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Review

High-frequency ventilation for non-invasive respiratory support of neonates

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SUMMARY

Non-invasive respiratory support is increasingly used in lieu of intubated ventilator support for the management of neonatal respiratory failure, particularly in very low birth weight infants at risk for bronchopulmonary dysplasia. The optimal approach and mode for non-invasive support remains uncertain. This article reviews the application of high-frequency ventilation for non-invasive respiratory support in neonates, including basic science studies on mechanics of gas exchange, animal model investigations, and a review of current clinical use in human neonates.

1. Introduction

Great strides have been made in the respiratory support of neonatal lung disease since the initial respirator efforts by Donald and Lord in 1953 [1]. Advances have included the introduction of continuous positive airway pressure (CPAP) (endotracheal, then nasal) [2], incorporation of CPAP (to provide positive end expiratory pressure, PEEP) as an integral component of the ventilator [3], development of extremely low tidal volume support via high-frequency ventilation (HFV) [4], surfactant replacement therapy [5], and sophisticated computer-based technical improvements in conventional mechanical ventilators [6]. Perhaps the most important of these was the introduction of CPAP, as first reported by Gregory et al. in 1971 [2].

Despite advances in neonatal respiratory care over the past 50 years, bronchopulmonary dysplasia (BPD) remains the most prevalent chronic morbidity affecting surviving preterm infants, with rates of >40% for infants <29 weeks of gestation and/or <1000 g at birth [7–10]. The importance of this problem in preterm infants is underscored by more than 5500 publications related to BPD since the first description by Northway in 1967. Pathologically, current BPD is most often defined as interrupted or simplified alveolization and represents the immature lung's response to a variety of inflammatory insults including perinatal infection, oxidative injury, nutritional deficiencies, and ventilator-mediated stretch [11–14].

It is indeed ironic that more than 40 years after the introduction of CPAP as the first effective therapy for neonatal respiratory distress syndrome (RDS) (survival rates improved by >50%), and despite the marked technological advances made during that time span, there has been a renewed emphasis on the application of non-invasive (NIV) respiratory approaches to support neonatal lung disease and reduce the frequency and severity of BPD [15]. The optimal NIV approach for neonatal respiratory disease, and especially for the prevention of BPD, remains unclear. In this article we describe what is known about the development and application of high-frequency ventilation as one potential approach to NIV in the neonate. One could describe this NIV mode in various ways; here we term it “high-frequency nasal ventilation” or HFNV, as an inclusive term for any NIV approach with high-frequency breath rates via any device designed to provide neonatal high-frequency ventilation.

2. High-frequency nasal ventilation: gas exchange

2.1. Ventilator features and interface factors

As shown in Fig. 1, various factors may contribute to the effectiveness of gas exchange during HFNV, including: (i) the specific mechanical features of the ventilator used to deliver HFNV, (ii) inspiratory time, (iii) the set pressure or amplitude, (iv) the high frequency rate, (v) the underlying lung pathophysiology, and (vi) characteristics of the nasal interface. Many of these factors are

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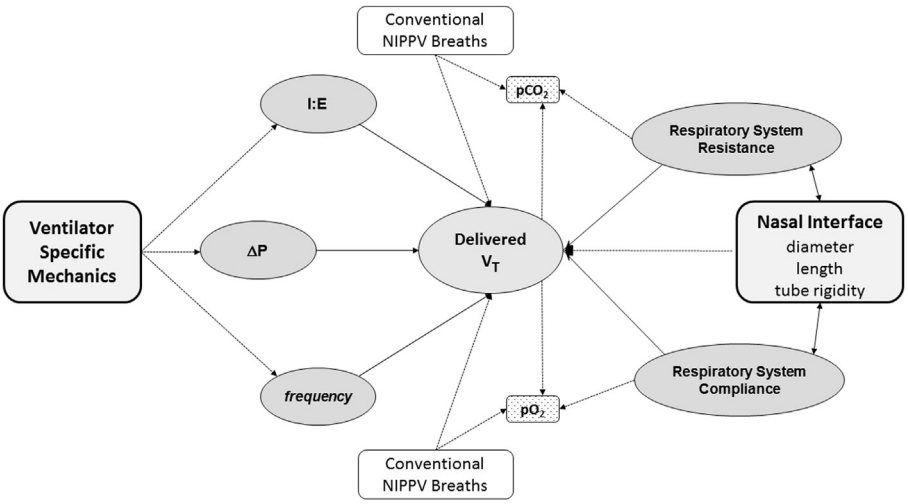

Fig. 1. Interactive factors contributing to delivered tidal volume (V_T) and effectiveness of gas exchange during non-invasive high-frequency nasal ventilation. I:E, inspiratory to expiratory ratio; ΔP, pressure amplitude. NIPPV, nasal intermittent positive pressure ventilation.

interactive. One additional variable involved in the efficacy of gas exchange during HFNV is the potential interposition of conventional breaths (i.e., combining nasal intermittent positive pressure ventilation, or NIPPV, with HFNV). This option is possible with most available high-frequency ventilators, though the 3110A (Care-Fusion, San Diego, CA, USA) is a notable exception (Table 1). The dynamics of gas exchange during HFNV remain less clear than during invasive HFV [16]. Laboratory evidence demonstrates substantial loss of pressure and volume across the non-invasive interface during conventional nasal ventilation [17,18]. Similar data have also been reported during HFNV in simulated studies on test lungs [19–21] and in clinical studies in preterm lambs [22].

2.2. Factors affecting tidal volume delivery

In test lung studies using the 3100A, De Luca et al. demonstrated that tidal volume (V_T) delivery is affected by the set amplitude, inspiratory time, and frequency; variables also known to impact V_T during invasive HFV [19,20] (Fig. 2a, b). As expected, V_T increased as pressure amplitude increased, though a plateau effect was noted at around 70% maximum amplitude for the 3100A. V_T also increased as inspiratory time increased, either by changing the I:E ratio from 33% to 50% or by decreasing frequency (with *f* at 10 Hz this change is accomplished by increasing the inspiratory time from 33 to 50 ms). De Luca et al. also found increased VT using larger nasal prongs interface [19] (Fig. 2b). Using the Dräger VN 500 in high-frequency mode, Mukerji et al. performed bench testing to assess the effect of high frequency rate on CO_2 removal via a non-invasive nasal prong interface [21]. With mean pressure, amplitude and I:E fixed, they found marked increase in CO_2 removal from a test lung at all HFNV rates compared to conventional NIPPV (Fig. 3). The optimal frequency for CO_2 removal was 8 Hz in their test lung model (Fig. 3). In unpublished data from our laboratory, using the Bronchotron (Percussionaire, Sand Point, ID, USA) interfaced via nasal CPAP prongs to a test lung, we found loss of pressure and volume with smaller nasal prongs, with lower pressure amplitude,

Table 1
Potential ventilator driver, nasal interface options and support features for initiation of neonatal high frequency nasal ventilation.

Variable	Comments
Ventilator	A variety of "drivers" are possible – see Table 7 Not all have been used clinically or studied in the lab
Frequency	Dependent on device & active v passive expiratory phase Optimum *f* unclear *Recommendation:* Start oscillators at 6–8 Hz; others at 4–6 Hz
Inspiratory time	May be expressed as I:E, I-time or "On-time" V_T >> at 50% I:E compared to 33% *Recommendation:* Set I:E at 50%; for Jet use longer "on-time" than 20 msec
Amplitude/ΔP	Device dependent Increased ΔP → larger V_T; appears to plateau ~ 70% *Recommendations:* Start ~ 50% max ΔP for device Adjust as possible to achieve visible chest wall vibration
Nasal interface	Single naso-pharyngeal tube Standard binasal CPAP prongs or nasal CPAP mask ? other nasal cannula interfaces *Recommendations:* Maximize internal diameter → Larger V_T Minimize dead space
Conventional breaths	Not all devices can provide this additional support Studied in animal studies, but not described in neonatal reports