Nasal Intermittent Mandatory Ventilation Versus Nasal Continuous Positive Airway Pressure for Respiratory Distress Syndrome: A Randomized, Controlled, Prospective Study

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Objective To evaluate whether nasal intermittent mandatory ventilation (NIMV) compared with nasal continuous positive airway pressure (NCPAP) would decrease the requirement for endotracheal ventilation in the treatment of respiratory distress syndrome (RDS) in preterm infants <35 weeks.

Study design Randomized, controlled, prospective, single-center study. Forty-one infants were randomized to NCPAP and 43 comparable infants to NIMV (birth weight 1533 ± 603 vs 1616 ± 494 g, gestational age 30.6 ± 3.0 vs 31.1 ± 2.3 weeks, $P = .5$, respectively).

Results Infants treated with NIMV and with NCPAP had comparable cardio-respiratory status at study entry. In the total cohort, infants treated initially with NIMV needed less endotracheal ventilation than infants treated with NCPAP (25% vs 49%, $P < .05$) with a similar trend in infants <1500 g; 31% vs 62%, $P = .06$). When controlling for weight and gestational age, NIMV was more successful in preventing endotracheal ventilation ($P < .05$). Infants treated with NIMV had a decreased incidence of bronchopulmonary dysplasia (BPD) compared with those treated with NCPAP (2% vs 17%, $P < .05$, in the total cohort and 5% vs 33%, $P < .05$, for infants <1500 g).

Conclusions NIMV compared with NCPAP decreased the requirement for endotracheal ventilation in premature infants with RDS. This was associated with a decreased incidence of BPD. *(J Pediatr 2007;150:521-6)*

Premature infants with respiratory distress syndrome (RDS) may require respiratory support. Because mechanical ventilation is associated with morbidity, mainly chronic lung disease (bronchopulmonary dysplasia [BPD]), the trend today is to minimize the use of mechanical ventilation. Nasal continuous positive airway pressure (NCPAP) was shown to be effective in treating infants with RDS and enables the avoidance of mechanical ventilation in a relatively large number of infants.[1-5] Individualized intubation strategy in delivery room was found to be safe.[6] Several centers administer surfactant, immediately extubate the infants and then use NCPAP,[7-9] to shorten the course of mechanical ventilation. The best option for treatment of RDS with respect to gestational age and RDS severity needs to be further investigated.[9] NCPAP may be used after extubation and thus decrease the incidence of reintubation.[10] NCPAP is currently a common practice for the treatment of premature infants with RDS.[9]

Nasal intermittent mandatory ventilation (NIMV) was shown to be more effective than NCPAP immediately after extubation in the treatment of RDS[11-16] and for apnea of prematurity.[17,18] The rationale behind the use of NIMV is the administration of "sighs" to the infant, thus opening microatelectasis and recruiting more ventilation units.[17] Moretti et al[11] found that application of synchronized NIMV was associated with increased tidal volume and minute volume as compared with NCPAP. Synchronized NIMV was associated with reduction in thoracoabdominal asynchrony, and thus stabilized the chest wall, and improved lung mechanics.[19] Synchronized NIMV may have advantages over NIMV. The positive pressure ventilator breath is delivered only after initiation of respiratory effort by the infants, when the glottis is likely to be open, or after an apneic interval. Synchronized NIMV also may decrease the work of breathing.[17] Although NIMV was more beneficial than NCPAP after extubating infants ventilated for RDS[11-16] and for apnea of prematurity,[17,18] the 2 methods have not been compared yet

BPD	Bronchopulmonary dysplasia	PDA	Patent ductus arteriosus
IVH	Intraventricular hemorrhage	PEEP	Positive end expiratory pressure
NCPAP	Nasal continuous positive airway pressure	RDS	Respiratory distress syndrome
NIMV	Nasal intermittent mandatory ventilation	VLBW	Very low birth weight

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for the initial treatment for RDS. Our study was designed to evaluate the hypothesis that NIMV would decrease the requirement for endotracheal ventilation when compared with NCPAP in the initial treatment of premature infants with RDS.

METHODS

Procedure

This was a prospective, open, controlled, single-center, clinical trial comparing the effectiveness of NCPAP and NIMV in the treatment of RDS. RDS was defined in the presence of clinical features and a positive chest x-ray film. The study was approved by the institutional review board in our center. All the parents signed informed consent before participating in the study. Endotracheal intubation was performed in the delivery room if the heart rate did not increase to >100 beats/min, or if the infant had insufficient spontaneous respiratory effort or if he showed marked and increasing dyspnea.[6] Exogenous surfactant (100 mg/kg, 1 to 2 doses as needed, Curosurf; Chiesi Farmaceutici, Parma, Italy) was given only as rescue therapy. Early nasal respiratory support (NCPAP or NIMV) was initiated in any spontaneous breathing premature infant showing signs of respiratory distress (tachypnea, grunting, flaring of nostrils, retractions).[2] If nasal respiratory support was indicated, the mode was randomized between NCPAP and NIMV. Crossover was not allowed between groups. The randomization was performed with a system of randomly prepared cards in sealed nontransparent envelopes containing NCPAP or NIMV group assignments. There were separate envelopes for infants weighing less than or 1500 g or more.

Subjects

Infants that were born in Bnai Zion Medical Center from September 2004 to April 2006 participated in the study. Inclusion criteria included gestational age between 24 to 34 and 6/7 weeks assessed by the obstetrical team from dating of last menstrual period or ultrasound, infants with RDS who needed nasal respiratory support, and informed consent. Infants were excluded if there was significant morbidity apart from RDS including cardiac disease (not including patent ductus arteriosus [PDA]), congenital malformation, or if they had cardiovascular or respiratory instability because of sepsis, anemia or severe intraventricular hemorrhage (IVH), parents refused consent, or the unavailability of a suitable ventilator.

Respiratory Management

Both modes of nasal respiratory support were delivered by the SLE 2000 (Specialized Laboratory Equipment Ltd., South Croydon, United Kingdom) via nasal prongs (INCA; Ackrad Labs, Berlin, Germany). NCPAP was set at 6 to 7 cm H_2O, and NIMV was set at a synchronized mode, rate of 12 to 30 breaths/min (according to $PaCO_2$), inspiratory time of 0.3 seconds, positive end expiratory pressure (PEEP) of 6 to 7 cm H_2O, and positive peak inspiratory pressure of 14 to 22 cm H_2O according to chest excursion and the infant's weight. FiO_2 was adjusted to keep oxygen saturation by pulse oximetry between 88% to 92%

Assessment of the Effectiveness of NIMV and NCPAP

The primary outcome measure was the percent of infants in whom nasal respiratory support failed and who needed endotracheal ventilation. The criteria for failure of nasal support were clinical deterioration (increased respiratory distress) accompanied by at least one of the following or worsening of the following: a pH <7.20 and PCO_2 >60 mm Hg, a PaO_2 <50 mm Hg, or arterial oxygen saturation by pulse-oximetry (SpO_2) < 88% on FiO_2 >50%, or recurrent significant apnea requiring repeated stimulation or bag-and-mask ventilation in spite of the use of methylxanthines or adequate nasal support (proper ventilatory settings and no technical problems).

Secondary outcome measures were as follow: clinical features during treatment (hourly): blood pressure, heart rate, respiratory rate, pulse oximetry saturation, and respiratory status prior to mechanical ventilation if needed according to arterial blood gas (PaO_2, PCO_2, pH), and "time to stop nasal support" (only oxygen or low nasal cannula flow, <1 L/min, and allowed when infants on nasal support were on FiO_2 <30%, had normal blood gases, and no respiratory distress or apnea. We also assessed neonatal clinical outcomes including incidence of intraventricular hemorrhage (IVH), duration of mechanical ventilation, incidence of BPD (oxygen at 36 weeks after conceptional age to keep saturation >92%), time until full feeds, and length of hospital stay.

Statistics

Sample size calculations for the primary outcome (need for endotracheal ventilation) were based on our rate of mechanical ventilation in previous years (55%-65%) and studies that have shown a decrease in the need for endotracheal ventilation when using NIMV as compared with NCPAP after mechanical ventilation for RDS.[12,13] We estimated that there would be a more than 80% chance of detecting a 50% difference between the groups (alpha = 0.05) when sample size (n) is 40 patients for each mode of treatment. Two-sample unpaired *t* tests (Student's *t*) were used for continuous variables with normal distribution and Wilcoxon rank-sum test was used where distribution was skewed. Differences for categorical variables were tested by use of χ^2 analysis. For the primary outcome measure (need for endotracheal ventilation) we used a multivariate regression model to correct for birth weight and gestational age (Minitab, Version 12.23, State College, Pa). For all tests the level of significance was set at $P < .05$. Data are presented as mean ± standard deviation or median (range).

RESULTS

Of 232 infants born <35 weeks during the study period, 10 infants were excluded (1 infant because of hydrops

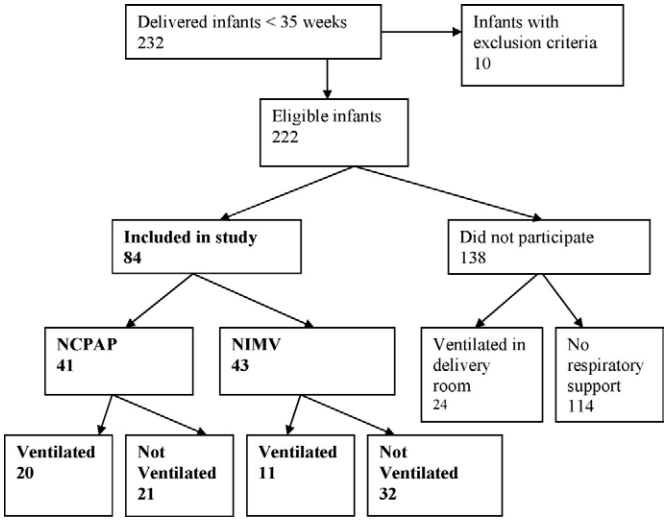

Figure 1. Infant enrollment into study.

fetalis, 1 infant because of esophageal atresia and tracheoesophageal fistula, 1 infant because of unstable clinical condition caused by sepsis and disseminated intravascular coagulation, 3 infants because of no available respirator with synchronized NIMV, 2 infants because of lack of parental consent, and 2 infants who started on nasal support without prior randomization). Of the eligible infants, 24 infants underwent ventilation within 15 minutes after delivery, and 114 infants did not need respiratory support or received only oxygen treatment. Eighty-four infants were randomized to the study; 41 infants were assigned to NCPAP and 43 infants to NIMV. Two infants in the NCPAP group were switched by the medical team to NIMV in violation of the study protocol but were included in the intention-to-treat analysis according to their primary assignment (Figure 1).

The NCPAP and the NIMV groups had comparable demographic characteristics (Table I). Although there was a significant statistical difference in the 5-minute Apgar score in the infants <1500 g, this difference does not seem to be of clinical significance. The cardiorespiratory status before study entry was comparable between the infants treated with NCPAP and NIMV (Table II). Grunting or retractions occurred in 35/41 infants placed on NCPAP and in 40/43 placed on NIMV ($P = .30$). There was no significant difference in the number of infants placed on nasal support within the first hour of life between the 2 groups (32/41 and 29/43, $P = .46$ in total cohort, and 20/21 and 16/19, $P = .33$, in infants <1500 g, respectively).

Failure of nasal support (need for endotracheal ventilation) was higher after initial treatment with NCPAP compared with NIMV in the total cohort ($P < .05$), with a similar trend not reaching statistical significance in very low birth weight (VLBW) infants ($P = .06$) (Table III, Figure 2; available at www.jpeds.com). One of the 2 infants switched from NCPAP to NIMV was ventilated. Even when excluding these 2 infants from analysis for the primary outcome of failure of nasal support, the results were similar, $P < .05$ for

Table I. Demographic data

Total cohort	NCPAP (n = 41)	NIMV (n = 43)	P value
Birth weight (g)	1533 ± 603	1616 ± 494	.49
Gestational age (weeks)	30.6 ± 3.0	31.1 ± 2.3	.55
Male/female	25/16	28/15	.82
Born by cesarean section (%)	76%	69%	.81
High-risk pregnancy*	25%	25%	1.00
Apgar score at 1 minute	8 (1-10)	8 (4-10)	.22
Apgar score at 5 minutes	9 (2-10)	9 (7-10)	.11
Prenatal steroids	70%	72%	1.00
Methylxanthine usage	39%	37%	1.00
Infants <1500 g	**NCPAP (n = 21)**	**NIMV (n = 19)**	**P value**
Birth weight (g)	1039 ± 238	1155 ± 193	.10
Gestational age (weeks)	28.2 ± 1.9	29.0 ± 1.4	.13
Male/female	10/11	12/7	.36
Born by cesarean section (%)	90%	79%	.39
High-risk pregnancy*	33%	31%	1.00
Apgar score at 1 minute	8 (1-10)	9 (6-10)	.20
Apgar score at 5 minutes	9 (7-10)	10 (8-10)	.01
Prenatal steroids	81%	84%	1.00
Methylxanthine usage	57%	68%	.52

*High-risk pregnancy was defined as preeclampsia, maternal hypertension, and gestational diabetes.

the total cohort and $P = .05$ for the VLBW infants. The same findings were found when analyzing the need for mechanical ventilation within the first 72 hours from birth, which may represent mainly RDS morbidity. When checking success or failure for the primary outcome (need for endotracheal ventilation) in the total cohort, both birth weight and gestational age were significant ($P < .01$, and $P < .05$, respectively). To correct for the effects of birth weight and gestational age, we performed a multivariate regression analysis, and the nasal mode of support (NIMV or NCPAP) remained a significant factor for failure or success ($P < .05$). We did not find a significant difference between NCPAP and NIMV in the reasons for failure in the total cohort: oxygenation, 10 vs 6 infants; ventilation, 4 vs 3 infants; apnea, 6 vs 3 infants; and in VLBW infants: oxygenation, 5 versus 4 infants; ventilation, 2 versus 2 infants; and apnea, 6 versus 2 infants, respectively. There could be more than 1 reason for an infant to fail.

As expected, mean airway pressure on NIMV was significantly higher than on NCPAP (Table III). On the other hand, the PEEP was statistically lower on NIMV in infants <1500 g (Table III). Peak inspiratory pressure on NIMV was 19.5 ± 2.4, and 18.8 ± 1.8 cm H_2O, and the NIMV rate was 22.2 ± 5.0 and 22.7 ± 5.5 breaths/min, for the total cohort and for VLBW infants, respectively. Time to "stop nasal support" (only oxygen or low nasal flow) in case of success, or time to mechanical ventilation in case of failure were comparable between the 2 treatment groups (Table III).

While treated with nasal support, there was no difference between the 2 treatment groups in the clinical variables (mean blood pressure, heart rate, respiratory rate), oxygen-

Table II. Cardiorespiratory status before study entry

Total cohort	NCPAP (n = 41)	NIMV (n = 43)	P value
FiO_2	0.37 ± 0.17	0.32 ± 0.14	.09
SpO_2 (%)	86 ± 16	91 ± 9	.12
PaO_2 (mm Hg)*	78 ± 24 (n = 15)	71 ± 22 (n = 7)	.55
PcO_2 (mm Hg)	52 ± 7	51 ± 7	.80
pH	7.24 ± 0.05	7.22 ± 0.07	.43
Respiratory rate (breaths/min)	44 ± 9	44 ± 13	.52
Heart rate (beats/min)	148 ± 12	151 ± 14	.33
Mean BP (mm Hg)	37.7 ± 7.1	37.1 ± 7.4	.71
Start of nasal support (min)	4 (3-3240)	17 (3-2940)	.16
Infants <1500 g	**NCPAP (n = 21)**	**NIMV (n = 19)**	**P value**
FiO_2	0.37 ± 0.16	0.33 ± 0.17	.41
SpO_2 (%)	89 ± 13	90 ± 7	.78
PaO_2 (mm Hg)*	72 ± 20 (n = 13)	67 ± 22 (n = 5)	.61
PcO_2 (mm Hg)	51 ± 7	47 ± 5	.16
pH	7.25 ± 0.05	7.26 ± 0.02	.37
Respiratory rate (breaths/min)	44 ± 9	45 ± 14	.60
Heart rate (beats/min)	146 ± 11	151 ± 15	.26
Mean BP (mm Hg)	36.4 ± 5.9	35.3 ± 7.5	.63
Start of nasal support (min)	4 (3-140)	10 (3-1260)	.26

BP, blood pressure.
*When arterial blood gas was available (number of infants).

Table III. Nasal respiratory support and respiratory short-term outcome

Total cohort	NCPAP (n = 41)	NIMV (n = 43)	P value
Initial MAP (cm H_2O)	6.2 ± 0.8	7.6 ± 1.4	<.0001
Initial PEEP or CPAP (cm H_2O)	6.2 ± 0.78	5.9 ± 0.99	.08
Respiratory rate (breaths/min)	43 ± 9	45 ± 14	.64
Time to stop nasal support (d)	4.9 ± 5.2	4.9 ± 4.3	.97
Failed nasal support (%)	49	25	.04
Time to MV (h)	32 ± 33	44 ± 62	.93
Initial FiO_2 on MV	0.49 ± 0.26	0.55 ± 0.27	.53
Initial MAP on MV	7.8 ± 1.2	8.1 ± 1.7	.47
Infants <1500 g	**NCPAP (n = 21)**	**NIMV (n = 19)**	**P value**
Initial MAP (cm H_2O)	6.2 ± 0.8	7.6 ± 1.6	.001
Initial PEEP or CPAP (cm H_2O)	6.2 ± 0.8	5.6 ± 0.7	.01
Respiratory rate (breaths/min)	43 ± 2	47 ± 4	.94
Time to stop nasal support (d)	9.0 ± 6.2	7.4 ± 4.9	.52
Failed nasal support (%)	62	31	.06
Time to MV (h)	28 ± 38	63 ± 79	.17
Initial FiO_2 on MV	0.39 ± 0.21	0.66 ± 0.31	.04
Initial MAP on MV	7.6 ± 1.2	9.0 ± 1.0	.03

MAP, mean airway pressure; *MV*, mechanical ventilation.

Table IV. Clinical outcome

Total cohort	NCPAP (n=41)	NIMV (n=43)	P value
Duration of MV (d)	13.2 ± 15.8	10.2 ± 23.8	.67
BPD	17%	2%	.03
IVH	8	8	1.00
Time to full feeds (d)	11 ± 8	9 ± 4	.75
Length of stay (d)	53 ± 39	39 ± 26	.20
Infants <1500 g	**NCPAP (n = 21)**	**NIMV (n = 19)**	**P value**
Duration of MV (d)	18.3 ± 17.7	16.8 ± 13.0	.08
BPD	33%	5%	.04
IVH	7	6	1.00
Time to full feeds (d)	15 ± 10	11 ± 3	.54
Length of stay (d)	81 ± 36	63 ± 23	.16

MV, mechanical ventilation; *BPD*, bronchopulmonary dysplasia; *IVH*, intraventricular hemorrhage.

ation (SpO_2 and PaO_2), and ventilation (PcO_2 and pH) during the 6 hours before mechanical ventilation in case of failure in the total cohort and in infants <1500 g (data not shown). Infants <1500 g in whom NIMV failed required higher initial respiratory support on mechanical ventilation (higher mean airway pressure and FiO_2 [$P < .05$]; Table III). However, there was no difference in the duration of mechanical ventilation between infants who failed NCPAP or NIMV (Table IV). Furthermore, the duration of mechanical ventilation tended to be shorter in the NIMV group of infants <1500 g ($P = .08$). The incidence of BPD was lower in infants treated with NIMV in the total cohort and in the group of VLBW infants ($P < .05$) (Table IV, Fig 2). One of the 2 infants switched from NCPAP to NIMV who was <1500 g had BPD. If these 2 infants are excluded from the analysis, the BPD rate decreased with NIMV in the total cohort ($P < .05$), and in the VLBW group this decrease did not reach statistical significance ($P = .09$).

Clinical outcomes during the neonatal period were similar in the 2 treatment groups (Table IV). Two infants had pneumothorax, 1 in the NCPAP group >1500 g and 1 in the NIMV group <1500 g; both occurred on mechanical ventilation. Two twin-infants had NEC in the group of infants treated with NIMV. No infant had gastric perforation on nasal support in either group during the study period. One infant in the NCPAP group <1500 g had periventricular leukomalacia, and the rate of IVH was comparable in the 2 treatment groups (in NCPAP group: 5 grade I-II, 2 grade

III-IV in infants <1500 g, and 1 grade I-II in an infant >1500 g that resolved in repeat ultrasound, and in the NIMV group: 6 grade I-II and 2 grade III-IV, out of which 2 with grade I-II in infants >1500 g, that resolved in repeat head ultrasound scanning).

DISCUSSION

We found that NIMV was more successful than NCPAP as the initial treatment of RDS in premature infants (<35 weeks) by reducing the rate of endotracheal ventilation. This was associated with a reduced incidence of BPD.

To our knowledge, there are no previous published studies that assessed whether NIMV or NCPAP is preferred in the initial treatment of RDS. However, a few studies have found that NIMV was superior to NCPAP post extubation, after mechanical ventilation and surfactant treatment, for RDS and for apnea of prematurity.[11-18] The same advantages of NIMV in these situations may be the cause for its beneficial effect in the initial treatment of RDS found in our study.[11,17,19]

Failure of nasal respiratory support was significantly associated with lower birth-weight. Other studies also correlated failure of nasal support with birth-weight or gestational age.[20,21] The rate of failure of nasal support varied in previous studies,[2,6,22] and our study failure rate is in accordance with the literature. The use of and the experience of medical teams with nasal support is increasing in recent years. Our study represents our single center experience.

We found that the level of support was comparable in the 2 modes of treatment (expressed by similar cardiorespiratory variables, as well as blood gases while being supported by NCPAP and NIMV). Previous studies also found similar P_{CO_2} levels when the 2 methods were used for apnea of prematurity.[17,18] In contrast to our study, Moretti et al[11] found a lower TcP_{CO_2} and respiratory rate on synchronized NIMV compared with NCPAP. As could be expected, mean airway pressure on NIMV was significantly higher than on NCPAP. On the other hand, PEEP that was set at around 6 cm H_2O initially was statistically significantly lower on NIMV in the VLBW group. This difference seems to be of no clinical significance. The difference could result from a compensatory reaction of the medical team to the needs of the infants in achieving similar targeted respiratory variables according to the clinical routines, probably because of the lower mean airway pressure on NCPAP. Furthermore, the reasons for failure of nasal support were also comparable.

While others "allowed" a trial of nasal support instead of immediate intubation in small premature infants,[6] our study demonstrates comparable safety of both methods of nasal support. It is not clear on the basis of the clinical variables and blood gases and the physiologic rationale why VLBW infants treated with NIMV required initially higher ventilatory settings (MAP, Fi_{O_2}), but it was reassuring that there was no significant difference in the length of mechanical ventilation. Furthermore, the incidence of BPD was lower in infants treated initially with NIMV. This may result from the lower rate of mechanical ventilation and its associated volutrauma/barotrauma in this group. A trend toward lower rate of BPD in NIMV compared with NCPAP was reported in studies comparing the modes in the postextubation period.[12,13,15]

Rates of IVH, or the length of hospital stay in the NCPAP and NIMV groups were comparable. There was a concern that NIMV might cause more gastrointestinal complications because of gastric distention leading to cessation of feeds or perforation.[18,23] In our study there were no gastrointestinal complications, and time to full feeds was similar in the 2 methods, in accordance with other studies.[12-15] Two twin-infants had NEC in the NIMV group, but the incidence of NEC was not statistically different compared with the NCPAP group.

We have used the synchronized intermittent mandatory ventilation mode for NIMV with maximal sensitivity with the ventilator (SLE 2000), and most of the time we did not get an alarm of not sensing infant's breath. However, we can not verify that the infants got pressure-synchronized ventilation all the time because the system was open and we used the pressure sensor of the ventilator. Thus we used the term *NIMV* to describe our mode of nasal support. Pressure-triggering ventilation is less effective compared with airflow-triggering in ventilated premature infants.[24] For synchronization of nasal support others have used an abdominal capsule.[12,13,16] Nasal intermittent positive pressure ventilation and NIMV are used interchangeably in the literature, and we took the common definition from Davis et al[10] that these are methods of augmenting NCPAP by delivering ventilator breaths via nasal prongs. We did not use the NIMV mode as an assist control, where the triggering might be of greater importance. Effectiveness of pressure-triggered ventilation and synchronization of intermittent mandatory ventilation were not evaluated previously in nasal support. Yet, whether synchronized or not, NIMV seems to be more effective than NCPAP. Future studies will need to compare the effectiveness of modes of synchronization via nasal support, and whether synchronization has an advantage over nonsynchronized ventilation delivered by nasal support in premature infants with RDS.

Our study limitations are that the mode of support assignment could not be blinded to the medical team. This could possibly explain the higher initial ventilator settings after NIMV in cases of nasal support failure in VLBW infants if we were unconsciously using a lower threshold to fail a patient in the control group. We used objective failure criteria and management protocols to reduce the possibility of such a bias. This was a clinical study that allowed the medical team to make clinical adjustments to assure that no infant would be compromised by the treatment mode. It is possible that the use of a strict PEEP of 6 cm H_2O in both groups would have even strengthened the benefits of NIMV found in our study. We had only a small number of infants <1500 g, and these infants should be the target population for further studies. Our results in the VLBW infants regarding the incidence of

endotracheal ventilation and BPD in the NIMV group should be taken with caution, because our study does not have statistical power for these outcome measures in this group of infants. Furthermore, the number of infants <1000 g in our cohort was small. The safety conclusions from our study should also be taken with caution, because our study did not have sufficient statistical power to detect differences in relatively infrequent complications such as NEC and IVH.

We conclude that NIMV was more successful than NCPAP in preventing endotracheal ventilation in the initial treatment of premature infants with RDS. This was associated with decreased incidence of BPD in infants treated with NIMV. Our study provides the basis for further, larger trials of this intervention before it can be concluded that NIMV is safe and is the preferred mode of nasal support in premature infants with RDS.

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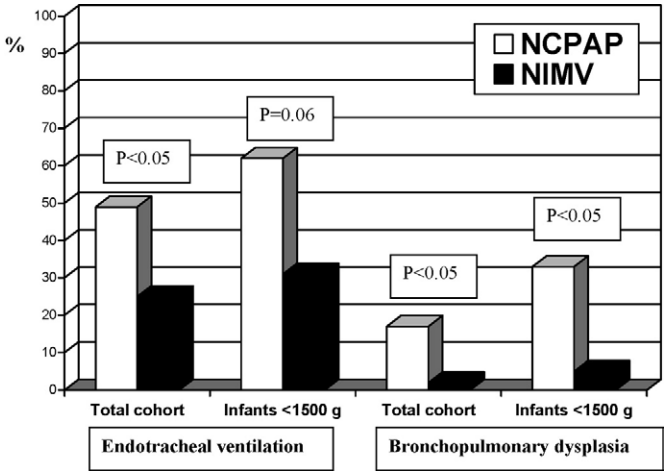

Figure 2. Mechanical ventilation and bronchopulmonary dysplasia (BPD) in infants treated with NIMV and NCPAP.