infant control everything else. Thus, PSV is considered more physiological mode than SIMV and SIPPV. Unfortunately, a marked lack of data prevents its sole use in neonates requiring full ventilator support for respiratory failure. PSV remains a promising tool in neonatal care. One examined use of PSV is in combination with SIMV. Data show that this combination reduces the work of breathing by decreasing mandatory ventilatory rate, mean airway pressure, and increases minute ventilation compared with SIMV alone [11]. Nevertheless, one randomized control trial of 107 preterm infants has compared the use of SIMV alone with the use of SIMV plus Pressure support ventilation and found that neonates assigned to the combination were less likely to require mechanical ventilation at 28 days of life than those assigned to SIMV alone [12]. All other morbidity including the total days of MV did not differ between the two groups.

Neurally-adjusted ventilatory assist (NAVA)

In this mode, a specialized nasogastric tube (NGT) in the lower esophagus records the electrical activity from the diaphragm (EAdi). The electrical activity is used to synchronize the mandatory mechanical breaths with infant's spontaneous respiratory effort. NAVA was examined by several studies in neonates. Observational reports found that NAVA improved patient-ventilator interaction, reduced peak inspiratory pressure (PIP), reduced sedation, and was adequately maintained similar blood gas values compared with other forms of synchronization [13]. However, recent Cochrane review published in 2017 found no difference between the two methods on any desired outcome [14]. Since the signal is not related to endotracheal tube, NAVA can be used with a noninvasive methods such as nasal intermittent positive pressure ventilation (NIPPV). In addition, NAVA appears to be effective even in the presence of large air leaks, and nasogastric feedings did not interfere with its signal integrity [15].

Modality of ventilation

Ventilator modalities include the ability to regulate the gas flow either by pressure or volume control. Either of these two modalities can be set with any of the previously mentioned mode to achieve different combination of modes/modalities.

Pressure-limited ventilation

Pressure-limited ventilation is basically the modality of first introduced TCPL ventilators. In this modality, peak inspiratory pressure (PIP) is set by the operator to limit the amount of pressure delivered during inspiration. The desired tidal volume is regulated by the preset of peak inspiratory time and PIP. In addition, infant's lung compliance, and the degree of synchrony between the infant's spontaneous breathing and mechanical ventilatory breaths directly affect the tidal volume. Low lung compliance will result in PIP with lower delivered volume. Inspiration is terminated at the end of the selected inspiratory time. Hence, adequate ventilation can only be ensured by adequate set of inspiratory time to maintain an inspiratory pressure plateau. The flow pattern in pressure-controlled ventilation characterizes by an initial acceleration of flow to achieve desired PIP followed by a deceleration toward the end of the inspiratory phase. Peak end expiratory pressure (PEEP) is set to maintain residual volume during expiration. Advancement has allowed different types of synchronized ventilation in pressure-limited ventilators. Hence, pressure-controlled modalities in NICU commonly take one of three main combination according to synchronization modes: pressure-control synchronized intermittent mandatory ventilation (PC-SIMV); pressure-control Assist control (PC-AC); pressure-control pressure support ventilation (PC-PSV).

Pressure-limited ventilators are relatively easy to use and less expensive. They allow infant's spontaneous breath as they provide a continuous flow, this facilitates weaning by progressively reducing PIP and mandatory ventilator rate. In addition, the risk of lung injury could be reduced by setting the PIP and mean airway pressure (MAP) with preserving adequate gas exchange. By contrast, these ventilators have the disadvantage of variation in tidal volume from breath to breath. As mentioned before, the tidal volume is influenced by infant's lung compliance and resistance, circuit compressed gas volume, and endotracheal tube leak. The instability in tidal may undermine effective ventilation. One study on preterm infant has found that the tidal volume was higher than targeted in one-quarter of delivered breath, and less than optimal in 36 percent of breath [16]. The consequences of large instability on the immature lungs of preterm include the risks of both hyperinflation (barotrauma) and collapse (atelectasis) of alveolar spaces. Administration of surfactant in preterm infants below 32 weeks gestation caused as rapid change in lung compliance. This may result in the delivery of excessive volume which increases the risk of progressive hypocarbia, pulmonary air leak. In turn, progressive hypocarba may lead to intraventricular hemorrhage (IVH). Other disadvantages include increased work of breathing and poor synchrony between spontaneous and mandatory breaths. Inadequate synchronization is associated with inadequate oxygenation, higher partial pressure of arterial carbon dioxide ($PaCO_2$), and reduction in tidal volume and minute ventilation [17]. Newer generations of TCPL ventilators that provide different synchronization option do not have such disadvantage.

Volume-targeted ventilation

Volume-targeted ventilators is considered more advanced and have been progressively improved since the late nineties. They are able to provide more consistent tidal volume during neonatal mechanical ventilation which is associated with lower risk of lung injury compared with pressure-limited ventilation. The main drive for volume-targeted modalities was the observed risks associated with volume distension of the lung [18]. As mentioned, the instability in tidal volume delivery causes harmful cycles of overdistension and atelectasis. Recently, 50 percent of neonatal tertiary units have replaced pressure-limited ventilation by volume-targeted modality according to international survey from in Australia, New Zealand, Sweden, Denmark, Finland and Norway [19]. Nowadays, three common modes of volume-targeted ventilation are being used: volume-controlled (VC) ventilation; volume-guarantee (VG); pressure-regulated volume control (PRVC) ventilation [20].

Volume-controlled (VC) ventilators were the first used mode of volume-targeted ventilation. In this mode, a preset tidal volume is delivered by variation in pressure (PIP pressure), regardless of underlying lung compliance. Hence, the rate of flow, PIP, and inspiratory time may vary from breath to breath. The usual tidal volume in neonate ranges between 4 to 6 mL/kg. For safety, a mandatory respiratory rate and an inspiratory time limit are frequently set. In contrast to pressure-limited ventilators which induce peak pressure and flow early in inspiration (front load), the peak flow and peak pressure in VC are generated at the end of inspiration in the form of back load.

Volume-guarantee (VG) ventilation is similar to pressure-targeted ventilatory modality but with installed microprocessor. The microprocessor acts by adjusting the pressure as needed to ensure a preset desired tidal volume. The inspired and expired tidal volume are detected by flow sensor placed at the endotracheal tube connection. In this modality, the clinician determine the expiratory tidal volume, inspiratory time, and a maximum inspiratory pressure limit (Pmax). The latter should be set high enough to allow fluctuation in actual pressure. Self-weaning occurs with the decrease in Inspiratory pressure associated with improvement in lung compliance and increased spontaneous respiratory effort by the infant. Insufficient Pmax, too short inspiratory time, and large endotracheal tube leaks are the main causes of failure to achieve the target tidal volume. VG ventilation can be used with different mode of synchronization such SIMV, AC, and PSV. VG mode is becoming the mode of choice in many neonate care centers.

Pressure-regulated volume control (PRVC) mode is also considered as modified pressure-targeted mode. The target inspiratory volume is ensured with lowest possible pressure by successive adjustment in inspiratory pressure. The operator presets the desired tidal volume and the maximum pressure allowed for delivery. The ventilator increases the inspiratory pressure subsequently until the targeted tidal volume or maximum allowable inspiratory pressure is reached. If the tidal volume is exceeded, inspiratory pressure is decreased. It is worthwhile mentioning that a small variation in tidal volume occurs during sequential adjustment the pressure.

Comparison between pressure- and volume-controlled ventilation

Compared with pressure-limited ventilation, the use of volume-targeted modalities are associated with more effective gas exchange while reducing the number of high volume mechanical breaths [21]; fewer fluctuations in tidal volume which reduce the incidence of hypocapnia;[16] decreased PIP while maintaining the desired tidal volume [22]. This finding was reinforced by a systematic review comparing volume-targeted ventilator to pressure-limited ventilation in the setting of acute respiratory failure in neonates [23]. The main findings of the systematic review include a lower rate of mortality or BPD, reduced rate of pneumothorax, mean days of ventilation, and hypocarbia.

Although the mentioned data suggest the superiority of volume-targeted modalities, some experts advocate the need for further evidence to recommend routine use in NICU [20]. Reasons for this belief emerges from the fact that most of studies evaluating volume-targeted ventilation were conducted by investigators with expertise in its use, which renders the results non-inferential as these ventilators are more difficult to operate. Another reason, these studies have used different modalities (VG, PRVC and VC) and modes (patient-triggered and mandatory ventilation) of volume-controlled ventilation and it is not possible to determine which ventilator or mode accounted for reported outcome. In addition, variable preset of tidal volume, inflation time, and peak pressures were used [24]. Accordingly, the optimal tidal volume set in volume-triggered ventilation uncertain [25]. In spite of this ongoing argument, many units prefer volume-targeted, patient-triggered ventilation for initial management of acute lung disease in neonates based on presented evidence.

Conclusion

There is two broad types of ventilator used in the neonatal intensive care unit (NICU): conventional mechanical ventilation (CMV), and high-frequency ventilation (HFV). Conventional mechanical ventilation could be classified by modalities to pressure-control or volume-control ventilation, and by modes to mandatory or synchronized ventilation. Either of the modalities can be used with either of the modes. Pressure-limited ventilators are associated with instability in the tidal volume that may harm the immature lungs of preterm. Volume-targeted ventilators are considered more advanced and safe. They can provide more consistent tidal volume during neonatal mechanical ventilation, which is associated with a lower risk of lung injury compared with pressure-limited ventilation.

Bibliography

1. Cullen AB., *et al*. "The impact of mechanical ventilation on immature airway smooth muscle: functional, structural, histological, and molecular correlates". *Biology of the Neonate* 90 (2006): 17.

2. Donn SM and Sinha SK. "Minimising ventilator induced lung injury in preterm infants". *Archives of Disease in Childhood: Fetal and Neonatal* 91 (2006): F226.

3. Donn SM and Sinha SK. "Newer modes of mechanical ventilation for the neonate". *Current Opinion in Pediatrics* (2001).

4. Cools F., *et al*. "Elective high-frequency oscillatory versus conventional ventilation in preterm infants: a systematic review and meta-analysis of individual patients' data". *Lancet* 375 (2010): 2082.

5. Cools F., *et al*. "Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants". *Cochrane Database of Systematic Reviews* (2009): CD000104.

6. Elective high-frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants". *Neonatology* 103 (2013): 7.

7. Bernstein G., *et al*. "Randomized multicenter trial comparing synchronized and conventional intermittent mandatory ventilation in neonates*". The Journal of Pediatrics* 128 (1996): 453.

8. Firme SR., *et al*. "Episodes of hypoxemia during synchronized intermittent mandatory ventilation in ventilator-dependent very low birth weight infants". *Pediatric Pulmonology* 40 (2005): 9.

9. Greenough A., *et al*. "Synchronized mechanical ventilation for respiratory support in newborn infants". *Cochrane Database of Systematic Reviews* 9 (2016): CD000456.

10. Ramanathan R and Sardesai S. "Lung protective ventilatory strategies in very low birth weight infants". *Journal of Perinatology* 28.1 (2008): S41.

11. Guthrie SO., *et al*. "A crossover analysis of mandatory minute ventilation compared to synchronized intermittent mandatory ventilation in neonates". *Journal of Perinatology* 25 (2005): 643.

12. Reyes ZC., *et al*. "Randomized, controlled trial comparing synchronized intermittent mandatory ventilation and synchronized intermittent mandatory ventilation plus pressure support in preterm infants". *Pediatrics* 118 (2006): 1409.

13. Beck J., *et al*. "Patient-ventilator interaction during neurally adjusted ventilatory assist in low birth weight infants". *Pediatric Research* 65 (2009): 663.

14. Rossor TE., *et al*. "Neurally adjusted ventilatory assist compared to other forms of triggered ventilation for neonatal respiratory support". *Cochrane Database of Systematic Reviews* (2017).

15. Stein H and Firestone K. "Application of neurally adjusted ventilatory assist in neonates". *Seminars in Fetal and Neonatal Medicine* 19 (2014): 60.

16. Keszler M and Abubakar K. "Volume guarantee: stability of tidal volume and incidence of hypocarbia". *Pediatric Pulmonology* 38 (2004): 240.

17. Bolivar JM., *et al*. "Mechanisms for episodes of hypoxemia in preterm infants undergoing mechanical ventilation". *The Journal of Pediatrics* 127 (1995): 767.

18. Dreyfuss D., *et al*. "High inflation pressure pulmonary edema. Respective effects of high airway pressure, high tidal volume, and positive end-expiratory pressure". *The American Review of Respiratory Disease* 137 (1988): 1159.

19. Klingenberg C., *et al*. "An international survey of volume-targeted neonatal ventilation". *Archives of Disease in Childhood - Fetal and Neonatal Edition* 96 (2011): F146.

20. Grover A and Field D. "Volume-targeted ventilation in the neonate: time to change?" *Archives of Disease in Childhood - Fetal and Neonatal Edition* 93 (2008): F7.

21. Herrera CM., *et al*. "Effects of volume-guaranteed synchronized intermittent mandatory ventilation in preterm infants recovering from respiratory failure". *Pediatrics* 110 (2002): 529.

22. McCallion N., *et al*. "Neonatal volume guarantee ventilation: effects of spontaneous breathing, triggered and untriggered inflations". *Archives of Disease in Childhood - Fetal and Neonatal Edition* 93 (2008): F36.

23. Klingenberg C., *et al*. "Volume-targeted versus pressure-limited ventilation in neonates". *Cochrane Database of Systematic Reviews* 10 (2017): CD003666.

24. Sharma A., *et al*. "Performance of neonatal ventilators in volume targeted ventilation mode". *Acta Paediatr* 96 (2007): 176.

25. Lista G., *et al*. "Lung inflammation in preterm infants with respiratory distress syndrome: effects of ventilation with different tidal volumes". *Pediatric Pulmonology* 41 (2006): 357.

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