Eur J Pediatr (2003) 162: 227–229
DOI 10.1007/s00431-002-1131-5

ORIGINAL PAPER

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Minimal handling and bronchopulmonary dysplasia in extremely low-birth-weight infants

Received: 29 August 2002 / Accepted: 30 October 2002 / Published online: 7 February 2003

Abstract Over the last 16 years a minitouch regime, i.e., nasal continuous positive airway pressure (n-CPAP) and/or nasal intermittent positive pressure ventilation (n-IPPV), together with a minimal intubation policy has been routinely used for the treatment of respiratory distress syndrome (RDS) in preterm infants. Only 1.39 (1 out of 72) of the extremely low-birth-weight babies admitted to our Neonatal Intensive Care Unit (NICU) and surviving for at least 36 weeks' postconceptional age developed bronchopulmonary dysplasia at 36 weeks (BPD 36-wk). The BPD-36wk incidence observed in our population is significantly lower than expected (30%) from the literature ($p = 0.000002$). *Conclusion*: Our experience supports the effectiveness of the minitouch regime as a way to ventilate premature babies, reducing BPD risk.

Keywords Nasal continuous positive airway pressure · Nasal intermittent positive pressure ventilation · Minimal handling · Bronchopulmonary dysplasia · Extremely low birth weight

Introduction

Bronchopulmonary dysplasia (BPD) is commonly defined as oxygen dependency at 28 days of postnatal age (BPD-28d) or 36 weeks' postconceptional age (BPD-36wk), with the latter definition increasingly used. Approximately 20% of infants with a birth weight less than 1500 g will have signs of bronchopulmonary dysplasia (BPD) at 36 weeks' postmenstrual age [13, 15, 18]. However, BPD is currently infrequent in infants with birth weight greater than 1200 g or with gestation exceeding 30 weeks, with a BPD prevalence of about 30% among infants with birth weight under 1000 g [2, 9].

Clinical evidence suggests that use of nasal continuous positive airway pressure (n-CPAP) and/or nasal intermittent positive pressure ventilation (n-IPPV), with minimization of intubation (i.e., the minitouch regime) is effective in preventing apnea of prematurity [14] and it has been reported to be associated with a lower incidence of BPD [1, 4, 5, 8, 11, 12, 16, 17, 21]. We tested the hypothesis that a minitouch regime reduces the incidence of BPD-36 wk in extremely low-birth-weight (ELBW) infants.

Methods

From July 1, 1986 to June 30, 2002, a total of 160 ELBW infants with gestational age at birth of 24 weeks or more (as determined on the basis of the first-trimester ultrasonography) were admitted to the Brindisi tertiary level Neonatal Intensive Care Unit (NICU) and 72 survived for at least 36 weeks' postconceptional age. Infants with congenital anomalies were excluded. The minitouch regime was used for the treatment of respiratory distress syndrome (RDS). A failure of the n-CPAP ventilation was defined as the presence of either one of the following conditions: $PaCO_2 > 70$ mmHg and/or a fraction of inspired O_2 (FiO_2) > 0.7 to maintain pulse oximeter saturation (SpO_2) $\geq 92\%$; severe recurrent apneas (more than 6 apneas lasting more than 20 s/day). Apnea was diagnosed from continuous pulse-oximeter monitoring records in the presence of bradycardia < 100 bpm or acute reduction in SpO_2 values $< 80\%$, with no obvious respiratory airflow. The same criteria were used to define the n-IPPV failure. Intubation time, n-CPAP and n-IPPV/hours, oxygen dependence at 28 days of postnatal age and 36 weeks of postconceptional age, percentage of intubated babies, total intubation time/total O_2 therapy and $FiO_2 < 0.40$/total O_2therapy ratios were determined.

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Data analysis

Comparisons between categorical variables were performed using the χ^2 test or the Fisher's exact test, whereas comparisons between continuous variables were evaluated using the unpaired Student's *t* test or Wilcoxon test as appropriate. The predicting values of gestational age and birth weight for endotracheal intubation, use of n-CPAP or n-IPPV were analyzed using receiver operating characteristic (ROC) curves, and an area under the curve (AUC) value above 0.5 was accepted to indicate a good discrimination [6].

A two-sided *P* value of < 0.05 was considered to be statistically significant and the Bonferroni corrected significance levels were used for multiple *t*-tests. The MedCalc ver. 5.0 statistical software package (MedCalc. Software, Mariakerke, Belgium) was used.

Results

Seventy-two out of 160 (45%) ELBW infants were alive at hospital discharge (Table 1). The nonsurviving population (53 male, 48 female, inborn 61/101 [60.4%] represented a population at increased risk for adverse outcome already at birth, as indicated by a significantly lower gestational age, birth weight and 1-min and 5-min Apgar score than the surviving population (23 male, 49 female; inborn: 53 [73.6%]).

BPD-28d was observed in 18 infants (25%), whereas only 1.38% (1/72) of the whole ELBW surviving population still needed ventilatory support and supplemental oxygen at 36 weeks postconceptional age, a figure which is significantly lower than expected (30%) from the literature ($P = 0.000002$). Over the years, an the survival rate has shown an increasing significant positive trend (1986–1989, 16%; 1990–1993, 25%; 1994–1997, 42.3%; 1998–2002, 68.2%; $\chi^2 = 28.7$, $df = 3$, $P < 0.0005$), whereas no statistically significant differences in the proportions of BPD-28d among the surviving infants were observed (1986–1989, 0%; 1990–1993, 22.2%; 1994–1997, 13.3%; 1998–2002, 31.1%; $\chi^2 = 3.38$, $df = 3$, $P = 0.34$). Gestational age and birth weight were found to be significant predictors of endotracheal intubation (gestational age, cut-off criterion ≤ 25 weeks, area under the curve, 0.582 ± 0.046; 95% CI, 0.501–0.659, $P < 0.05$; birth weight, cut-off criterion ≤ 820 g, area under the curve, 0.667 ± 0.044, 95% CI, 0.588–0.739, $P < 0.05$), use of n-CPAP (gestational age, cut-off criterion > 26 weeks; area under the curve, 0.624 ± 0.044; 95% CI, 0.545–0.699, $P < 0.05$; birth weight, cut-off criterion > 700 g; area under the curve, 0.595 ± 0.045; 95% CI, 0.515–0.671, $P < 0.05$) and n-IPPV use (birth weight, cut-off criterion > 680 g; area under the curve, 0.604 ± 0.045; 95% CI, 0.524–0.680, $P < 0.05$).

None of the associated complications of n-CPAP and/or n-IPPV [3, 14] were observed.

Discussion

Our experience supports the effectiveness of the minitouch strategy as a way to ventilate premature babies, resulting in an high survival rate and a reduction in BPD risk. Although the technique of n-CPAP administration is now quite different from that originally used and even if the characteristics of ELBW infants have changed over the years, possible explanations of the observed findings may include (1) a reduced oxygen-therapy and/or mechanical ventilation length; (2) and/or a low FiO_2 use; and/or (3) a reduced exposure to phthalates released from endotracheal tubes [12]. Early use of n-CPAP, with or without surfactant replacement, is safe and appears to reduce the need for mechanical ventilation [19]. On the other hand, the use of n-IPPV appears to reduce the frequency of apneas more effectively than n-CPAP [14].

Length of time on mechanical ventilation has been shown to be an important risk factor for developing BPD [20]. Moreover, a large number of reports seem to show that in respiratory distress syndrome (RDS)-

Table 1 Comparisons of relevant clinical and ventilatory variables in ELBWinfants as a function of survival at the hospital discharge

Variable	ELBW		
	Survival ($n = 72$)	Death ($n = 88$)	*P*-value
Gestational age (weeks)	27.3 ± 2.6	26.3 ± 2.4	0.0192
Birth weight (g)	846.8 ± 124.6	792.5 ± 152.4	0.0157
Apgar score			
1 min	5.13 ± 1.9	4.3 ± 1.92	0.0070
5 min	7.05 ± 1.4	5.4 ± 1.83	< 0.0001
BPD-28d	18 (25%)	N/A	
BPD-36wk	1 (1.4%)	N/A	
Endotracheal intubation	43 (59.7%)	48 (54.5%)	0.62
Intubation duration (h)	24 (0–193)	2.0 (0–66)	0.078
n-CPAP treatment	67 (93.0%)	29 (32.9%)	< 0.0001
n-CPAP duration (hr)	144 (72–392.5)	40 (9.5–84)	< 0.0001
n-IPPV treatment	38 (52.7%)	58 (65.9%)	0.11
n-IPPV duration (h)	279 (136–461)	40.5 (6–135)	< 0.0001
Total O_2 supplementation (h)	211(66–694)	37 (11–137)	< 0.0001
$FiO_2 < 0.40$ (h)	168 (38–642)	12 (0–72)	< 0.0001
Intubation/O_2-therapy ratio (%)	14.6 (0–65)	21.2 (0–100)	0.71
$FiO_2 < 0.40/O_2$ therapy ratio (%)	91.2 (68.9–98.6)	27.2 (0–86.7)	< 0.0001
Length of stay (days)	84.5 (75–96)	4 (1–10)[a]	< 0.0001

Continuous variables are expressed as mean ± SD or median (interquartile range), as appropriate. Categorical variables are expressed as number of cases with percentages in brackets*N*/*A* definition not applicable

[a]Corresponding to age at death

affected premature newborns, the use of n-CPAP or at least a minimal intubation policy is effective in the treatment of RDS and may reduce BPD risk [1, 4, 5, 8, 11, 12, 16, 17, 21]. Likewise, recent evidence indicates that in an animal model [10] n-CPAP reduces lung injury as compared to mechanical ventilation and that the lung injury begins antenatally, but only the ventilated preterm animals may develop BPD [7]. On the other hand, we had previously evidenced the occurrence of material degradation in endotracheal tubes after use and assumed a potential plasticizer release in contributing to causing BPD [12]. As a consequence, little doubt exists that a reduction in the aggressiveness of the respiratory approach in high-risk preterm infants would be highly desirable. However, the statistical significance here observed in birth weight and gestational age between the surviving and nonsurviving ELBW populations indicates that intubation and ventilation cannot always be avoided in ELBW infants, particularly in those at the lowest gestational age. But a minimal intubation policy may be effective in the treatment of RDS, especially in those above 750 g and/or 25 weeks of gestational age, reducing the lung injury related to mechanical ventilation. Future multicenter randomized clinical trials are necessary to validate our clinical experience and to explain the precise role, if any, of ventilation, intubation or leakage of plasticizers from endotracheal tubes in determining lung injury.

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