Synchronized Nasal Intermittent Positive Pressure Ventilation (SNIPPV) Decreases Work of Breathing (WOB) in Premature Infants With Respiratory Distress Syndrome (RDS) Compared to Nasal Continuous Positive Airway Pressure (NCPAP)

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Summary. Synchronized nasal intermittent positive pressure ventilation (SNIPPV) is non-invasive respiratory support that delivers ventilator breaths via the nasal prongs. We hypothesized that SNIPPV is more effective than nasal continuous positive airway pressure (NCPAP) in premature neonates due to decreased work of breathing (WOB). Fifteen infants (BW: 1,367 ± 325 g, GA: 29.5 ± 2.4 weeks) were studied on (a) NCPAP at 5 cmH2O (NCPAP5) and (b) three increasing SNIPPV settings achieved by NCPAP5 with additional delivered peak inspiratory pressures (PIP) of 10, 12, and 14 cmH2O. Tidal volumes and transpulmonary pressures were estimated via calibrated respiratory inductance plethysmography (RIP) and esophageal pressures, respectively. Inspiratory (WOBinsp), resistive (RWOB), and elastic (WOBE) components of WOB were calculated using standard methods. Compared to NCPAP5, (a) WOBinsp and RWOB were significantly lower with SNIPPV12, and were similarly lower with SNIPPV14 and (b) WOBE was significantly lower only with SNIPPV14. WOB components did not differ significantly for the three SNIPPV settings. Tidal volume, respiratory rate (RR), minute ventilation, compliance, and phase angle were similar for all four measurements. In conclusion, compared to NCPAP, the addition of ventilator-delivered PIP during SNIPPV decreases WOB in premature infants. Pediatr Pulmonol. 2006; 41:875–881. © 2006 Wiley-Liss, Inc.

Key words: work of breathing; synchronized nasal intermittent positive pressure ventilation; nasal continuous positive airway pressure; respiratory inductance plethysmography; respiratory distress syndrome.

INTRODUCTION

Preterm neonates who are intubated and mechanically ventilated for respiratory distress syndrome (RDS) are at increased risk of developing pulmonary complications including bronchopulmonary dysplasia (BPD).1–3 Increased concern about volutrauma in ventilator supported preterm infants and efforts to prevent BPD have...
resulted in renewed interest in the use of nasal continuous positive airway pressure (NCPAP). Use of NCPAP in premature neonates can decrease the need for mechanical ventilation and may reduce the incidence of BPD. However, preterm infants may fail NCPAP support and, consequently, require intubation and mechanical ventilation.

Synchronized nasal intermittent positive pressure ventilation (SNIPPV) is a promising non-invasive method to support respiration without endotracheal intubation. SNIPPV provides synchronized ventilatory breaths via the nasal prongs in addition to CPAP. SNIPPV has been used in preterm neonates with RDS as a primary mode as well as after extubation and for apnea. Santin et al. used SNIPPV as a primary mode of respiratory support over conventional ventilation and reported decreased oxygen requirement and hospital stay with support over conventional ventilation and reported decreased inspiratory effort during SNIPPV. In two small clinical trials, researchers have reported more successful extubation of premature neonates on SNIPPV compared to NCPAP. Alternatively, two clinical trials using SNIPPV for short duration in premature neonates with apnea reported conflicting results.

The mechanistic reasons why SNIPPV might be beneficial—or more effective—than NCPAP have not been fully elucidated. However, Moretti et al. reported that the application of SNIPPV versus NCPAP was associated with increased tidal ventilation and decreased esophageal pressure reflecting decreased inspiratory effort during SNIPPV. While these findings may indicate a decreased workload with SNIPPV, a decrease in work of breathing (WOB) in preterm neonates on SNIPPV has never been demonstrated, nor has the potential effects of varying the delivered peak inspiratory pressures (PIP) during SNIPPV been investigated. Accordingly, we compared NCPAP to varying levels of SNIPPV support in preterm infants with RDS.

We hypothesized that SNIPPV is more effective than NCPAP for respiratory support of premature neonates due to decreased inspiratory workload.

**MATERIALS AND METHODS**

The study was conducted in a 39 bed, level III NICU at Cooper University Hospital in Camden, New Jersey, between January 2003 and November 2004. The study was approved by the Institutional Review Board and signed informed consent was obtained from parent(s) or guardian(s) prior to the study.

Infants were eligible for study if <2,000 g birth weight and medically stable but requiring NCPAP for mild RDS. Infants with major congenital anomalies were also excluded. Each of the 15 infants was studied on both devices NCPAP and SNIPPV, applied in random order. The random sequence of starting device was determined by a sealed envelope drawn prior to start of study. Investigators were not blinded to the device type at the time of measurement. According to the randomization, seven of the infants started on NCPAP and eight started on SNIPPV.

Infants were studied supine, without sedation, and after feeding whenever possible. An Infant Star ventilator with INCA prongs was used to deliver NCPAP and SNIPPV using pneumatic StarSync capsule (Mallinckrodt, St. Louis, MO). Prongs used were the largest size that would easily fit into the infant’s nares without blanching the surrounding tissue.

Positive end expiratory pressure (PEEP) of 5 cmH₂O was used on NCPAP (NCPAPS). SNIPPV was always delivered in assist control mode with a constant PEEP set at 5 cmH₂O (i.e., equivalent to NCPAPS). Here, three increasing levels of support were delivered by adjusting PIP: 10 (SNIPPV10), 12 (SNIPPV12), and 14 (SNIPPV14) cmH₂O. The inspiratory time was kept constant at 0.35 sec for all modes. The SNIPPV data were collected in sequential order. All data were collected after a stabilization time of approximately 5 min at each level. When necessary, the infant’s mouth was closed gently during data collection to stop any air leak. Leak free breaths spanning the last 20–30 sec at each setting were selected for subsequent analysis.

The analysis methods are described elsewhere in detail. Briefly, abdominal and chest wall movements were recorded using respiratory inductance plethysmography (RIP; Respiband Plus and Respitrace, SensorMedics Corp., Yorba Linda, CA), and these were used as estimates of tidal ventilation [V RIP(t)]. Calibration of V RIP data was done via direct comparisons of tidal ventilation measured by face mask pneumotachography (Hans Rudolph, Inc., Kansas City, MO). Pleural pressures (and hence transpulmonary pressure or Ptp(t)) were estimated from continuous esophageal pressure...
monitoring via an esophageal balloon catheter (Ackrad Laboratories, Cranford, NJ) with validation of proper placement using the occlusion technique. Data were collected at 100 Hz using the Biopac MP100 data acquisition system (Biopac Systems, Inc., Santa Barbara, CA).

Calibrated \( V_{\text{RIP}}(t) \) tracings were used to obtain weight-adjusted tidal volume (\( V_T, \text{ml/kg} \)), respiratory rate (\( RR \)), and minute ventilation (\( V_E \)). Breath-to-breath lung compliance estimates were derived from changes in \( P_{tp} \) and \( V_T \) \[ CL = \frac{V_T}{\Delta P_{tp}} \]. Additionally, phase angle (in degrees, time lag between chest and abdominal movement) was calculated from RIP tracings. Finally, \( V_{\text{RIP}}(t) \) and \( P_{tp}(t) \) were used to calculate individual breaths’ inspiratory, elastic, and resistive work (\( \text{WOB}_{\text{insp}}, \text{WOB}_E, \) and \( \text{RWOB} \)) as shown in Figure 1 and as previously described.\(^{12–15}\)

Paired \( t \)-tests were used to determine the significance of differences between NCPAP5 (control) and SNIPPV at delivered PIP 10, 12, and 14 cmH\textsubscript{2}O. Data were also compared among the three SNIPPV support. A Bonferroni correction was used to account for the multiple significance tests run on each infant, holding the family-wise Type I error rate to 0.05.\(^{16,17}\) Post hoc ("observed") power calculations were done to gauge the strength of the design for the various tests run, and to point to outcomes where increased sample sizes may be required to determine effects in future studies. Observed power calculations, based on the observed effect sizes for outcomes averaged over all three interventions, showed adequate sample sizes for all significance tests run, using a one-tailed alpha = 0.05 and power = 0.80.

\[ \text{WOB}_{\text{insp}} = \text{WOB}_{\text{E}} + \text{WOB}_R \]
\[ \text{RWOB} = \text{RWOB}_{\text{insp}} + \text{RWOB}_R \]

**RESULTS**

Fifteen infants were enrolled in the study. Demographics and clinical settings at the time of study are outlined in Table 1. Mean birth weight and gestational age of infants were 1,367 ± 325 g and 29.5 ± 2.4 weeks and mean age at time of study was 4 ± 4 days. Infants were on minimal NCPAP support at the time of study (FiO\textsubscript{2} 0.26 ± 0.1, NCPAP 4.2 ± 0.4 cmH\textsubscript{2}O). Prior to the study, four infants received surfactant therapy and six required ventilatory support.

Figure 2 shows sample tracings from one infant of \( V_T, P_{tp}, \) and the corresponding P–V loops recorded during SNIPPV14 and NCPAP5. Respiratory pattern parameters, lung compliance (\( C_L \)) and WOB components are summarized in Table 2. There was no significant difference in \( C_L, \) RR, \( V_T, \) \( V_E, \) or phase angle on NCPAP versus SNIPPV.

Compared to NCPAP5 (Table 2), (1) \( \text{WOB}_{\text{insp}} \) was significantly lower (\( P = 0.01 \)) whereas \( \text{WOB}_E \) (\( P = 0.06 \)) and \( \text{WOB}_R \) (\( P = 0.09 \)) were not significant for SNIPPV10; (2) \( \text{WOB}_{\text{insp}} \) and \( \text{RWOB} \) were significantly decreased for SNIPPV12 (\( P = 0.03 \) for both) while the corresponding decrease in \( \text{WOB}_E \) did not reach significance (\( P = 0.10 \)); and (3) \( \text{WOB}_{\text{insp}}, \text{WOB}_E, \) and \( \text{RWOB} \) were all significantly lower (\( P = 0.02, \) \( P = 0.03, \) and \( P = 0.01, \) respectively) with SNIPPV14.

The percent change in \( \text{WOB}_{\text{insp}}, \text{WOB}_E, \) and \( \text{RWOB} \) with each SNIPPV relative to NCPAP5 are detailed in Figure 3. For SNIPPV10, SNIPPV12, and SNIPPV14, respectively, (a) \( \text{WOB}_{\text{insp}} \) was decreased in 12 of 15, 11 of 15, and 13 of 15 patients, respectively; (b) \( \text{WOB}_E \) was decreased in 12 of 15, 12 of 15, and 12 of 15 patients, respectively; and (c) \( \text{RWOB} \) was decreased in 11 of 15, 12 of 15, and 11 of 15 patients, respectively.

The decrease in \( \text{WOB}_{\text{insp}}, \text{WOB}_E, \) and \( \text{RWOB} \) was more evident with increasing PIP support but did not differ significantly among the three SNIPPV settings.

**DISCUSSION**

SNIPPV, like NCPAP, is a non-invasive way to support respiration without endotracheal intubation. SNIPPV not only provides CPAP but also generates extra pressure during spontaneous breathing. By providing extra support,
SNIPPV may be better than NCPAP alone. SNIPPV may decrease inspiratory effort and improve patency of the upper airway by creating intermittently elevated pharyngeal pressure. However, data on lung mechanics comparing SNIPPV and NCPAP are scarce in premature neonates. To our knowledge this is the first study demonstrating decreased WOB with SNIPPV compared to NCPAP in preterm neonates. Earlier, two small

**TABLE 2**—Actual Data on Respiratory Parameters at Various Levels of Respiratory Support (mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>NCPAP5</th>
<th>SNIPPV10</th>
<th>SNIPPV12</th>
<th>SNIPPV14</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT, ml/kg</td>
<td>2.9 ± 1.2</td>
<td>2.8 ± 1.32</td>
<td>2.8 ± 1.1</td>
<td>2.9 ± 1.0</td>
</tr>
<tr>
<td>RR, per min</td>
<td>53 ± 23</td>
<td>58 ± 22</td>
<td>53 ± 26</td>
<td>59 ± 23</td>
</tr>
<tr>
<td>Minute ventilation, ml/min - kg</td>
<td>115 ± 72</td>
<td>119 ± 67</td>
<td>114 ± 70</td>
<td>127 ± 62</td>
</tr>
<tr>
<td>Phase angle, degrees</td>
<td>46 ± 58</td>
<td>49 ± 38</td>
<td>47 ± 53</td>
<td>56 ± 54</td>
</tr>
<tr>
<td>WOB_{insp} per ml, cmH&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>2.69 ± 2.24</td>
<td>2.26 ± 1.94</td>
<td>2.29 ± 2.29*</td>
<td>1.91 ± 1.68*</td>
</tr>
<tr>
<td>RWOB per ml, cmH&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>1.81 ± 1.67</td>
<td>1.32 ± 1.10</td>
<td>1.50 ± 1.56</td>
<td>1.01 ± 0.95*</td>
</tr>
<tr>
<td>RWOB per ml, cmH&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>2.16 ± 2.04</td>
<td>1.71 ± 1.79*</td>
<td>1.79 ± 2.05*</td>
<td>1.56 ± 1.61*</td>
</tr>
<tr>
<td>CL (ml/kg · cmH&lt;sub&gt;2&lt;/sub&gt;O)</td>
<td>1.61 ± 1.68</td>
<td>1.38 ± 2.73</td>
<td>3.37 ± 4.89</td>
<td>2.42 ± 2.86</td>
</tr>
</tbody>
</table>

*P = 0.01–0.03.
randomized clinical trials compared extubation failure rate on SNIPPV and NCPAP in premature neonates with RDS. Khalaf et al. demonstrated higher success rate of extubation with SNIPPV compared to NCPAP. Barrington et al. also reported similar reduction in extubation failure with SNIPPV. Santin et al. used SNIPPV as a primary mode of ventilation in premature neonates with RDS requiring surfactant treatment. They reported significant reduction in ventilation in premature neonates with RDS requiring surfactant treatment. SNIPPV has also been used in premature neonates with apnea. Ryan et al. in a cross-over study of 20 infants found no significant difference in rates of apnea on SNIPPV compared to NCPAP. However, Lin et al. reported significant reduction in frequency of apnea with SNIPPV compared to NCPAP. The conflicting results from these small clinical trials may be due to the short period of intervention (4–6 hr) in their studies. The Cochrane review on the use of SNIPPV for apnea of prematurity and after extubation from conventional ventilator concluded that SNIPPV may be a useful method of augmenting the beneficial effect of NCPAP in preterm infants.

In our study, compared to NCPAP support, SNIPPV with increasing PIP at the same NCPAP (5 cmH₂O) decreased WOB with WOB_E as well as RWOB. SNIPPV probably decreases WOB by reducing the infant’s inspiratory effort, making the pressure–volume curve narrow and straight. Moretti et al. found a similar reduction in inspiratory effort as indicated by lower esophageal pressure during SNIPPV compared to NCPAP. Even with lowest delivered PIP of 10 cmH₂O (SNIPPV10) there was a reduction in WOB by 15–23%. The largest reduction in WOB with WOB_E (22–28%) was seen at delivered PIP of 14 cmH₂O. One of the major causes of CPAP failure in spontaneously breathing premature neonates with RDS is fatigue in the diaphragm and accessory respiratory muscles. SNIPPV by decreasing WOB—while maintaining the lung volume recruitment of NCPAP—is an attractive alternative to NCPAP in premature neonates with RDS.

There is a concern that increasing PIP in SNIPPV may alter the infant’s respiratory pattern and increase breathing asynchrony. In our study we used lower delivered PIP to find the minimal pressure required to decrease the WOB parameters without affecting the respiratory pattern and asynchrony. There was no significant change in phase angle (indicating asynchrony in breathing) at any PIP setting. The lack of change in compliance, breathing pattern and asynchrony with NCPAP versus the SNIPPV might be explained by the application of same PEEP of 5 cmH₂O at all levels of respiratory support studied. The constant PEEP applied at all measurements may have attributed to similar end expiratory lung volumes (i.e., similar lung recruitments) that will primarily determine the effective lung compliance, the breathing patterns (RR, Vₚ), and even breathing asynchrony or phase angles. Furthermore, the infants in our study had mild RDS and changes in lung compliance might be evident if SNIPPV was used in sicker neonates.
With SNIPPV, there are also the risks of gastric and intestinal distension, feeding intolerance, and possible gastrointestinal perforation. Garland et al. reported increased risk of developing gastric and intestinal perforation with cycled ventilation by nasal prongs compared with ventilation and endotracheal intubation using intermittent mandatory ventilation. 20 Recent Cochrane reviews on SNIPPV showed no significant increase in gastrointestinal morbidities with SNIPPV compared to NCPAP. 18, 19 Our data report a decrease in WOBinsp, WOBE, and RWOB even at the lower delivered pressure, which can further minimize gastrointestinal complications with SNIPPV.

Morretti et al. reported increased tidal volume, minute ventilation, and decreased RR with SNIPPV compared to NCPAP. 11 Our study did not find significant difference in these parameters. We speculate that this disparity is probably due to the study population. Morretti et al. studied all infants immediately after extubation with similar delivered PIP as on ventilator (only 6 of 15 of our infants were on the ventilator before study), the median age of their study population was 6 days (2 days in our study), 9 of 11 of their infants were treated with surfactant (4 of 15 in our study) and 3 of 11 infants were on steroids for extubation (0 of 15 in our study). Another potential explanation for the difference in respiratory parameters in these two studies is the PEEP applied during the data acquisition. Moretti et al. used PEEP of 3 cmH2O on NCPAP and SNIPPV, whereas we used PEEP of 5 cmH2O. We speculate that with the higher PEEP level used in our study, the baseline lung recruitment (end expiratory lung volume) on NCPAP5 was more optimal and did not change significantly with addition of PIP. Alternatively, in the Moretti et al. study, the addition of PIP at the low-level PEEP of 3 cmH2O, may have been significant enough to change the respiratory parameters.

One of the limitations of our study results is that the data were obtained over a short time span. It is not possible to draw conclusions about long-term clinical importance from statistically significant short-term physiologic studies. However, our study supports the benefit of SNIPPV over NCPAP from previous smaller clinical trials. Better outcomes in previous clinical trials are probably due to decreased WOB with SNIPPV compared to NCPAP. Indeed, here we are able to provide the mechanistic evidence (decreased WOB) for the clinical findings of earlier trials. Another limitation of this study is that our study population consisted of larger neonates (birth weight mean ± SD, 1367 ± 325 g) that had mild RDS. Additional studies are needed on extremely low birth weight premature neonates (<1,000 g) with more severe RDS to find the optimal PIP in this group of infants.

The Infant Star ventilator used in this and other previous studies 6–8 is no longer commercially available. Infant flow® SiPAP™ plus and comprehensive (Viasys Healthcare, Inc., Palm Springs, CA) used in Europe and Canada can deliver SNIPPV. Puritan Bennett, Inc. (Pleasanton, CA) is modifying its 840™ ventilator system to deliver SNIPPV (personal communication).

In conclusion, SNIPPV decreases WOB without altering the breathing patterns and synchrony compared to NCPAP in premature neonates with mild RDS. Our study also indicates that WOB is decreased at lower delivered pressure, which can further minimize gastrointestinal complications and lung barotrauma.

REFERENCES


