

Partial Pressure of Carbon Dioxide in Extremely Low Birth Weight Infants Supported by Nasal Prongs Continuous Positive Airway Pressure

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ABSTRACT. *Objective.* Traditionally, delivery room management of extremely low birth weight (ELBW) infants consisted of immediate intubation and mechanical ventilation. There have been recent reports of success using nasal prongs continuous positive airway pressure (NCPAP) in this population. Data on the partial pressure of carbon dioxide (P_{CO_2}) in spontaneously breathing ELBW infants is very limited. The objective of this study was to determine the trend of the average P_{CO_2} in the spontaneously breathing ELBW infants, while on NCPAP, during the first week of life and to determine whether a brief period of mechanical ventilation affects the P_{CO_2} levels after extubation.

Methods. This is a retrospective cohort study of infants who had birth weights <1000 g and were admitted to the neonatal intensive care unit at our institution. These ELBW infants were divided into groups on the basis of whether they were never intubated (group 1) or were intubated for <48 hours (group 2). Average daily P_{CO_2} levels while on NCPAP were compared between the 2 groups. Minimum and maximum P_{CO_2} levels were also compared with a third group of infants (group 3), who were intubated for >48 hours and treated mainly with mechanical ventilation during the first week of life.

Results. Sixty-two ELBW infants were included in this study: 24 infants in group 1, 19 infants in group 2, and 19 infants in group 3. There was no significant difference between the average P_{CO_2} levels of group 1 and group 2 during the first week of life. The daily P_{CO_2} level during the first week of life for infants who were breathing spontaneously on NCPAP had a mean value of 39.73 ± 1.78 mm Hg. There was no difference between the daily average minimum P_{CO_2} levels among the 3 groups. Group 3, however, had significantly higher maximum P_{CO_2} levels compared with the first 2 groups during days 2 through 7 of life.

Conclusions. Daily average P_{CO_2} levels in the spontaneously breathing ELBW infants during the first week of life remains at approximately 40 mm Hg. These levels seem to be unaffected by an initial brief period of mechanical ventilation. Infants who are treated with longer periods of mechanical ventilation have higher daily maximum P_{CO_2} levels during the first week of life. Additional studies are required to detect neurodevelopmental outcomes of these 3 groups. *Pediatrics* 2003;112:e208–e211.

URL: <http://www.pediatrics.org/cgi/content/full/112/3/e208>; nasal CPAP, extremely low birth weight infants, carbon dioxide, chronic lung disease.

ABBREVIATIONS. ELBW, extremely low birth weight; NCPAP, nasal prongs continuous airway pressure; CLD, chronic lung disease; P_{CO_2} , partial pressure of carbon dioxide; NICU, neonatal intensive care unit; IVH, intraventricular hemorrhage; CO_2 , carbon dioxide, RDS, respiratory distress syndrome.

Treatment of extremely low birth weight (ELBW) infants continues to change in the postsurfactant era. Recently, there have been several reports of success using an immediate strategy toward nasal prongs continuous airway pressure (NCPAP) support in place of intubation and mechanical ventilation in the delivery room.^{1–4} The use of NCPAP has brought much excitement because there have been many reports linking the barotrauma and high fraction of inspired oxygen levels associated with mechanical ventilation to the risk for chronic lung disease (CLD).^{4–7}

There have been many reports and significant controversy about the role of partial pressure of carbon dioxide (P_{CO_2}) in the respiratory management of the ELBW infant.⁸ However, without a clear definition of “normocapnia” in this population, these studies are difficult to interpret. It would be of interest to know where these ELBW infants would keep their P_{CO_2} if they were given the chance to breathe spontaneously. It would also be helpful to determine whether ELBW infants experience hypercapnia without the support offered by mechanical ventilation.

Previously, examining the P_{CO_2} in spontaneously breathing ELBW infants has been difficult because the majority of ELBW infants were mechanically ventilated beyond the peripartum period. The aim of this study was to determine the average P_{CO_2} level of the spontaneously breathing ELBW infant during the first week of life and to determine whether brief and more extended periods of mechanical ventilation affect these levels.

METHODS

Subjects

All infants who were born at our institution and weighing <1000 g at birth and were admitted to the neonatal intensive care unit (NICU) between 1997 and 2001 were identified retrospectively. Infants were excluded when they were transferred to another hospital or died during the first week of life. They were divided into groups on the basis of the length of intubation and

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TABLE 1. Demographic Data

	Group 1 (n = 24)	Group 2 (n = 19)	Group 3 (n = 19)	P Value
Birth weight	782 ± 151	766 ± 131	742 ± 140	.56
Gestational age	26.8 ± 1.7	26.2 ± 1.2	25.7 ± 1.6	.34
Gender (% male)	20.8	26.3	31.6	.72*
Multiple gestation	37.5%	15.8%	25%	.33*
Maternal infection	30.4%	47.4%	31.6%	.50*
Apgar <4 at 1 min	8.7%	36.8%	47.4%	.008*

* Fisher exact test.

TABLE 2. Daily Average CO₂ Values (± Standard Deviation)

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Group 1	41.56 ± 5.88	37.55 ± 6.53	37.92 ± 7.65	38.04 ± 6.28	38.64 ± 5.69	40.75 ± 5.61	40.29 ± 5.52
Group 2	43.25 ± 10.76	37.79 ± 6.61	39.52 ± 6.47	38.94 ± 5.91	39.37 ± 6.70	40.13 ± 6.36	42.47 ± 6.36
P value	0.80	0.97	0.49	0.74	0.77	0.89	0.39

mechanical ventilation in the first week of life: never intubated (group 1), intubated for <48 hours (group 2), or intubated for >48 hours (group 3).

Respiratory Management

Our unit practice consists of infants who are initially dried, stimulated, and assessed in the delivery room. ELBW infants with spontaneous respiratory efforts are offered distending pressure using facial CPAP with a Carden valve to maintain a continuous pressure of 5 cm of water. ELBW infants are then immediately transported to the NICU. A water-seal CPAP unit⁹ is always ready in the NICU. Infants are immediately placed on NCPAP using the nasal prongs of Hudson Respiratory Care (Temecula, CA). With signs of respiratory compromise, such as severe retraction, frequent apnea, or increased oxygen requirement (fraction of inspired oxygen >60%), the infant will be intubated for mechanical ventilation. In the delivery room, ELBW infants who do not breathe spontaneously are immediately intubated and supported with conventional mechanical ventilators. Intratracheal surfactant therapy is offered on an individual rescue basis depending on the clinical and radiographic findings.

Measurement

All Pco₂ values during the first week of life were compiled from the medical records for each infant in group 1 and group 2. Our practice is to maintain an umbilical artery catheter in place during the first 3 days of life. After this period, capillary blood gases are then collected as indicated. A peripheral arterial line is placed only when additional intensive monitoring is needed. Average daily Pco₂ levels of group 1 were sequentially compared with those of group 2, who had been weaned to NCPAP at that time. Daily minimum and maximum Pco₂ values for days 1 through 7 of life were collected for group 3. These values were compared among the 3 groups.

Data Analysis

Data were analyzed using The SAS System Version 6.12.¹⁰ The χ^2 test was used to compare differences in sex distribution of the 3 groups. The Kruskal-Wallis test (χ^2 approximation) was used to determine statistically significant differences between the mean birth weight, mean gestational age, and Pco₂ levels of the test groups. The Fisher exact test was used to compare the percentages of ELBW infants with multiple gestation, maternal infection, and Apgar score <4 in the 3 groups.

RESULTS

Seventy-six neonates who weighed <1000 g were sequentially born at our institution and admitted to the NICU during the study period. Five infants died, and 2 were transferred to the Children’s Hospital for surgical reasons during the first week of life. Of the

surviving 69 infants, 62 medical records were available for review.

Twenty-four infants were never intubated and were treated with NCPAP alone (group 1). Nineteen infants were initially intubated and ventilated but weaned to NCPAP in <48 hours of life (group 2). Another 19 infants were treated mainly with mechanical ventilation during the first week of life (group 3). The demographic and perinatal data of this study population are included in Table 1.

There was no significant difference between the daily average Pco₂ levels of group 1 and group 2 during the first week of life (Table 2). For both groups, average Pco₂ levels were highest on the first day of life (group 1: 41.56 ± 5.88 mm Hg; group 2: 43.25 ± 10.76 mm Hg) and lowest on the second day of life (group 1: 37.55 ± 6.53 mm Hg; group 2: 37.79 ± 6.61 mm Hg). Overall mean Pco₂ level during the first week of life for infants who were breathing spontaneously on NCPAP was 39.73 ± 1.78 mm Hg. The trend of daily Pco₂ averages for both groups is shown in Fig 1. Average daily pH values for the infants in group 1 ranged from 7.30 to 7.35 (Table 3).

There was no difference between the daily average minimum Pco₂ levels among the 3 groups (Fig 2). The infants who were treated mainly with mechanical ventilation, however, had significantly higher maximum Pco₂ levels compared with the other 2

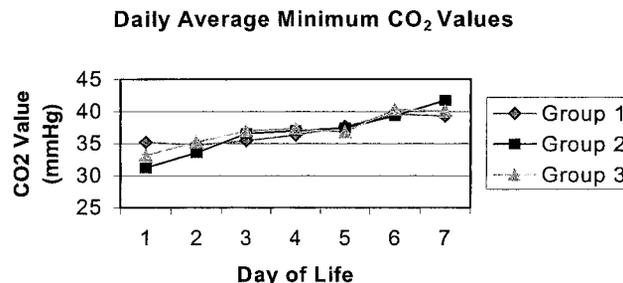


Fig 1. Average daily Pco₂ during the first week of life are shown as a function of days of life (DOL) in infants who were treated with NCPAP (group 1) and mechanically ventilated and weaned to NCPAP within the first 48 hours of life (group 2). The Pco₂ averages near 40 mm Hg and are similar for both groups.

TABLE 3. Daily Average pH Values (\pm Standard Deviation)

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
pH	7.35 \pm 0.06	7.35 \pm 0.06	7.32 \pm 0.05	7.32 \pm 0.03	7.31 \pm 0.03	7.30 \pm 0.04	7.31 \pm 0.04
Range	7.24–7.46	7.24–7.46	7.23–7.42	7.27–7.41	7.26–7.37	7.24–7.36	7.25–7.38

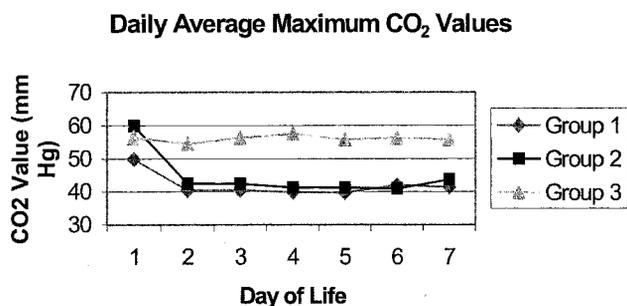


Fig 2. Average daily minimum Pco₂ for groups 1 and 2 and in infants who were mechanically ventilated for >48 hours (group 3), as a function of DOL. There is no significant difference among the 3 groups.

groups during days 2 through 7 of life ($P < .05$). This difference was not found on the first day of life ($P = .27$). Group 3 had daily average maximum Pco₂ levels ranging between 54.51 and 57.52 mm Hg (Fig 3).

None of the infants in group 1 or 2 had grade 3 or higher intraventricular hemorrhage (IVH) or stage 3 or higher retinopathy of prematurity. In group 3, 3 infants developed IVH grade 3 or 4 ($P = .05$) and 2 infants developed retinopathy of prematurity stage 3 ($P = .18$). There was a trend for a decreased incidence of BPD in group 1 (16.7%) compared with group 2 (36.8%) and group 3 (42.1%) that did not reach significance ($P = .14$). A total of 5 infants died; 3 from group 1 (necrotizing enterocolitis, sepsis and airway obstruction) and 2 from group 3 (pulmonary hemorrhage and hyaline membrane disease).

DISCUSSION

ELBW infants who were supported with early NCPAP could maintain Pco₂ levels that averaged approximately 40 mm Hg. ELBW infants who were treated solely with NCPAP did not show any significant difference in their Pco₂ levels when compared with those who were initially ventilated and then weaned to NCPAP at a later time.

Pco₂ of blood is determined by carbon dioxide

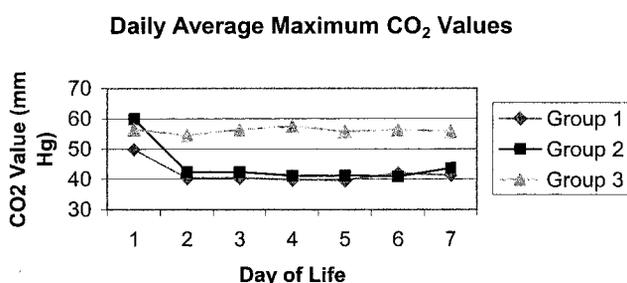


Fig 3. Average daily maximum Pco₂ levels for all 3 groups are shown as a function of age in days (DOL). The maximum Pco₂ in group 3 is significantly higher than in groups 1 and 2 on days 2 through 7 of life.

production and alveolar ventilation, and the latter is affected by minute ventilation, dead space volume, and blood flow. The normal reference range for Pco₂ levels in children has been generally accepted to be between 33 and 45 mm Hg.¹¹ Healthy term infants between 2 weeks and 9 months of life have been reported to have Pco₂ levels of 40.5 \pm 3 kPa (5.4 \pm 0.4 kPa).¹² This information has been adapted to the treatment of the ELBW infant; however, no data are available to determine whether these respiratory mechanics are applicable to this population.

In a previous report by Lindner et al,³ initial Pco₂ in ELBW infants who were supported with NCPAP was higher when compared with those who were intubated and mechanically ventilated in the delivery room (54 \pm 13 vs 42 \pm 17 mm Hg, respectively). These levels did decrease within the first day of life to 48 mm Hg (range: 32–57 mm Hg) and were maintained during the first week at 47 mm Hg (range: 39–49 mm Hg). Their management practice was different from ours. ELBW infants in their study were initially given distending pressure of 20 cm of water via a mechanical ventilator through a nasal pharyngeal tube before CPAP initiation. In addition, we use a water-seal CPAP device in place of ventilator-delivered CPAP. Finally, we have a strict policy with airway care requiring appropriate positioning and airway suctioning every 2 to 3 hours.

Extreme levels of Pco₂ in the ELBW infant can have adverse effects on neonates. Hypocapnia has been reported to increase the risk for CLD^{7,8,13,14} and has been associated with poor neurologic outcomes, including periventricular leukomalacia,^{8,15–17} cerebral palsy, and neurodevelopmental delay.^{8,15} Severe hypercapnia, however, has likewise been linked to adverse outcomes such as IVH.^{8,18,19}

We found that ELBW infants who were maintained on NCPAP did not develop carbon dioxide (CO₂) retention, with results similar to those seen with intermittent mechanical ventilation (group 3). Many of these infants, when allowed to breathe independently, settled at a Pco₂ level in the low 30s during the first few days of life. This low Pco₂ level does not seem to be a compensatory response to significant metabolic acidosis. This may be of relevance because CPAP has been associated with a decreased incidence of IVH.^{2,3} IVH in the premature infant is attributed to the lack of cerebral autoregulation.¹⁸ We speculate that low Pco₂ levels in this subgroup may serve as a protective measure to compensate for this lack of autoregulation. Of note, none of the infants in groups 1 and 2 had any grade 3 or 4 IVH or periventricular leukomalacia.

Our finding that prolonged mechanical ventilation during the first week after birth is associated with higher daily maximum Pco₂ levels can be attributed to increased severity of respiratory distress syn-

drome (RDS) and could be an early harbinger of ongoing lung disease. This more severe RDS in the mechanical ventilation group may be reflected in the lower Apgar scores of this group. Another important perinatal factor is maternal glucocorticoid use, for which data were not available for this study. However, in other aspects that may suggest a more severe degree of illness in the ventilation group (gestational age, birth weight, percentage of boys), we did not find significant differences from the other 2 groups. In fact, all 3 groups had similar numbers of ELBW infants with birth weight between 500 and 750 g (10 of 24 for group 1, 9 of 19 for group 2, and 10 of 19 for group 3). Even so, it came as no surprise that patients who require prolonged mechanical ventilation have some form of intrinsic lung disease with hypercapnia. It is not the aim of this study to compare P_{CO_2} levels of these infants with those on NCPAP. Rather, these data show that ELBW infants with moderate RDS can be supported adequately with NCPAP and not show evidence of respiratory insufficiency or P_{CO_2} retention.

The clinical practice to allow P_{CO_2} to rise to ameliorate the incidence of CLD in the premature infant has been revisited recently.^{20,21} There is no consensus on acceptable P_{CO_2} levels. Instead, one may look at P_{CO_2} levels in neonates who are breathing spontaneously without distress. The parameters seen in these spontaneously breathing infants can help us to arrive at optimal settings for infants who require mechanical ventilation.

The results of this study show that a short period of mechanical ventilation does not affect the P_{CO_2} level in the ELBW infant after extubation. However, this comparison was limited only to the first week of life, and no additional information can be determined regarding other effects of this intervention. Surprising, ELBW infants who are intubated for brief period (<24 hours) experience a significantly higher incidence of CLD compared with ELBW infants on NCPAP.²² Although infants who are treated for the most part with mechanical ventilation during the first week of life seem to have a higher daily maximum P_{CO_2} , any clinical impairment associated with such hypercapnia remain unknown.

CONCLUSIONS

During the first week of life, the spontaneously breathing ELBW infant has an average daily P_{CO_2} near 40 mm Hg. Those levels of P_{CO_2} seem to be unaffected by any brief time on mechanical ventilation. Infants who are mechanically ventilated for more extensive periods of time (>48 hours) have an elevated maximum P_{CO_2} during the first week of life. Additional studies are required to detect possible adverse neurodevelopmental and pulmonary changes associated with increased levels of P_{CO_2} .

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