

Non-invasive ventilation in premature infants

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Non-invasive respiratory support in preterm infants traditionally consisted of the application of continuous distending positive pressure at the nose. More recently, the continuous distending pressure has been combined with intermittent positive pressure cycles using conventional ventilators or devices developed specifically for this purpose. One of the common terms used to refer to these modalities is nasal intermittent positive pressure ventilation (NIPPV). These modalities or devices vary depending on the peak pressure of each cycle, how fast it rises, the duration of the cycle and cycling frequency and whether the positive pressure cycle can be synchronised to the spontaneous inspiration. The mechanisms of action, benefits and limitations of the different devices, modalities and/or applied settings have not been fully explored. Three separate studies sought to improve the understanding of some of these modalities of respiratory support.^{1–3}

Bi-level positive airway pressure (BiPAP) has been proposed as a way to provide higher mean airway pressure (MAP) without the possible side effects of a continuously high distending pressure while the infant is able to breathe at both pressure levels. Lampland *et al* tested the hypothesis that applying BiPAP without increasing MAP would improve gas exchange compared with nasal continuous positive airway pressure (NCPAP). Twenty preterm infants of median gestational age (GA) of 26 weeks and 33 days old were crossed over twice between NCPAP and BiPAP for 1 h each. During BiPAP, positive end-expiratory pressure (PEEP) and peak pressure were adjusted to provide a minimum Δ pressure of 3 cm H₂O for 1 s at a rate of 20/min and match the MAP to the NCPAP level of 6 cm H₂O. These investigators found arterial oxygen saturation (SpO₂), fraction of inspired oxygen (FiO₂), transcutaneous CO₂ tension (TcPCO₂), respiratory rate (RR) and frequency of apnoea, bradycardia

or hypoxaemia spells did not differ between NCPAP and BiPAP. These findings differ from those obtained in a similar study where BiPAP provided higher MAP than NCPAP.⁴ This difference in results suggests the gains achieved by the relatively small Δ pressure cycles might have been counteracted by the lower PEEP during BiPAP. It is unknown if cycles with a larger Δ pressure or a longer duration would have achieved different effects. The lack of effect may also be because these infants were already stable on NCPAP and thus did not need the additional support.

Another proposed benefit of BiPAP is that the positive pressure cycle would improve tidal volume (VT) or facilitate its generation by assisting every spontaneous inspiration. This requires synchronising the BiPAP cycle to the onset of the spontaneous inspiration. Owen *et al* assessed the synchronisation achieved by a BiPAP device using the Graseby pressure capsule applied on the infant's abdomen and its effects on VT and the backup ventilation provided during apnoea. Ten premature infants of 26 weeks GA were studied at a mean age of 29 days. Thirty-minute recordings while on BiPAP set at a PEEP of 7 and Δ pressure cycle of 3 cm H₂O lasting 0.3 s to assist every spontaneous inspiration or provide a backup rate of 30/min in case of apnoea.

Examination of the recordings found the Graseby capsule reliably followed spontaneous breaths and that 82% of spontaneous breaths triggered a BiPAP cycle. Most of these cycles occurred in early inspiration (83% were within 50 ms from the onset of spontaneous inspiration). It was noted that for some periods (10% of the time in 6/10 infants) the capsule pressure waveform showed inspiration, but a BiPAP cycle was not triggered. This appeared to be influenced by the spontaneous RR with 89% of spontaneous breaths triggering a BiPAP cycle when RR was <55/min compared with 75% with a higher RR. Interestingly, the measured VT in BiPAP-assisted spontaneous breaths was not larger than VT in non-assisted spontaneous breaths and the positive pressure cycles during apnoea did not produce a detectable VT. These findings clearly indicate the Graseby capsule is adequate for use as a trigger signal for

synchronised NIPPV. The achieved synchronisation may be influenced by refractory times programmed in the device or by the manner in which the changes in pressure are achieved in each cycle.

An important observation is that synchronised BiPAP cycles did not increase VT. This may be due to the relatively small Δ pressure. However, it was previously shown that even larger Δ pressures applied in synchrony led to a reduction in inspiratory effort instead of an increase in VT.^{5–6} Also of interest is that backup cycles delivered during apnoea episodes did not deliver measurable VT's.

An inconsistent respiratory drive and oxygenation instability are common in the preterm infant and recurrent episodes of apnoea, hypoxaemia and bradycardia often lead to intubation and mechanical ventilation. Studies have shown inconsistent effects of NIPPV on apnoea compared with NCPAP^{7–10} and it is unknown if synchronised NIPPV may be advantageous compared with non-synchronised NIPPV.

Gizzi *et al* compared the effects of synchronised NIPPV vs. non-synchronised NIPPV or CPAP on the frequency of apnoea, hypoxaemia and bradycardia spells in premature infants. Nineteen infants of 27 weeks GA were studied at a median postmenstrual age of 30 weeks in a crossover study of CPAP, NIPPV at 20 cycles/min and flow synchronised NIPPV in assist/control mode with a backup rate of 20/min, for 4 h each.

Recordings showed a significantly lower frequency of hypoxaemia spells (SpO₂ <80%) and apnoea during synchronised NIPPV compared with NCPAP or non-synchronised NIPPV while these events did not differ between NCPAP and non-synchronised NIPPV.

Whether the improved oxygenation stability with synchronised NIPPV was related to the assistance of every inspiration, a higher ventilator rate or higher MAP is unknown but it is in contrast with the increase in hypoxaemia spells noted with non-synchronised BiPAP and non-synchronised ventilator NIPPV compared with NCPAP alone.¹⁰ Similar to other observations,¹¹ backup NIPPV cycles during apnoea did not appear to maintain ventilation, which suggests a stimulatory effect on apnoea that could attenuate episodic hypoxaemia.

These and previous studies^{5–6–12–13} report adequate synchrony can be achieved during NIPPV by means of the Graseby pressure capsule placed on the abdomen or an inline flow sensor. This is important because these techniques were used in 4 of the trials that showed higher

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extubation success with synchronised NIPPV compared with NCPAP.^{14–17}

The findings of these three studies must be carefully interpreted in the context of the respiratory status of the enrolled infants when contrasting to data from randomised clinical trials or to clinical experiences. Physiologic studies tend to enrol infants who are for the most part stable on a specific mode of non-invasive support with the settings determined by the clinical team. In contrast, infants with more severe respiratory failure or those who were recently extubated may be more likely to benefit from the additional support.

The factors that influence the efficacy of NIPPV and enhance transmission of the positive pressure to the airway need to be further explored along with the possible effects of NIPPV on respiratory control. Well-conducted physiologic studies like those reported^{1–3} greatly contribute to our understanding of the modalities of NIPPV and the manner in which they are applied.

These studies highlight the variability that exists between NIPPV devices and how these are used in clinical practice. Specific device features, e.g. synchronisation, combined with the selected settings of pressure and time can vary considerably and may account for the differences in clinical results. The effects of the different forms of NIPPV and the settings may differ within a given population as well as between populations of preterm infants due to the fact that there are multiple indications for non-invasive respiratory support and that respiratory conditions vary between preterm infants. It is therefore important to consider differences in NIPPV modalities, settings and populations when interpreting the evidence from NIPPV studies.

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