Seminars in Fetal & Neonatal Medicine 21 (2016) 146–153

Contents lists available at ScienceDirect

Seminars in Fetal & Neonatal Medicine

journal homepage: www.elsevier.com/locate/siny

Review

Nasal intermittent positive pressure ventilation in preterm infants: Equipment, evidence, and synchronization

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Keywords:
Premature infant
Neonatal intensive care
Continuous positive airway pressure
Respiratory distress syndrome
Newborn

SUMMARY

The use of nasal intermittent positive pressure ventilation (NIPPV) as respiratory support for preterm infants is well established. Evidence from randomized trials indicates that NIPPV is advantageous over continuous positive airway pressure (CPAP) as post-extubation support, albeit with varied outcomes between NIPPV techniques. Randomized data comparing NIPPV with CPAP as primary support, and for the treatment of apnea, are conflicting. Intrepretation of outcomes is limited by the multiple techniques and devices used to generate and deliver NIPPV. This review discusses the potential mechanisms of action of NIPPV in preterm infants, the evidence from clinical trials, and summarizes recommendations for practice.

1. Introduction

NIPPV has been used as a form of non-invasive respiratory support in newborn infants since the 1970s [1]; however, uncertainty remains regarding its mechanism of action, and how best to apply it and in which infants.

This review evaluates the evidence currently available to assess whether NIPPV should be used, and under which clinical circumstances. It examine hows NIPPV may be applied, with particular reference as to whether or not NIPPV should be synchronized (sNIPPV) with spontaneous breathing.

2. Terminology and techniques

"NIPPV" is an umbrella term for multiple techniques combining the application of positive distending pressure (continuous positive airway pressure: CPAP) with intermittent pressure increases applied at the nose, without an endotracheal tube. The various abbreviations used to describe NIPPV in the literature reflect whether synchronization was attempted, and the ventilation strategy applied, e.g. N-SIMV: nasal synchronized intermittent mandatory ventilation [2]; or NI-PSV: non-invasive pressure support ventilation [3].

Bi-level CPAP is often included under the umbrella of NIPPV. This mode also combines CPAP with intermittent pressure increases via a nasal interface, but describes alternating high and low levels of CPAP. Throughout both levels the infant breathes independently. Bi-level CPAP has also been called nasal BiPAP [4] and biphasic nasal CPAP [5].

3. Generating and delivering NIPPV

3.1. Pressure

In theory, any ventilator can be used to generate non-synchronized (ns)NIPPV and many have been used in published studies [6–9]. However, the most cited ventilator in the NIPPV literature, and one of very few that have been used to provide sNIPPV, is the Infant Star (Infrasonics Inc., San Diego, CA, USA). However, this ventilator is no longer in production and consequently its use has almost ceased. Some manufacturers are introducing ventilators with incorporated synchronization mechanisms, two of which have been used in published NIPPV studies: Giulia (Giulia Neonatal Nasal Ventilator, Ginevri Medical Technologies, Rome, Italy [10–12]) and Sophie (Fritz Stephan Medizintechnik GmbH, Gackenbach, Germany [13]).

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http://dx.doi.org/10.1016/j.siny.2016.01.003
1744-165X/

The set pressures and rates used during ventilator-generated NIPPV are usually similar to peri-extubation endotracheal ventilation settings (peak pressures 14–24 cmH_2O and positive end expiratory pressure (PEEP) 3–6 cmH_2O) [7–9,14–17]. Typically, peak pressure duration is short (<0.5 s) with a range of 10–60 cycles/min [7–9,14–17].

There are few devices capable of delivering biphasic CPAP to newborns. The flow-driver "SiPAP" and its predecessor the Infant Flow Driver Advance – IFDa (both Care Fusion, Yorba Linda, CA, USA) were developed to deliver CPAP and biphasic CPAP. At least one new device designed to deliver these modes is available, but is yet to be clinically evaluated: Medin CNO (Medical Innovations GmbH, Puchheim, Germany). Biphasic CPAP uses lower set pressures and lower rates than traditional ventilator-generated NIPPV, partly due to limitations within the delivery devices, and partly because there is no intent to mimic or fit in with spontaneous breathing patterns.

Both the SiPAP and IFDa devices have a maximum deliverable pressure of 11 cmH_2O in the biphasic mode, except under certain circumstances. Studies using biphasic CPAP describe longer high-pressure duration (0.5–1.0 s), cycle rates of 10–30/min and 3–4 cmH_2O differences between high (typically 8–9 cmH_2O) and low (typically 4–6 cmH_2O) CPAP pressure settings [5,18–22].

Additionally, SiPAP and IFDa can be set to deliver traditional NIPPV patterns with shorter, more frequent high-pressure intervals. In this setting synchronization may be desired, and in synchronized mode SiPAP can deliver peak pressure of 15 cmH_2O. Some studies have used the SiPAP in this way [23,24].

Whether these devices and strategies should be considered different modes of support or simply a spectrum of NIPPV is unclear. However, for the purpose of this review, NIPPV is considered to have high-pressure duration $\leq$0.5 s, and biphasic CPAP >0.5 s.

3.2. Patient interface

NIPPV and biphasic CPAP studies have mostly used short binasal prongs as the patient interface. Binasal prongs have been shown to reduce re-intubation rates during CPAP, in comparison to single nasal prongs [25]. Several NIPPV studies have used binasal nasopharyngeal prongs [6,8,15,26,27]; however, two groups have reported abdominal distension with these longer prongs [8,26]. Recently, nasal cannulae have been used to deliver NIPPV in a lung model [28]. However, the NIPPV pressure transmission was greatly attenuated by the small diameter nasal cannulae, compared with traditional CPAP prongs. There have been no studies using NIPPV delivered via nasal mask, nor direct comparisons between interfaces during NIPPV or biphasic CPAP. With all interfaces there are likely to be large and variable leaks from the nose and mouth, which may limit the effectiveness of the applied pressures.

4. How are NIPPV and biphasic CPAP thought to work?

4.1. NIPPV: pressure and volume

It has been suggested that NIPPV pressure changes micro-recruit alveoli and improves functional residual capacity (FRC) [16,29,30], but no clinical trials support these theories. Nasal intermittent positive pressure ventilation is so called because it was initially presumed that pressure changes delivered into the nose would translate into lung inflations. However, observational data have shown that during NIPPV the delivered peak pressure is variable and often substantially below the set peak pressure [31,32], likely related to leak. These observations measured intra-prong pressure, not intra-thoracic pressure, which is likely to be lower still, and more variable [28] due to pressure loss across different prongs [33]. However, these observations have demonstrated slightly higher delivered mean airway pressures (MAP) during NIPPV than CPAP alone: this in itself may be enough to account for the apparent advantages of NIPPV [31,34]. Most studies comparing CPAP with NIPPV have not aligned MAP between study groups and therefore the variable is unaccounted for. One study directly examining MAP found no difference in oxygenation, carbon dioxide (CO_2) levels or respiratory rate (RR) between nsNIPPV and CPAP delivered at NIPPV-MAP level [35]; tidal volume (V_T) and desaturation events were better during MAP-level CPAP.

So do applied NIPPV pressures translate to lung volume change? NIPPV may slightly increase end expiratory lung volume, compared with CPAP [23], although this also could be due to increased MAP. However, data have demonstrated that during nsNIPPV the majority of pressure peaks occur during spontaneous expiration and have no effect on V_T [11,36]. When pressure peaks occur during spontaneous inspiration those volumes increase by ~15% [36]. This suggests that timing of pressure change is important to confer volume change. One group has demonstrated higher V_T during sNIPPV (NIPPV pressures 12/3 cmH_2O, compared with CPAP 3 cmH_2O), reporting 40% higher volumes during sNIPPV [11]. In this study infants were enrolled immediately after extubation, and very low PEEP was used in the CPAP group. Other similar studies enrolled infants already stable on CPAP, used higher PEEPs, and failed to demonstrate V_T difference between CPAP and sNIPPV [3,23,37,38]. A study that directly compared sNIPPV (~90% of pressure peaks delivered during inspiration) with nsNIPPV (~20% of pressure peaks during delivered during inspiration) found no difference in V_T between modes [37].

NIPPV pressure peaks may not effectively reach the lungs during central (non-obstructive) apnea [10,36]. Data have demonstrated that during 95% of central apneas no NIPPV pressure changes produced lung volume change (Fig. 1), possibly due to obstructive components of central apnea [39]. In 5% of central apneas NIPPV pressures produced V_T change one-quarter the volume of spontaneous breaths [36]

Therefore, it does not seem likely that pressure or volume change are the prime mechanisms of action during NIPPV.

4.2. NIPPV: gas exchange

Given the limited pressure and volume effects of NIPPV it could be anticipated that there would be minimal effect on gas exchange. Of six studies investigating oxygenation and CO_2 clearance, two reported lower CO_2 during NIPPV [11,40], one reported lower oxygen saturation (by 1%) during NIPPV [41], and the remainder (all using sNIPPV) found no difference in either parameter [3,10,37]. Infants in all six studies were adequately supported with CPAP at study entry, potentially limiting any difference in these parameters. In contrast, Huang et al.'s study enrolled infants shortly after extubation and found improved oxygen and CO_2 levels during sNIPPV, compared with nsNIPPV [13].

4.3. NIPPV: work of breathing

Five studies investigating work of breathing (WOB) during sNIPPV found reduced WOB compared with CPAP [3,11,13,37,38]; a sixth reported improved thoraco-abdominal synchrony [2]. Two direct comparisons of sNIPPV with nsNIPPV found that sNIPPV improved thoraco-abdominal synchrony [37] and reduced WOB [13,37]. Less WOB may seem of small benefit, but over a prolonged period may influence need for intubation or re-intubation, or frequency of apnea.