Published in final edited form as:
J Perinatol. 2014 January ; 34(1): 27–32. doi:10.1038/jp.2013.120.

Work of breathing indices in infants with respiratory insufficiency receiving high-flow nasal cannula and nasal continuous positive airway pressure

BE de Jongh[1,2], **R Locke**[3,4], **A Mackley**[3], **J Emberger**[3], **D Bostick**[3], **J Stefano**[3,4], **E Rodriguez**[5], and **TH Shaffer**[4,5]

[1]Department of Neonatology, St Christopher's Hospital for Children, Philadelphia, PA, USA

[2]Department of Pediatrics, Drexel University College of Medicine, Philadelphia, PA, USA

[3]Department of Neonatology, Christiana Care Health System, Newark, DE, USA

[4]Department of Pediatrics/Neonatology, Thomas Jefferson University, Philadelphia, PA, USA

[5]Nemours Research Lung Center, Alfred I duPont Children's Hospital, Wilmington, DE, USA

Abstract

OBJECTIVE—To compare work of breathing (WOB) indices between two nCPAP settings and two levels of HFNC in a crossover study.

STUDY DESIGN—Infants with a CGA 28–40 weeks, baseline of HFNC 3–5 lpm or nCPAP 5–6 cmH_2O and fraction of inspired oxygen ≤40% were eligible. WOB was analyzed using respiratory inductive plethysmography (RIP) for each of the four modalities: HFNC 3 and 5 lpm, nCPAP 5 and 6 cmH_2O. $N = 20$; Study weight 1516 g (±40 g).

RESULT—Approximately 12 000 breaths were analyzed indicating a high degree of asynchronous breathing and elevated WOB indices at all four levels of support. Phase angle values (means) ($P<0.01$): HFNC 3 lpm (114.7°), HFNC 5 lpm (96.7°), nCPAP 5 cmH_2O (87.2°), nCPAP 6 cmH_2O (80.5°). The mean phase relation of total breath (PhRTB) (means) ($P<0.01$): HFNC 3 lpm (63.2%), HFNC 5 lpm (55.3%), nCPAP 5 cmH_2O (49.3%), nCPAP 6 cmH_2O (48.0%). The relative labored breathing index (LBI) (means) ($P\leq0.001$): HFNC 3 lpm (1.39), HFNC 5 lpm (1.31), nCPAP 5 cmH_2O (1.29), nCPAP 6 cmH_2O (1.26). Eighty-two percent of the study subjects—respiratory mode combinations displayed clustering, in which a proportion of breaths either occurred predominantly out-of-phase (relative asynchrony) or in-phase (relative synchrony).

CONCLUSION—In this study, WOB indices were statistically different, yet clinically similar in that they were elevated with respect to normal values. These infants with mild-to-moderate respiratory insufficiency demonstrate a meaningful elevation in WOB indices and continue to require non-invasive respiratory support. Patient variability exists with regard to biphasic clustered

---

Correspondence: Dr BE de Jongh, Division of Neonatal-Perinatal Medicine, Department of Pediatrics, Drexel University College of Medicine, 3601 A Street, Philadelphia, PA 19134, USA., Beatriz.dejongh@drexelmed.edu or bedejongh@gmail.com.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

breathing patterns and the level of supplemental fraction of inspired oxygen ≤40% alone does not provide guidance to the optimal matching of WOB indices and non-invasive respiratory support.

Keywords

preterm; infant; respiratory inductive plethysmography

INTRODUCTION

Despite advances in critical care neonatal-perinatal medicine, ventilator-induced lung injury remains an unresolved contributor towards neonatal morbidity and mortality.[1] In an effort to decrease ventilator-induced lung injury, many centers have implemented a less-invasive approach to ventilation. These efforts include increased use of nasal continuous positive airway pressure (CPAP) and, more recently, a heated high-flow humidified nasal cannula system.[2,3]

Nasal CPAP (nCPAP) is beneficial in improving gas exchange in preterm infants. It is able to do so by increasing the functional residual capacity, decreasing atelectasis and reducing the right-to-left intrapulmonary shunt.[4,5] Conversely, the principal mechanism of action of high-flow therapy is through dead space washout of the nasopharyngeal cavity, therefore, reducing overall dead space and resulting in alveolar ventilation as a greater fraction of minute ventilation.[6–8] In addition, high-flow therapy most likely minimizes the inspiratory resistance associated with the nasopharynx by providing nasopharyngeal gas flows that match or exceed a patient's peak inspiratory flow, and thus, reducing the resistive work of breathing (WOB).[7]

High-flow nasal cannula (HFNC) has been widely adopted as an alternative to nCPAP as clinical evidence suggests that HFNC provides improved levels of arterial CO_2, independent of changes in minute ventilation.[8] HFNC has been found to be well tolerated with no apparent differences in adverse outcomes when compared with the infants managed with nCPAP.[2] HFNC is able to deliver higher flow rates than regular nasal cannula through the addition of sufficient warmth and high levels of humidification to the inspired gas. Properly conditioned gas provides for patient comfort and minimizes deterioration of nasopharyngeal structures.[2,7,9,10] Previous reports estimated the airway end-distending pressures with the use of esophageal manometry and found a wide distribution of the pressure data, with differences only when comparing HFNC of 5 lpm and nCPAP of 6 cmH_20.[11] There was no increase in WOB when comparing nCPAP of 6 cmH_2O with HFNC of 3, 4 and 5 lpm.[11] Uncontrolled intrapulmonary pressure can be generated with nasal cannula devices when creating a relatively closed system that does not permit the exhalation or loss of flow.[12] Most recently, Sivieri *et al.*,[13] using a bench/analytical model, further demonstrated the multiple factors (flow, prong size, nares anatomy, mouth opening and lung mechanics) associated with intrapulmonary pressure generation.

In contrast to intrapulmonary pressures, intrapharyngeal pressures may be generated with greater consistency in a linear fashion with flow. The variability in the intrapharyngeal pressures has been linked to oral and nasal hygiene, mouth position and patient size, in addition to flow rates.[14,15] However, in these studies no pressure was generated with the mouth open at any flow rate and no documentation of intrapulmonary end-distending pressure or changes in FRC was established.[15]

Proper use of HFNC includes minimizing the nasal cannula size to the nare opening. This permits for a pop-off gas leak, limiting uncontrolled pressure generation while optimizing the benefits of CO_2 elimination and gas washout during exhalation. This method allows for entrainment of gas around the nasal cannula when using flow rates that are less than the infant's own peak inspiratory flow.

Flow rate (lpm) and end-distending pressure (cmH_2O) are not equivalent. Devices that deliver a controlled end-distending pressure to improve FRC, and devices that primarily operate through the reduction of nasopharyngeal dead-space to enhance CO_2 elimination and inspiratory respiratory unloading, may have differential efficacy depending upon the degree of an individual infant's underlying pulmonary pathology.

The decision to support an infant with nCPAP or HFNC is made mostly by personal preference and clinical experience. HFNC has been perceived to have greater ease of use and improved patient tolerance.[16] This crossover study compared WOB indices in infants with respiratory insufficiency that were receiving HFNC or nasal continuous airway pressure as part of their clinical care.

The primary outcome measured was WOB indices using respiratory inductive plethysmography (RIP), which is a tool used to assess thoraco-abdominal motion, as well as thoraco-abdominal asynchrony.[17–26] RIP is used in the Neonatal Intensive Care Unit setting for the measurement of non-invasive pulmonary function testing. There are no known risks of RIP use.[27] RIP obtains tidal breathing measurements via thoraco-abdominal motion analysis performed on volume signals collected at the chest wall and abdomen.[18] Thoraco-abdominal motion analysis examines the chest and abdominal motion asynchrony. Typically, patients are observed for a short period of time to establish a stable breathing pattern, after which thoraco-abdominal motion measurements are recorded for 10 to 20 representative breaths. In the healthy infant, the rib cage moves outward with inspiration in conjunction with the abdominal wall.[17] Thoraco-abdominal asynchrony refers to the non-coincident movement of the rib cage (RC) and the abdomen (ABD).[17] With increased WOB, the rib cage lags behind abdominal wall movement. Thoraco-abdominal asynchrony is increased in the setting of increased respiratory resistance, decreased lung compliance and increased chest wall compliance.[28]

The null hypothesis was that there would be equivalent efficacy in the WOB indices between HFNC (3 and 5 lpm) and nCPAP (5 and 6 cmH_2O) in these infants with mild respiratory insufficiency. In addition, we reasoned that determining the relative effects of HFNC and CPAP on pulmonary function measurements in infants may help improve the clinical determination for choice of methodology and provide evidence on the mechanism of action for each method.

METHODS

Study methodology utilized a two group pre-test/post-test experimental study in the tertiary neonatal intensive care unit at Christiana Care Health System, Newark, DE, USA. The study was designed to identify differences in WOB indices while administering HFNC (VT; Vapotherm, FDA approved device for the delivery of HFNC) or nCPAP (nCPAP: Drager Evita: demand flow, flow is variable (0.25 to 30 lpm), pressure remains constant) to infants as measured by RIP.

Infants were eligible for inclusion if they were: (1) between 28 and 40 weeks of corrected gestational age at the time of entry in the study, (2) receiving HFNC of 3 to 5 lpm or nCPAP of 5 to 6 cmH_2O as determined by the clinical care team for clinical care purposes independent from this study and (3) had an fraction of inspired oxygen requirement ≤40%. Subjects needed to have been on their current mode of ventilatory support for ≥12 h and have been extubated from a mechanical ventilator for ≥48 h. Patients were excluded if they had skeletal or neuromuscular disorders that affected the accuracy of RIP measurements. All patients received care at the Level III Neonatal Intensive Care Unit at Christiana Care Hospital.

In this study thoraco-abdominal motion was performed by means of RIP using the Respitrace QDC Unit (Yoma Linda, CA, USA) and recorded over a period of 2–4 min in order to ascertain a better estimate of breathing characteristics. The pulmonary function measurements were collected during quiet respiratory breathing with the infant in supine position, while wearing soft elastic cloth bands (RespiBands Plus, Viasys, San Diego, CA, USA), that comfortably encircled the RC and ABD. Contained within the soft elastic bands is a flexible sinusoidal wire that can measure motion. Real-time raw signals and Konno–Mead loops were monitored during the test to ensure proper signal and adequate quality using RespiEvents software 5.2 g (Nims, Miami, FL, USA).

Commonly used settings of both nCPAP and HFNC rates used in the Neonatal Intensive Care Unit were evaluated. Using the RIP methodology, WOB indices were measured initially on the patient’s baseline mode of therapy followed by the alternate mode of therapy. A stabilization time of ~5 min was completed before recording the testing.[29] While on nCPAP, measurements were recorded at 5 and 6 cmH_2O, on HFNC they were assessed at 3 and 5 lpm in a randomized order. All infants received all four levels of respiratory support (HFNC 3 lpm, HFNC 5 lpm, nCPAP 5 cmH_2O, nCPAP 6 cmH_2O).

Safety measures were set in place for termination of the study if the infant was not tolerating the study procedures. These measures included the following parameters: oxygen saturation <80% consistently for more than 30 s; heart rate <80 bpm or >200 bpm for more than 30 s; respiratory rate >100 per minute for more than 30 s.

WOB indices analyzed included phase angle, phase relation of the total breath, uncalibrated labored breathing index and uncalibrated inspired volume. Phase angle: this parameter is defined by the equation $\sin\theta = m/s$, where m is the line parallel to the abscissa on the RC–ABD plot at one-half the distance between the maximal RC perpendicular intercept and the origin, and s is the length of a line from the maximal ABD perpendicular intercept minus the origin. A phase angle of 0° represents perfect synchrony between the chest and abdominal compartments. Higher phase angles represent greater degrees of asynchronous breathing. A phase angle of 180° represents complete asynchrony.[28,27]

Phase relation total breath refers to the total time spent in asynchrony in a single breath, with values ranging between 0 and 100%.[29] High numbers reflect greater time spent in asynchrony. Labored breathing index refers to the sum of maximal excursion of RC and ABD divided by the tidal volume. One equals perfect thoraco-abdominal coordination. Greater than one reflects paradoxical motion of either the RC or the ABD.[27] This parameter is a relative number because RIP measurements were uncalibrated. Uncalibrated inspired volume is an arbitrary volume, measured by RIP, which is relative to other breaths for each patient. The mean for each mode of therapy of each patient was used. Values were normalized by empirically setting the standard to HFNC of 3 lpm, and then the relative differences were compared.

Demographic data were collected from chart review including the following: birth weight, weight at the time of the study, gestational age, corrected gestational age, baseline respiratory support and fraction of inspired oxygen. A power analysis to detect a 20% change in the phase angle ($\alpha = 0.05$, $\beta = 0.80$) yielded an estimate of 20 patients required for evaluation. Demographic data were analyzed by parametric means if normally distributed and nonparametric means if assumptions of normality were not reached. The analysis of the data of the WOB indices was performed applying mixed linear analysis, controlling for patient and breath-number influences. Bimodal analysis of the phase angle data for all modes of therapy for each patient utilized k-means clustering with $k = 2$ cluster means, accompanied by calculation of the variance reduction score (VRS)[30] to determine whether the distribution of phase angles was truly bimodal or merely unimodal with outliers. Clustering of the VRS across all analyzed data sets (again, k-means clustering with $k = 2$) established a VRS of <0.25 as representing a bimodal distribution. We arbitrarily used a phase angle of <60 for synchrony and ≥60 for asynchrony. Determination of sequential randomness utilized Runs testing.[31]

Written informed consent was obtained before enrollment in the study from a parent by one of the members of the research team. The study was approved by the Christiana Care Health System Institutional Review Board.

RESULTS

Twenty infants were evaluated. Demographics are shown in Table 1. A total of 52 patients were approached for entry into the study. Twenty-two consented with two being removed before entry into the study due to clinical changes leading to ineligibility after consent was obtained. There was greater tendency of parents to assent for participation if their infant was on CPAP compared with HFNC at the start of the study ($P = 0.09$). All study subjects tolerated the procedures. A total of 12 102 breaths were analyzed; this is the total number of breaths from the 20 patients on the four different modes of therapy. There was a high degree of asynchronous breathing at all four levels of support.

Eighty-two percent of the study subject—respiratory mode combinations displayed clustering (VRS <0.25; *k*-means clustering with *k* =2 centers) in which a proportion of breaths either occurred predominantly out-of-phase (relative asynchrony) or in-phase (relative synchrony). (Figures 1 and 2). This has not been previously reported. There was a greater tendency to demonstrate two-cluster pattern breathing with infants on nCPAP compared with HFNC ($P<0.01$) and in infants with higher mean phase angles measurements ($P=0.01$), though the clinical impact of the change on VRS was small and unlikely to be clinically meaningful (0.05 for HFNC vs nCPAP; 0.011 maximum impact of phase angle). Seventy-two percent of the phase angle distributions were random. The study was not prospectively designed to investigate this newly detected phenomenon and factors that may influence this occurrence may not have been included in the study protocol.

Phase angle, labored breathing index and phase relation of the total breath means for all breaths for each mode of therapy are presented in Figures 3–5.

The mean phase angle across the four different support levels varied between 80–140°, demonstrating significant ongoing WOB in the study population. There were different degrees of variability in the phase angle across the study group with 10% of patients on HFNC 3 lpm, 30% on HFNC 5 lpm, 20% nCPAP 5 cmH_2O and 40% nCPAP 6 cmH_2O. The highest phase angle values were seen in the measurements made on HFNC of 3 lpm, followed by HFNC of 5 lpm, nCPAP of 5 cmH_2O and finally nCPAP of 6 cmH_2O, which had the lowest phase angle measured ($P<0.01$). Although statistically significant because of the sensitivity associated with the large number of breaths measured, the overlap of the 95% confidence interval for the phase angle parameters, especially between HFNC 5 lpm, nCPAP 5 cmH_2O and nCPAP of 6 cmH_2O, suggest that there is a lack of a clinical meaningful difference (Figure 3). At the time that the infants were receiving HFNC of 3 lpm, they had less breath-to-breath variation when compared with the other three modes of therapy; however, they had the highest mean phase angle. The percentage of breaths with a phase angle >90 was greater in HFNC 3 lpm>HFNC 5 lpm>nCPAP 5 cmH_2O>nCPAP 6 cmH_2O ($P<0.01$).

The mean relative labored breathing index showed statistical differences ($P\leq 0.001$), but the clinically similar means and high degree of overlap of the 95% confidence interval suggest a lack of clinical meaningful differences (Figure 4). Similarly, the mean phase relation of total breath was statistically different ($P<0.01$) though with clinically similar means and high degree of overlap of the 95% confidence interval (Figure 5).

The composite data for the uncalibrated inspired volume revealed that HFNC of 3 lpm had a mean size breath that was 11.8% smaller when compared with HFNC of 5 lpm ($P=0.01$); 23.2% smaller when compared with nCPAP of 5 cmH_2O ($P<0.01$); and 21.3% smaller when compared with nCPAP of 6 cmH_2O ($P<0.01$). The median size breath for HFNC of 5 lpm was 11.4% smaller when compared with the mean size breath of nCPAP of 5 cmH_2O ($P=0.19$); 9.4% smaller when compared with nCPAP of 6 cmH_2O ($P=0.22$). The mean breath size of nCPAP of 5 cmH_2O was 1.9% smaller when compared with nCPAP of 6 cmH_2O ($P=0.78$).

DISCUSSION

Statistically different, but clinically similar, WOB indices were detected in our population of infants with mild-to-moderate respiratory support receiving HFNC of 3–5 lpm or NCPAP of 5–6 cmH_2O. There was high intra- and inter-patient variability for the respiratory support mode that was associated with the optimal WOB indices. The composite group clinical efficacy and the individual intra-patient variability leave opportunity for the value of clinical judgment in optimizing the type for respiratory support for a particular infant.

The findings of this study extend the confidence range in which HFNC may be successfully used within the context of good clinical judgment. Although non-intubated and receiving <40% fraction of inspired oxygen, the study population had significant underlying disease as evident by the high WOB indices. This study population had greater underlying respiratory disease than other nCPAP–HFNC comparative efficacy studies. Saslow *et al.*[11] studied the WOB in 18 premature infants while on HFNC and nCPAP, they reported similar compliance and phase angle values on all HFNC and nCPAP settings. The mean phase angle in their study ranged from 35.2–45.2, considerably different from our study population.

CPAP achieves efficacy primarily through the improvement of functional residual capacity, whereas HFNC achieves efficacy through CO_2 washout and respiratory unloading. HFNC and CPAP may not be interchangeable in all clinical circumstances.[32] Variability existed in our patient population with regards to the type and level of respiratory support that was associated with the greatest synchrony and associated WOB indices.

This study provides the first report of biphasic-clustered breathing in this population of infants with mild-to-moderate respiratory insufficiency. Pulmonary function analysis and WOB indices analysis typically utilize 10–20 breaths. We observed this unexpected phenomenon through the analysis of a greater number of sequential breaths per patient per mode (mean n =152), which were obtained in a 2–4 min period. As a fairly consistent finding in 83% of the patient-mode combinations, there is high confidence that this cluster pattern breathing represents a true event. Since unexpected, our study was not prospectively designed to completely analyze this occurrence. Our interpretation of these bimodal patterns is that infants are conserving energy by partitioning the use of respiratory muscle groups (intercostals; RC vs diaphragm; ABD). Rather than fatiguing both muscle groups with continuous synchronous breathing, these infants are sparing muscle efforts by switching between thoracic and abdominal contributions to tidal breathing. These bimodal patterns are reflected by our observations of ‘in-phase (low phase angles)’ and ‘out-of-phase (high phase angles)’ over extended time periods. These patterns are quite different from either all synchronous patterns (normal respiratory muscle function associated with a normal lung and chest wall combination) or all asynchronous patterns (weak respiratory muscle function associated with an abnormal lung and chest wall combination). Infants with ongoing mild-to-moderate respiratory insufficiency may be engaging in breathing pattern strategies to balance energy expenditure and gas exchange.

The limitations of our study include the difficulty to enroll patients who were on a baseline therapy of HFNC. There appeared to be reluctance on the parents’ part to have their infant placed on nCPAP once they were already on HFNC. Technical difficulties prevented measurement of esophageal pressure; however, this has been studied previously.

The application of our data to different devices should be undertaken with caution. All HFNC devices are not equivalent in their ability to provide high humidification at flows greater than 4 lpm. The HFNC device used in this study maintains high humidification at 5 lpm. A device that is unable to maintain adequate heated humidification at this flow rate may not yield equivalent results. It is known that the provision of adequately warmed and humidified gas to the conducting airways improves conductance and pulmonary compliance compared with dry, cooler gases.[7] The nasal cannula interface we used permitted >50% of the nasal opening to be patent, limiting the risk of providing uncontrolled intrapulmonary pressures or obstructing the entrainment of inspired gas necessary to meet infant’s peak demand.[12] In addition to safety concerns, the use of improperly sized nasal cannula can reduce the efficacy of HFNC by limiting the effectiveness of the jet stream gas flow and nasal washout.[33] The nCPAP device we used involved a ventilator interface that maintains constant end-distending pressure while varying the inspiratory flow rate.[34] nCPAP devices that utilize constant flow may yield different results. The prongs we used with the nCPAP were sized to fit snugly in the nares and short in length permitting the accurate delivery of end-distending pressure as well as permitting the expiration of gas through the nCPAP circuit. The use of small diameter prongs that do not seal at the nasal opening do not meet the definition of an nCPAP interface, as they cannot consistently deliver intrapulmonary end-distending pressure or have the capacity to permit expiratory flow through the device.

As measured by WOB indices and comparative level of supplemental oxygen support, heated high humidity HFNC and nCPAP are viable non-invasive respiratory support options for infants with mild-to-moderate respiratory insufficiency. Patient variability exists and a level of supplemental fraction of inspired oxygen ≤40% does not alone provide guidance to the optimal matching of improved WOB indices and the non-invasive mode of support. Clinical judgment, patient comfort and other factors remain important. We acknowledge that RIP is a research tool that is not readily available to the clinician and further research is needed to practically guide clinical care decisions. Infants with ongoing mild-to-moderate respiratory insufficiency may be engaging in variable breathing pattern strategies to balance energy expenditure and gas exchange. Further investigation into these findings may help guide methods to improve neonatal outcomes.

Acknowledgments

We would like to thank the parents and families in the Neonatal Intensive Care Unit. This study was supported by Nemours Biomedical Research (THS), NIH COBRE P20 GM 103464-8 (THS), Christiana Neonatal Research (RL, BDJ) and NIGMS T32-GM08562 (ER) pediatric clinical pharmacology fellow funded by NICHD.

References

1. Donn SM, Sinha SK. Minimising ventilator induced lung injury in preterm infants. Arch Dis Child Fetal Neonatal Ed. 2006; 91(3):F226–F230. [PubMed: 16632652]
2. Holleman-Duray D, Kaupie D, Weiss MG. Heated humidified high-flow nasal cannula: use and a neonatal early extubation protocol. J Perinatol. 2007; 27(12):776–781. [PubMed: 17855805]

3. Shoemaker MT, Pierce MR, Yoder BA, DiGeronimo RJ. High flow nasal cannula versus nasal CPAP for neonatal respiratory disease: a retrospective study. J Perinatol. 2007; 27(2):85–91. [PubMed: 17262040]
4. DeLemos RA, McLaughlin GW, Robison EJ, Schulz J, Kirby RR. Continuous positive airway pressure as an adjunct to mechanical ventilation in the newborn with respiratory distress syndrome. Anesth Analg. 1973; 52(3):328–332. [PubMed: 4574960]
5. Chernick V. Hyaline-membrane disease: therapy with constant lung-distending pressure. N Engl J Med. 1973; 289(6):302–304. [PubMed: 4577904]
6. Chatila WMD, Nugent TMD, Vance GRN, Gaughan JP, Criner GJMD. The effects of high-flow vs low-flow oxygen on exercise in advanced obstructive airways disease. Chest. 2004; 126(4):1108–1115. [PubMed: 15486371]
7. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: mechanisms of action. Respir Med. 2009; 103(10):1400–1405. [PubMed: 19467849]
8. Frizzola M, Miller TL, Rodriguez ME, Zhu Y, Rojas J, Hesek A, et al. High-flow nasal cannula: impact on oxygenation and ventilation in an acute lung injury model. Pediatr Pulmonol. 2011; 46(1):67–74. [PubMed: 21171186]
9. Miller SM, Dowd SA. High-flow nasal cannula and extubation success in the premature infant: a comparison of two modalities. J Perinatol. 2010; 30(12):805–808. [PubMed: 20237485]
10. Spentzas TMDM, Minarik MMD, Patters AB, Vinson BCRTL, Stidham GMD. Children with respiratory distress treated with high-flow nasal cannula. J Intens Care Med. 2009; 24(5):323–328.
11. Saslow JG, Aghai ZH, Nakhla TA, Hart JJ, Lawrysh R, Stahl GE, et al. Work of breathing using high-flow nasal cannula in preterm infants. J Perinatol. 2006; 26(8):476–480. [PubMed: 16688202]
12. Locke RG, Wolfson MR, Shaffer TH, Rubenstein SD, Greenspan JS. Inadvertent administration of positive end-distending pressure during nasal cannula flow. Pediatrics. 1993; 91(1):135–138. [PubMed: 8416477]
13. Sivieri EM, Gerdes JS, Abbasi S. Effect of HFNC flow rate, cannula size, and nares diameter on generated airway pressures: an *in vitro* study. Pediatr Pulmonol. 2012; 48(5):506–514. [PubMed: 22825878]
14. Spence KL, Murphy D, Kilian C, McGonigle R, Kilani RA. High-flow nasal cannula as a device to provide continuous positive airway pressure in infants. J Perinatol. 2007; 27(12):772–775. [PubMed: 17762844]
15. Kubicka ZJ, Limauro J, Darnall RA. Heated, humidified high-flow nasal cannula therapy: yet another way to deliver continuous positive airway pressure? Pediatrics. 2008; 121(1):82–88. [PubMed: 18166560]
16. de Klerk A. Humidified high-flow nasal cannula: is it the new and improved CPAP? Adv Neonat Care. 2008; 8(2):98–106.
17. Hammer JNC. Assessment of thoraco-abdominal asynchrony. Paediatr Resp Rev. 2009; 10(2):75–80.
18. Gappa M, Pillow JJ, Allen J, Mayer O, Stocks J. Lung function tests in neonates and infants with chronic lung disease: lung and chest-wall mechanics. Pediatr Pulmonol. 2006; 41(4):291–317. [PubMed: 16493664]
19. Wolfson MR, Greenspan JS, Deoras KS, Allen JL, Shaffer TH. Effect of position on the mechanical interaction between the rib cage and abdomen in preterm infants. J Appl Physiol. 1992; 72(3):1032–1038. [PubMed: 1533209]
20. Allen JL, Greenspan JS, Deoras KS, Keklikian E, Wolfson MR, Shaffer TH. Interaction between chest wall motion and lung mechanics in normal infants and infants with bronchopulmonary dysplasia. Pediatr Pulmonol. 1991; 11(1):37–43. [PubMed: 1833720]
21. Allen JL, Wolfson MR, McDowell K, Shaffer TH. Thoracoabdominal asynchrony in infants with airflow obstruction. Am Rev Respir Dis. 1990; 141(2):337–342. [PubMed: 2137313]
22. Locke R, Greenspan JS, Shaffer TH, Rubenstein SD, Wolfson MR. Effect of nasal CPAP on thoracoabdominal motion in neonates with respiratory insufficiency. Pediatr Pulmonol. 1991; 11(3):259–264. [PubMed: 1758748]

23. Deoras KS, Greenspan JS, Wolfson MR, Keklikian EN, Shaffer TH, Allen JL. Effects of inspiratory resistive loading on chest wall motion and ventilation: differences between preterm and full-term infants. Pediatr Res. 1992; 32(5):589–594. [PubMed: 1480462]
24. Miller TL, Palmer C, Shaffer TH, Wolfson MR. Neonatal chest wall suspension splint: a novel and noninvasive method for support of lung volume. Pediatr Pulmonol. 2005; 39(6):512–520. [PubMed: 15678504]
25. Miller TL, Cox T, Blackson T, Paul D, Weiss K, Shaffer TH. Pulmonary function assessment in an infant with Barnes syndrome: proactive evaluation for surgical intervention. Pediatrics. 2006; 118(4):e1264–e1267. [PubMed: 16950944]
26. Rodriguez ME, Mackenzie WG, Ditro C, Miller TL, Chidekel A, Shaffer TH. Skeletal dysplasias: evaluation with impulse oscillometry and thoracoabdominal motion analysis. Pediatr Pulmonol. 2010; 45(7):679–686. [PubMed: 20575094]
27. Warren RH, Horan SM, Robertson PK. Chest wall motion in preterm infants using respiratory inductive plethysmography. Eur Respir J. 1997; 10(10):2295–2300. [PubMed: 9387956]
28. Newth, CJL.; Hammer, J. Paediatric Pulmonary Function Testing. Basel: Karger; 2005. Measurements of Thoraco-Abdominal Asynchrony and Work of Breathing in Children; p. 9
29. Rusconi F, Gagliardi L, Aston H, Silverman M. Respiratory inductive plethysmography in the evaluation of lower airway obstruction during methacholine challenge in infants. Pediatr Pulmonol. 1995; 20(6):396–402. [PubMed: 8649920]
30. Hellwig B, Hengstler JG, Schmidt M, Gehrmann MC, Schormann W, Rahnenfuhrer J. Comparison of scores for bimodality of gene expression distributions and genome-wide evaluation of the prognostic relevance of high-scoring genes. BMC bioinformatics. 2010; 11:276. [PubMed: 20500820]
31. Technology NIoSa. Guide to the Statistical Tests. 2000. csrc.nist.gov/groups/ST/toolkit/rng/stats_tests.html[updated June 19, 2012; cited 2013 January]
32. Campbell DM, Shah PS, Shah V, Kelly EN. Nasal continuous positive airway pressure from high flow cannula versus infant flow for preterm infants. J Perinatol. 2006; 26(9):546–549. [PubMed: 16837929]
33. Miller TL. High flow nasal cannula therapy in neonatology. Resp Ther. 8(2):30–35.
34. Chang GY, Cox CA, Shaffer TH. Nasal cannula, CPAP, and high-flow nasal cannula: effect of flow on temperature, humidity, pressure, and resistance. Biomed Instr Technol. 2011; 45(1):69–74.

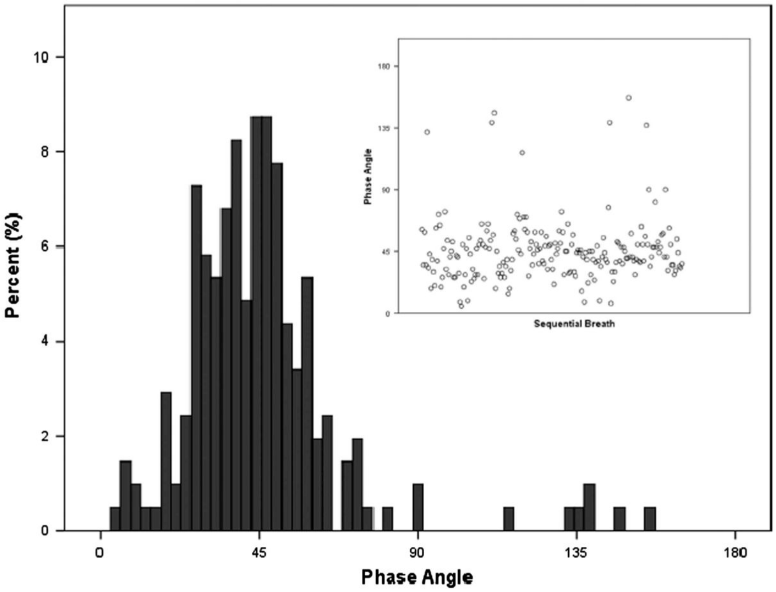

Figure 1.

Example patient no. 1: histogram and scatter representation of the phase angles for one of the patients studied on nasal CPAP 6 cmH_2O.

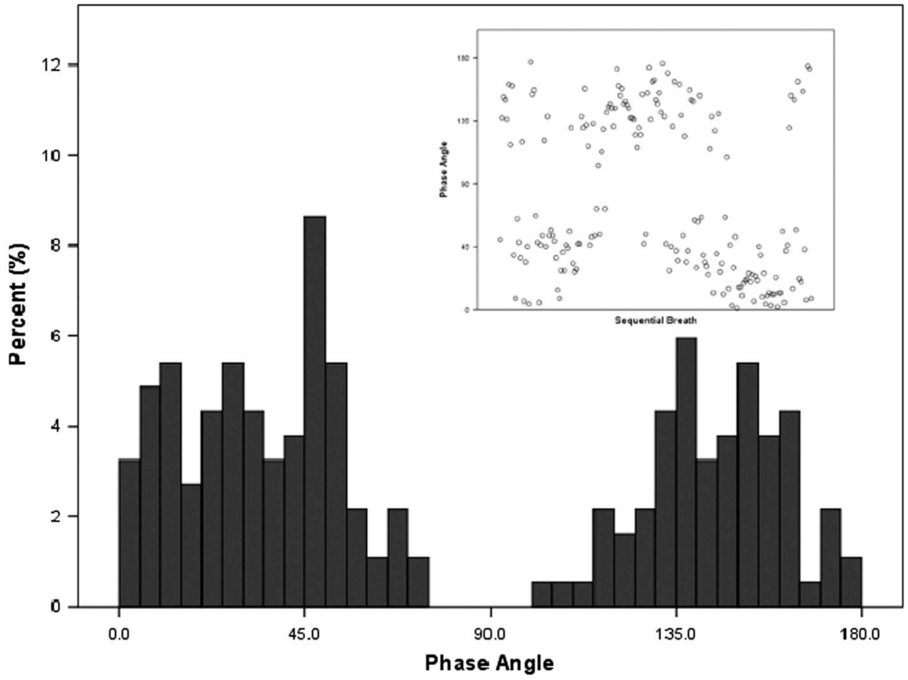

Figure 2.

Example patient no. 2: histogram and scatter representation of the phase angles for one of the patients studied on nasal CPAP 6 cmH_2O.

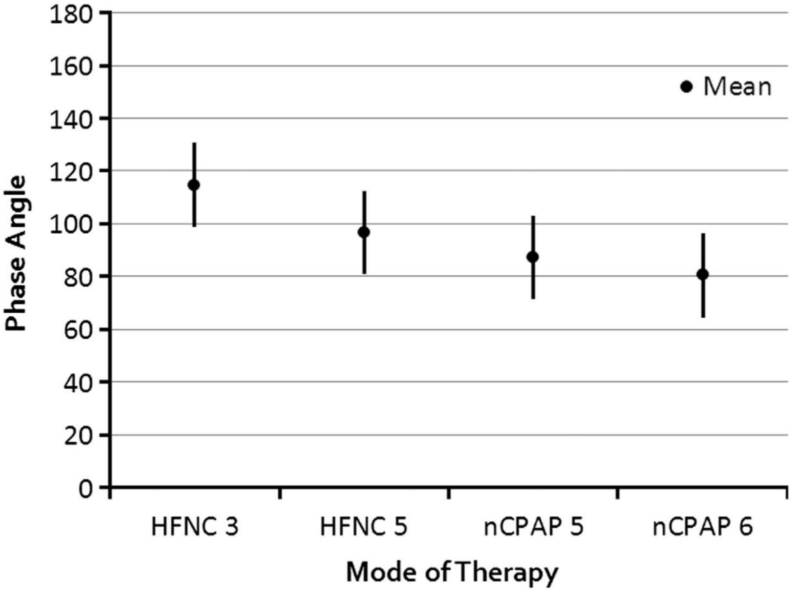

Figure 3.

Mean phase angle and 95% confidence interval results for all analyzed breaths in each group studied. Note: lower phase angle value indicates greater chest–abdomen synchrony.

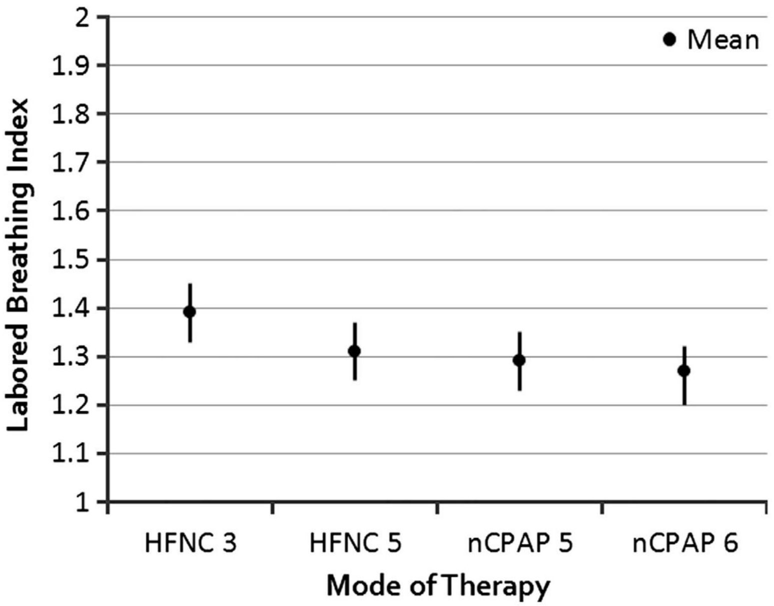

Figure 4.

Mean labored breathing index and 95% confidence interval results for all analyzed breaths in each group studied. Note: labored breathing index: closer to 1 relates to greater chest–abdomen synchrony.

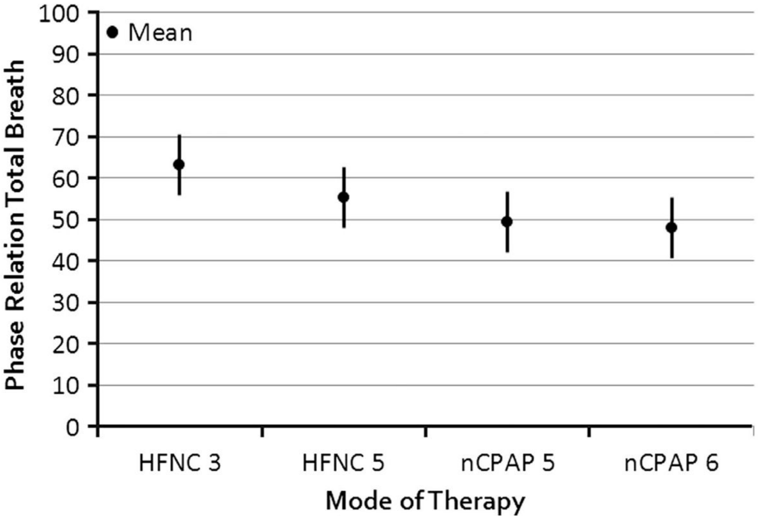

Figure 5.

Mean phase relation total breath and 95% confidence interval results for all analyzed breaths in each group studied. Note: phase relation of total breath: lower numbers relate to greater chest–abdomen synchrony.

Table 1

Patient demographics $N = 20$

	Mean (s.d.)	Range
Birth weight (g)	1175 (555)	615–2790
Gestational age (weeks)	28 (3.5)	24.5–39
Study weight (g)	1516 (470)	870–2790
Corrected gestational age (weeks)	32 (2.6)	28–39
FiO_2 (%)	26 (4)	21–32

Abbreviation: FiO_2, fraction of inspired oxygen.