Published in final edited form as:

Pediatrics. 2009 August ; 124(2): 517–526. doi:10.1542/peds.2008-1302.

SYNCHRONIZED NASAL INTERMITTENT POSITIVE PRESSURE VENTILATION AND NEONATAL OUTCOMES: A RETROSPECTIVE STUDY

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Abstract

Background—Current literature suggests that use of synchronized nasal intermittent positive pressure ventilation (SNIPPV), following extubation, reduces the rate of reintubation compared to nasal continuous positive airway pressure (NCPAP). However, there is limited information available on the outcomes of infants managed with SNIPPV.

Objectives—To compare the outcomes of infants managed with SNIPPV (postextubation or for apnea) to infants not treated with SNIPPV at 2 sites.

Methods—Clinical retrospective data was used to evaluate the use of SNIPPV in infants ≤ 1250 g birth weight (BW); and 3 BW subgroups (500–750, 751–1000, and 1001–1250 g, decided a priori). SNIPPV was not assigned randomly. Bronchopulmonary dysplasia (BPD) was defined as treatment with supplemental oxygen at 36 weeks' postmenstrual age.

Results—Overall, infants who were treated with SNIPPV had significantly lower mean BW (863g vs. 964g) and gestational age (26.4 weeks vs. 27.9 weeks), more frequently received surfactant (85% vs. 68%), and had a higher incidence of BPD or death (39% vs. 27%) (all $p < 0.01$), compared to infants treated with NCPAP. In the subgroup analysis, SNIPPV was associated with lower rates of BPD (43% vs 67%, $P = .03$) and BPD/death (51% vs 76%, $P = .02$) in the 500- to 750g infants, with no significant differences in the other BW groups. Logistic regression analysis, adjusting for significant covariates, revealed infants with 500–700-g BW who received SNIPPV were significantly less likely to have the outcomes of BPD (OR: 0.29 [95% CI: 0.11–0.77]; $P = .01$), BPD/death (OR: 0.30 [95% CI: 0.11–0.79]; $P = .01$), neurodevelopmental impairment (NDI) (OR: 0.29 [95% CI: 0.09–0.94]; $P = .04$), and NDI/death (OR: 0.18 [95% CI: 0.05–0.62]; $P = .006$).

Conclusion—SNIPPV use in infants at greatest risk of BPD or death (500-750g) was associated with decreased BPD, BPD/death, NDI, and NDI/death when compared to infants managed with NCPAP.

Keywords

premature newborn; respiratory distress syndrome; non-invasive ventilation

INTRODUCTION

Disorders related to prematurity accounted for 17% of all infant deaths in the USA in 2003¹. Almost half (49%) of all infant deaths occurred in those with birth weights <1000 grams (g)¹. Respiratory distress syndrome (RDS) and its sequelae, bronchopulmonary dysplasia (BPD), are both frequent complications in such infants. Despite an increased frequency of antenatal steroid use and surfactant replacement therapy for management of RDS, the incidence of BPD in very low birth weight (VLBW) infants has not changed significantly in the last decade². The pathogenesis of BPD is complex³. While genetic predisposition accounts for about half of the susceptibility to this disease⁴, important environmental factors include chorioamnionitis, hyperoxia, ventilator-induced injury, pulmonary edema, and hospital acquired infections⁵.

Noninvasive ventilation strategies using nasal continuous positive airway pressure (NCPAP), with or without surfactant therapy⁶⁻⁸, and nasal intermittent positive pressure ventilation (NIPPV)⁹ have been applied to VLBW infants with RDS and apnea in an effort to decrease ventilator-induced lung injury. A significant number of infants (20 to 63%) with respiratory distress treated with NCPAP alone (either as initial management or post-extubation) still require intubation and mechanical ventilation¹⁰⁻¹³, without an impact on the incidence of BPD^{14, 15}.

NIPPV is a form of non-invasive respiratory support that combines NCPAP with intermittent ventilator breaths and has been used as a treatment strategy for apnea of prematurity¹⁶⁻²⁰. One study using NIPPV as initial treatment for RDS²¹ and others using synchronized NIPPV (SNIPPV) for supporting infants as an extubation mode after a period of endotracheal tube positive pressure ventilation (ETTPPV) have found it to be more effective than NCPAP, especially in extremely low birth weight (ELBW) infants²²⁻²⁶. All the SNIPPV studies used the same ventilator and achieved synchronization using an abdominal sensor.²²⁻²⁶ A decrease in the incidence of BPD has been noted in some of these studies.^{21, 22, 26, 27} Recent reviews have suggested that SNIPPV is an effective method of augmenting the beneficial effects of NCPAP.²⁸⁻³²

We hypothesized that use of SNIPPV in premature infants with birth weight (BW) ≤1250 grams (g) would be associated with a lower incidence of BPD or death. The short- and long-term outcomes of infants 500-1250 g as well as the 3 BW sub-groups (500-750, 751-1000, 1001-1250 g) that were treated with SNIPPV, were compared with those infants who were not treated with SNIPPV in 2 centers (Yale University and University of California, San Diego [UCSD]) participating in the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network (NRN) benchmarking trial. These 2 centers were selected because they had the most experience with SNIPPV, and used similar protocols.^{22, 24}

MATERIAL AND METHODS

Clinical retrospective data were obtained from infants born January 1, 2002, to December 31, 2004, with BW of ≤ 1250 g from the Yale and UCSD sites participating in the benchmarking trial.³³ All of the infants were included. Maternal and infant data were collected by using common definitions developed by the investigators (with institutional review board approval), as described previously.³⁴

The criteria for intubation at both sites included need for resuscitation and/or respiratory failure necessitating surfactant administration (ie, fraction of inspired oxygen [FIO_2] ≥ 0.4 to maintain arterial oxygen saturation at $\geq 90\%$ and a diagnosis of RDS). The criteria for extubation were peak inspiratory pressure (PIP) of ≤ 16 cm H₂O, positive endexpiratory pressure (PEEP) of ≤ 5 cm H₂O, ventilator rate of 15 to 25, and FIO_2 of ≤ 0.35 . Acceptable blood-gas parameters were a pH of 7.25 to 7.45, Paco_2 of 40 to 55 mm Hg, and Pao_2 of 50 to 80 mm Hg. Postnatal steroids were used if the infants remained ventilator dependent with an FIO_2 of ≥ 0.4 beyond a postnatal age of 3 weeks despite use of diuretic therapy.

At both sites, the Infant Star with a synchronized intermittent mandatory ventilation box (Star Sync [Infrasonics, Inc, San Diego, CA]) was used for the infants assigned to SNIPPV. The StarSync module provides thoracoabdominal synchronization via the Graseby capsule placed on the abdomen. SNIPPV was generally used as a means of respiratory support for infants after extubation, although some infants were treated with SNIPPV for apnea without having had a previous intubation. Information was not available from the database about the specific indications for SNIPPV in each case. The use of SNIPPV was neither randomly assigned nor standardized. However, guidelines were very similar for the use of SNIPPV at Yale²⁶ and UCSD.²⁴ In brief, infants extubated to SNIPPV received synchronized nasal ventilation at the same rate as they were receiving before extubation, PIP was increased by 2 to 4 cm H₂O, and the PEEP was kept at ≤ 6 cm H₂O. FIO_2 was adjusted to maintain oxygen saturations of 88% to 96% at Yale and 85% to 95% at UCSD. The flow rate was kept at 8 to 10 L/minute. To avoid excessive leak of pressure, an attempt was made on all infants on SNIPPV to have their mouths closed (using pacifiers and/or chin straps). All infants on SNIPPV had a large-bore nasogastric tube in place, open to the atmosphere, to avoid distension of the stomach.

The SNIPPV group included infants who were on SNIPPV at any time during their hospitalization. The no-SNIPPV group included infants who never received SNIPPV but did receive NCPAP.

NCPAP settings were 4 to 6 cm H₂O. No specific protocol was applied for mouth closure or use of the nasogastric tubes in these infants, in terms of keeping it open to the atmosphere or suctioning air purposely from it.

BPD was defined as treatment with supplemental oxygen at 36 weeks' postmenstrual age.³⁵ In addition to demographic and common short-term outcome information (see "Results"), data on spontaneous gastrointestinal perforations (which was documented at surgery or post-mortem) were collected. Neurodevelopmental impairment (NDI) at 18 to 22 months of corrected age was defined as the presence of any of the following: cerebral palsy, Bayley Mental Developmental Index <70 , Bayley Psychomotor Developmental Index <70 , deafness/hearing loss requiring amplification in both ears, or bilateral blindness.³⁶

Infants ($n = 83$) who did not receive noninvasive ventilation, either NCPAP or SNIPPV, were excluded from the analysis. Out of these 83 infants, 30 infants survived to discharge from NICU, and 10 of these 30 infants had birth weight less than 1000 grams and hence

were eligible for the 18-month follow up. Eight infants completed follow up and 4 (50%) had NDI. Two infants were lost to follow-up.

Statistical analyses

To describe the effect of SNIPPV on outcomes of interest such as BPD, BPD/death, NDI, and NDI/death, first descriptive analyses were performed to compare several demographic, perinatal and neonatal characteristics of infants in the 2 groups (SNIPPV and no SNIPPV). χ^2 and Fisher's exact tests were used to test categorical data. For continuous data, t tests were used.

Analysis for all infants with BW ≤ 1250 g, was performed. With sample sizes available, we had a power of 80% for detecting a difference of 20%. Further analysis by BW categories (500-750, 751-1000, and 1001-1250 g, decided a priori) was also performed.

Logistic regression models were used to evaluate the effect of SNIPPV on BPD, BPD/death, NDI, and NDI/death. In all the logistic regression models we have initially included center, BW, gestational age (GA), small for GA, race, gender, antenatal steroids, Apgar scores at 1 and 5 minutes, RDS, surfactant use, postnatal steroids, late-onset sepsis, patent ductus arteriosus (PDA), severe intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), birth year, and duration of CPAP and/or mechanical ventilation as covariates. The final logistic regression model included only those covariates which were significant at $P < .05$. No significant differences were observed with the results on varying the sequence of entering the covariates in the logistic regression models. A stepwise or backward selection procedure was used to produce best-fit models.

The overall (500- to 1250-g BW) logistic regression models also included the interaction between the treatment and the 3 BW categories. The interaction showed $P < .05$ for the outcomes BPD or BPD/death always. This justified a subgroup analysis by the prespecified BW categories³⁷. A P value of $< .05$ was considered statistically significant for the treatment effect.

RESULTS

CHARACTERISTICS AND OUTCOMES OF INFANTS WITH BW 500 to 1250g

The baseline characteristics of infants receiving ($n = 242$ [52%]) or not receiving ($n = 227$ [48%]) SNIPPV at the Yale and UCSD sites during their hospital stay are depicted in Table 1, with their outcomes shown in Table 2. Infants who were treated with SNIPPV were significantly smaller in BW, of younger GA with a greater incidence of RDS and received more surfactant doses (Table 1). In addition, more of these infants had Apgar scores of ≤ 3 at 1 minute (Table 1). Infants treated with SNIPPV had significantly longer duration of ETTPPV, SNIPPV, and NCPAP days (Table 2). In addition, they had late-onset sepsis, retinopathy of prematurity (ROP) and (PVL) diagnosed more often, were more likely to be given postnatal steroids, and stayed in the hospital longer (Table 2). In accord with spending more time on supplemental oxygen (Table 2), infants who were treated with SNIPPV, were more likely to have BPD at 36 weeks postmenstrual age and BPD/death (Table 3).

We obtained average blood gas data for the 2 groups of infants on postnatal days 1, 3, 7, 14, 21 and 28. Regarding blood gas values, pH was significantly higher (data not shown) and pCO_2 lower on days 7, 21 and 28 in the SNIPPV group (Figure 1), with no differences in PaO_2 , bicarbonate or base deficit values (data not shown).

We had follow-up rates of 78.4% of the infants in the CPAP group, while 82.9% did so in the SNIPPV group. There was no difference in NDI in the 2 groups (Table 3).

Outcome analysis of BPD and NDI by BW—When the analysis was performed in the 3 predesignated BW categories, the overall rates of BPD and BPD/death were significantly lower in the BW category of 500-to 750-g for infants treated with SNIPPV (Table 3). Logistic regression analyses adjusting for center, BW, GA, small for GA, race, gender, antenatal steroids, Apgar scores at 1 and 5 minutes, RDS, surfactant use, postnatal steroids, late-onset sepsis, PDA, severe IVH, PVL, birth year, and duration of CPAP and/or mechanical ventilation showed that infants treated with SNIPPV in the weight category 500-to 750-g BW category were significantly less likely to develop BPD (odds ratio [OR]: 0.29 [95% confidence interval (CI): 0.11-0.76; $P = .01$], or BPD/death (OR 0.30 [95% CI: 0.11-0.79]; $P = .01$), overall (Table 4A and 4B). There were no significant differences between the SNIPPV and no-SNIPPV groups in BPD or BPD/death noted in the other BW categories.

NDI was not computed for the group with BW of 1001 to 1250 g, because only infants with BW up to 1000 g are followed up at 18 months in this NRN cohort. For the predesignated BW categories, the overall rates of NDI and NDI/death were not different in the 2 smaller BW categories (Table 3). Logistic regression analyses adjusting for the covariates (listed above) showed that infants treated with SNIPPV in the 500- to 750-g weight category were significantly less likely to have NDI (OR 0.29 [95% CI: 0.09-0.94; $P = .04$] or NDI/death (OR 0.18 [95% CI: 0.05-0.62]; $P = .006$), overall (Table 5A and 5B). There were no significant differences between the SNIPPV and no-SNIPPV groups in NDI or NDI/death noted in the 751- to 1000-g BW category.

DISCUSSION

This retrospective study has some limitations. The indications and techniques for using SNIPPV were not standardized at the 2 sites, although the protocols were similar and we had an equivalent sample size in the 2 groups. The study was not randomized and the 2 groups differed significantly (BW, GA, severity of disease etc.). There could be a selection bias in the SNIPPV and no-SNIPPV groups in terms of clinical severity of illness and the choice made by the treating physician to use this mode of therapy for a specific infant in a specific BW category. In addition, data were not available for some factors known to be associated with BPD and NDI, such as chorioamnionitis. Despite these limitations, we believe that this is the largest population of premature neonates treated with SNIPPV reported.

Given the potential benefits of avoiding endotracheal tube intubation, namely, decreased laryngeal and tracheal injury, decreased incidence and severity of BPD, and decreased nosocomial pneumonia and sepsis^{23, 38, 39}, there has been a renewed interest in the use of (S)NIPPV in extremely low BW infants^{19, 21-24, 31, 32}. (S)NIPPV has been shown to be associated with a decrease in BPD when introduced into a NICU setting.^{26, 40} Two recent prospective trials reported that (S)NIPPV as a form of ventilatory support in the early phase of RDS was associated with a significant decrease in the incidence of BPD and/or BPD and death.^{21, 27} While 1 prospective study has reported on long-term outcomes, it had a small sample size.²⁷ We evaluated the short-and long-term outcomes in the largest population reported to date.

Overall, the SNIPPV group was composed of smaller, younger, and sicker infants, and had a higher overall incidence of BPD and BPD/death. Despite this, for the 500- 750-g BW strata, there were improved BPD and BPD/death outcomes when compared with the no-SNIPPV group (Table 3). This remained true even after correcting for confounding variables (Tables 4). It is important note that the infants in the SNIPPV and no-SNIPPV groups are almost equal in number and the 2 centers had similar styles of providing SNIPPV. We speculate

that BPD and BPD/death rates were lower due to a more aggressive approach to avoid endotracheal tube placement by using SNIPPV.

An important caveat about our blood gas data is that it is not necessarily reflective of the infants while on SNIPPV or NCPAP. We have reported the average levels of blood gas data that were measured on specific postnatal days, without taking into account the type of the mechanical ventilation support on that day. Low PCO_2 values have been associated with PVL. However, the mean values of PCO_2 were 49, 54 and 54 mm Hg in the SNIPPV group, on days 7, 21, and 28 respectively. These values of PCO_2 have not been associated with PVL.⁴¹⁻⁴⁶

Furthermore, after correcting for confounding variables (the final logistic regression model did not include PVL), there was significantly decreased NDI in the infants receiving SNIPPV in the same BW category. Our data is based on ~80% follow-up rates. Interestingly, increased NDI in babies has been reported in babies with BPD⁴⁷; hence, we speculate that decreased NDI in this population of babies receiving SNIPPV could be attributed to lower rates of BPD.

We found no difference in the 2 groups in the incidence of air leaks, early-onset sepsis, PDA, severe intraventricular hemorrhage (IVH) or ROP requiring laser therapy (Table 2). In contrast, there was more ROP stage ≥ 2 , late-onset sepsis, use of postnatal steroids, PVL and longer duration of hospitalization in the SNIPPV group (Table 2). These outcomes could be reflective of the younger GA, smaller BW, and higher severity of illness of the infants in the SNIPPV group (Table 1). Importantly, it is reassuring to note that there were no differences in the rates of proven necrotizing enterocolitis or spontaneous gastrointestinal perforations in infants receiving SNIPPV and no SNIPPV. Concern for perforations had been raised in a previous study using NIPPV,⁴⁸ but our study confirms recent reports that gastrointestinal complications with SNIPPV use were not found.²⁸ One study reported earlier achievement of full enteral feeds in infants who were receiving SNIPPV²⁵.

Several explanations may account for the effectiveness of SNIPPV. Kiciman et al⁴⁹ have shown that thoracoabdominal motion asynchrony and flow resistance through the nasal prongs is decreased in neonates on SNIPPV, with improved stability of the chest wall and pulmonary mechanics. Addition of a PIP above PEEP by using SNIPPV could be adding increased intermittent distending pressure above PEEP, with increased flow delivery in the upper airway²³. Moretti et al¹⁷ reported that application of SNIPPV was associated with increased tidal and minute volumes when compared to NCPAP in the same infant. It is also possible that SNIPPV recruits collapsed alveoli and increases functional residual capacity. Aghai et al⁵⁰ recently reported that infants receiving SNIPPV have decreased work of breathing. Thoracoabdominal synchronization with SNIPPV may account, in part, for its efficacy. The use of synchronization is an important issue that needs additional investigation³².

The Infant Star ventilator with the StarSync® module has been used in most of the published studies^{22-27, 50}. In the United States, the Infant Star ventilator is being phased out of production, although it is still being used at some centers, including UCSD. In Europe and Canada, synchronization is accomplished with the Infant Flow® SiPAP™ Comprehensive ventilator (Viasys Healthcare, Yorba Linda, CA). In the United States, the comprehensive model has not yet been approved by the Food and Drug Administration. The 840TM ventilator system (Puritan Bennett Inc., Pleasanton, CA) is being modified to deliver SNIPPV. A recent study used a nasal ventilator that detected the inspiratory effort by means of a pneumotachograph⁵¹.

Recently, the nonsynchronized mode (ie, NIPPV) has been found beneficial^{21,52}. To date, however, no randomized, controlled trials comparing SNIPPV versus nonsynchronized NIPPV have been reported.

CONCLUSION

Given our findings for improved BPD, BPD/death, NDI and NDI/death and the reports of randomized trials using (S)NIPPV showing beneficial effects on BPD^{19, 21, 27}, we believe that a large, multicenter trial of (S)NIPPV in infants with BW of <1000g is warranted.

Acknowledgments

The NRN benchmarking (2002-2004) and follow-up (2003-2006) studies were supported by grants from the National Institutes of Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The funding agency provided overall oversight for study conduct. All data analyses and interpretation were independent of the funding agency.

The following investigators (listed with applicable grant numbers) participated in this study: NRN chair: Alan Jobe, MD, PhD (University of Cincinnati); Brown University, Women & Infants Hospital of Rhode Island (U10 HD27904): William Oh, MD, Abbot R. Laptook, MD, Betty R. Vohr, MD, Angelita Hensman, BSN, RNC, Lucy Noel, RN, Bonnie Stephens, MD, Victoria E. Watson, BA, MS, CAS, and Teresa M. Leach, BA, MA, MEd, CAES; Case Western Reserve University, Rainbow Babies & Children's Hospital (GCRC M01 RR80 and U10 HD21364): Michele C. Walsh, MD, MS, Avroy A. Fanaroff, MD, Deanne Wilson-Costello, MD, Nancy S. Newman, BA, RN, Bonnie S. Siner, RN, and Duncan Neuhauser, PhD; Duke University, University Hospital, Alamance Regional Medical Center, and Durham Regional Hospital (GCRC M01 RR30, CCTS UL1 RR24128, and U10 HD40492): Ronald N. Goldberg, MD, C. Michael Cotten, MD, Ricki Goldstein, MD, Kathy Auten, BS, and Melody Lohmeyer, RN; Emory University, Children's Healthcare of Atlanta, Grady Memorial Hospital, and Emory Crawford Long Hospital (GCRC M01 RR39 and U10 HD27851): Barbara J. Stoll, MD, Ira Adams-Chapman, MD, Susie Buchter, MD, Ellen Hale, RN, BS, Marcia Bishop, MS, NNP-BC, and Irma Seabrook, RRT; Indiana University, Indiana University Hospital, Methodist Hospital, Riley Hospital for Children, and Wishard Health Services (GCRC M01 RR750 and U10 HD27856): James A. Lemons, MD, Brenda B. Poindexter, MD, MS, Anna M. Dusick, MD, William A. Engle, MD, Diana D. Appel, RN, BSN, Dianne Herron, RN, Lucy Miller, RN, BSN, CCRC, Leslie Richard, RN, and Richard Hooper, RRT; Eunice Kennedy Shriver National Institute of Child Health and Human Development: Linda L. Wright, MD, Rosemary D. Higgins, MD, and Elizabeth M. McClure, MEd; Research Triangle Institute (U01 HD36790): W. Kenneth Poole, PhD, Abhik Das, PhD, Betty Hastings, Elizabeth McClure, MEd, Jamie Newman, Rebecca L. Perritt, MS, Qing Yao, PhD, Carolyn Petrie Huitema, MS, and Kristin Zaterka-Baxter, RN; Stanford University, Lucile Packard Children's Hospital (GCRC M01 RR70 and U10 HD27880): David K. Stevenson, MD, Krisa P. Van Meurs, MD, Susan R. Hintz, MD, MS, William D. Rhine, MD, M. Bethany Ball, BS, CCRC, Carol Kibler, RN, Jeffrey R. Parker, RRT, and Joan M. Baran, PhD; University of Alabama at Birmingham Health System and Children's Hospital of Alabama (GCRC M01 RR32 and U10 HD34216): Waldemar A. Carlo, MD, Ambalavanan Namasivayam, MD, Myriam Peralta-Carcelen, MD, Monica V. Collins, RN, BSN, Shirley S. Cosby, RN, BSN, and Vivien Phillips, RN, BSN; University of California San Diego Medical Center and Sharp Mary Birch Hospital for Women (U10 HD40461): Neil N. Finer, MD, Yvonne E. Vaucher, MD, MPH, Maynard R. Rasmussen, MD, Paul R. Wozniak, MD, Greg Heldt, MD, Kathy Arnell, RN, Clarence Demetrio, RN, Martha G. Fuller, RN, MSN, Chris Henderson, RCP, CRTT, Wade Rich, BS, RRT, CCRC, Mindy Grabarczyk, BSN, Christina Joseph, RRT, Renee Bridge, RN, and Jim Goodmar, RRT; University of Cincinnati, University Hospital, Cincinnati Children's Hospital Medical Center, and Good Samaritan Hospital (GCRC M01 RR8084 and U10 HD27853): Edward F. Donovan, MD, Kurt Schibler, MD, Jean Steichen, MD, Barb Alexander, RN, Cathy Grisby, BSN, CCRC, Marcia Mersmann, RN, Holly Mincey, RN, Jody Shively, RN, and Teresa Gratton, PA; University of Miami, Holtz Children's Hospital (GCRC M01 RR16587 and U10 HD21397): Charles R. Bauer, MD, Shahnaz Duara, MD, Ruth Everett, RN, MSN, Silvia Frade Eguaras, MS, and Silvia Fajardo-Hiriart, MD; University of Rochester, Golisano Children's Hospital at Strong (GCRC M01 RR44 and U10 HD40521): Dale L. Phelps, MD, Robert A. Sinkin, MD, Gary Myers, MD, Linda Reubens, RN, Diane Hust, RN, PNP, and Rosemary Jensen; University of Texas Southwestern Medical Center at Dallas, Parkland Health & Hospital System and Children's Medical Center Dallas (GCRC M01 RR633 and U10 HD40689): Abbot R. Laptook, MD, Walid A. Salhab, MD, Charles R. Rosenfeld, MD, Roy J. Heyne, MD, Jackie F. Hickman, RN, Gay Hensley, RN, Nancy A. Miller, RN, Janet Morgan, RN, Melissa Martin, RN, and James Allen, RRT; University of Texas Health Science Center at Houston, Medical School, and Children's Memorial Hermann Hospital (CCTS KL2 RR24149, CCTS UL1 RR24148, and U10 HD21373): Jon E. Tyson, MD, MPH, Kathleen Kennedy, MD, MPH, Brenda H. Morris, MD, Pamela J. Bradt, MD, MPH, Laura L. Whiteley, MD, Esther G. Akpa, RN, BSN, Patty A. Cluff, RN, Anna E. Lis, RN, BSN, Georgia E. McDavid, RN, Nora I. Alaniz, BS, and Patti L. Tate, RCP; Wake Forest University, Baptist Medical Center, Brenner Children's Hospital, and Forsyth Medical Center (GCRC M01 RR7122 and U10 HD40498): T. Michael O'Shea, MD, MPH, Robert G. Dillard, MD, Lisa Washburn, MD, Nancy Peters, RN, CCRP,

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We are indebted to our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

ABBREVIATIONS

BW	Birth weight
BPD	Bronchopulmonary dysplasia
DR	Delivery room
ELBW	Extremely low birth weight
ETTPPV	Endotracheal tube positive pressure ventilation
GA	Gestational age
IMV	Intermittent mandatory ventilation
IVH	Intraventricular hemorrhage
MDI	Mental developmental index
NCPAP	Nasal continuous positive airway pressure
NDI	Neurodevelopmental impairment
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
NIPPV	Nasal intermittent positive pressure ventilation
PEEP	Positive end expiratory pressure
PDA	Patent ductus arteriosus
PDI	Psychomotor developmental index
PIH	Pregnancy-induced hypertension
PIP	Peak inspiratory pressure
PVL	Periventricular leukomalacia
RDS	Respiratory distress syndrome
ROP	Retinopathy of prematurity
SNIPPV	Synchronized nasal intermittent positive pressure ventilation

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Figure 1.

Blood gas values of p_{CO_2} in infants in the SNIPPV vs. no-SNIPPV groups on postnatal days 1, 3, 7, 14, 21 and 28. Data expressed as mean $\pm$ SEM. p_{CO_2} values were significantly lower on days 7, 21, and 28 in the SNIPPV group (all $P \leq .01$).

Table 1

Patient Characteristics for Infants With BW of 500 to 1250 g

Variable	No SNIPPV (n=227)	SNIPPV (n=242)	p value
Maternal Race **			
White	84 (37)	93 (38)	.493
Black	46 (20)	55 (23)	
Hispanic	52 (23)	59 (24)	
Asian	17 (8)	17 (7)	
Other	28 (12)	18 (7)	
Male Gender **	124 (55)	131 (54)	0.915
Antenatal steroids **	208 (92)	228 (94)	0.274
Vaginal Delivery **	53 (23)	59 (24)	0.793
BW (g) *	964 ± 183	863 ± 198	<0.0001
GA (wks) *	27.9 ± 2.4	26.4 ± 1.7	<0.0001
Apgar ≤ 3 at 1 min **	33 (15)	64 (26)	0.002
Apgar ≤ 3 at 5 min **	7 (3)	10 (4)	0.544
DR Resuscitation **	222 (98)	239 (99)	0.492
RDS **	222 (98)	242 (100)	0.026
Surfactant therapy **	145/212 (68)	203/238 (85)	<0.0001
Systolic BP on admission (mmHg)	55.9 ± 12.5	51.7 ± 12.6	0.0003
Diastolic BP on admission (mmHg)	28.4 ± 11.1	27.9 ± 12.1	0.668

Abbreviations and definitions as in the text.

* Mean ± SD

** n, %.

Table 2

Neonatal Outcomes for infants with BW 500 to 1250 g

Variable	No SNIPPV (n=227)	SNIPPV (n= 242)	p value
ETTPPV **	227 (100)	242 (100)	.9999
Duration of ETTPPV (days) *	11.1 ± 17.8	20.5 ± 21.6	<0.0001
Duration of SNIPPV (days) *	0	8.7 ± 7.6	<0.0001
Duration of NCPAP (days) *	6.7 ± 7.7	8.7 ± 8.4	0.008
Duration of supplemental oxygen by nasal cannula (days) *	15.7 ± 18.1	16.3 ± 16.6	0.723
Duration of Supplemental Oxygen (days) *	31.2 ± 32.3	51.1 ± 32.7	<0.0001
Air leaks **	8 (4)	16 (7)	0.129
PDA **	91/226 (40)	106 (44)	0.439
IVH (≥ grade 3) **	13/225 (6)	17 (7)	0.583
PVL **	1/185 (0.5)	12/213 (6)	0.004
NEC or Spontaneous gastrointestinal perforations **	22 (10)	32 (13)	0.231
ROP (≥ stage 2) **	37/183 (20)	75/222 (34)	0.002
ROP requiring laser **	15/183 (8)	26/222 (12)	0.243
Early sepsis (≤72 hrs after birth) **	2 (0.9)	2 (0.8)	.9999
Late-onset sepsis (>72 hrs after birth) **	33 (15)	81 (34)	<0.0001
Postnatal steroids **	19 (8)	48 (20)	<0.001
Time to full feeds (days) *	18.2 ± 11.8	23.4 ± 14.1	<0.0001
Survival to discharge **	220 (97)	226 (93)	0.0771
Duration of hospitalization (days) *	72.1 ± 39.6	88.0 ± 33.9	<0.0001
Weight at discharge (g) *	2444 ± 592	2533 ± 604	0.148

Abbreviations and definitions as in the text.

* Mean ± SD

**
n, %

Table 3

BPD*/death and NDI*/Death Outcomes for Infants with BW 500 to 1250 g

Variable**	No SNIPPV (n=227)	SNIPPV (n= 242)	p value
BPD	50/202 (25)	78/226 (35)	0.028
BW (g): 500-750	18/27 (67)	36/84 (43)	0.031
751-1000	18/77 (23)	30/85 (35)	0.097
1001-1250	14/98 (14)	12/57 (21)	0.277
Death	7/227(3)	16/242 (7)	0.077
BW (g): 500-750	4/32 (12)	10/87 (11)	1.000
751-1000	2/85 (2)	3/89 (3)	1.000
1001-1250	1/110 (1)	3/66 (5)	0.149
BPD/Death	56/204 (27)	89/226 (39)	0.009
BW (g): 500-750	22/29 (76)	43/84 (51)	0.021
751-1000	19/77 (25)	32/85 (38)	0.076
1001-1250	15/98 (15)	14/57 (25)	0.154
NDI	25/83 (30)	37/130 (29)	0.795
BW (g): 500-750	12/22 (55)	24/62 (39)	0.197
751-1000	13/61 (21)	13/68 (19)	0.756
1001-1250	No Follow up		
NDI/Death	32/90(36)	53/146(36)	0.9077
BW (g): 500-750	16/26(61)	34/72(47)	0.2107
751-1000	15/63(24)	16/71(22)	0.8614
1001-1250	No Follow up		

Abbreviations used as in the text.

* As defined in the text

** n, %

Table 4A

Logistic Regression Analysis to Assess the Effect of SNIPPV vs. No SNIPPV on BPD.

Birth Weight	Odds Ratio	95% CI	p value
Overall 500-1250g	12.47	0.80-194.52	0.0719
500-750g	0.29	0.11-0.77	0.0123
751-1000g	1.17	0.49-2.82	0.7247
1001-1250g	0.52	0.16-1.71	0.2809

Table 4B

Logistic Regression Analysis to Assess the Effect of SNIPPV vs. No SNIPPV on BPD or Death.

Birth Weight	Odds Ratio	95% CI	p value
Overall 500-1250g	12.86	0.92-180.10	0.0579
500-750g	0.30	0.11-0.79	0.0146
751-1000g	1.40	0.60-3.30	0.4391
1001-1250g	0.64	0.22-1.91	0.4268

Table 5A

Logistic regression analysis to assess the effect of SNIPPV vs. No SNIPPV on NDI.

Birth Weight	Odds Ratio	95% CI	p value
Overall 500-1000g	0.52	0.25-1.07	0.0770
500-750g	0.29	0.09-0.94	0.0396
751-1000g	0.94	0.34-2.64	0.9129
1001-1250g	-	-	-

Table 5B

Logistic regression analysis to assess the effect of SNIPPV vs. No SNIPPV on NDI or Death.

Birth Weight	Odds Ratio	95% CI	p value
Overall 500-1000g	0.59	0.30-1.17	0.1312
500-750g	0.18	0.05-0.62	0.0061
751-1000g	0.73	0.29-1.83	0.5052
1001-1250g	-	-	-