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The Breathing Effort of Very Preterm Infants at Birth

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Objective To compare the respiratory effort of very preterm infants receiving positive pressure ventilation (PPV) with infants breathing on continuous positive airway pressure (CPAP), directly after birth.

Study design Recorded resuscitations of very preterm infants receiving PPV or CPAP after birth were analyzed retrospectively. The respiratory effort (minute volume and recruitment breaths [>8 mL/kg], heart rate, oxygen saturation, and oxygen requirement were analyzed for the first 2 minutes and in the fifth minute after birth.

Results Respiratory effort was analyzed in 118 infants, 87 infants receiving PPV and 31 infants receiving CPAP (median gestational age, 28 weeks [IQR, 26-29] vs 29 weeks [IQR, 29-30; $P < .001$); birth weight, 1059 g [IQR, 795-1300] vs 1205 g [IQR, 956-1418; $P = .06$]). The minute volume of spontaneous breaths of infants receiving PPV was lower at 2 minutes (37 mL/kg/minute [IQR, 15-69] vs 188 mL/kg/minute [IQR, 128-297; $P < .001$]) and at 5 minutes (112 mL/kg/minute [IQR, 46-229] vs 205 mL/kg/minute [IQR, 174-327; $P < .001$]). Recruitment breaths occurred less in the PPV group at 2 minutes (0 breaths/minute [IQR, 0-1] vs 4 breaths/minute [IQR, 1-8; $P < .001$]) and 5 minutes (0 breaths/minute [IQR, 0-3] vs 2 breaths/minute [IQR, 0-11; $P = .01$). The heart rate was lower in the PPV group (94 beats/minute [IQR, 68-128] vs 124 beats/minute [IQR, 100-144; $P = .02$]) as was oxygen saturation (50% [IQR, 35%-66%] vs 67% [IQR, 34%-80%; $P = .04$]), but not different at 5 minutes (heart rate, 149 beats/minute [IQR, 131-162] vs 150 beats/minute [IQR, 132-160; P = NS]; oxygen saturation , 91% [IQR, 80%-95%] vs 92% [IQR, 89%-97%; P = NS]). The oxygen requirement was higher (at 2 minutes, 30% [IQR, 21%-53%] vs 21% [IQR, 21%-29%; $P = .05$]; at 5 minutes, 39% [IQR, 22%-91%] vs 22% [IQR, 21%-31%; $P = .003$]).

Conclusion Very preterm infants breathe at birth when receiving PPV, but the respiratory effort was significantly lower when compared with infants receiving CPAP only. The reduced breathing effort observed likely justified applying PPV in most infants. *(J Pediatr 2017;■■:■■-■■).*

During transition at birth, very preterm infants need respiratory support for clearing their airways of lung liquid and replacing it with air to establish a functional residual capacity (FRC).[1] To minimize lung injury during this stabilization period, intubation and mechanical ventilation are avoided. This practice is reflected by a shift in the focus toward noninvasive ventilation using a facemask: continuous positive airway pressure (CPAP) is applied when spontaneous breathing is present or positive pressure ventilation (PPV) when breathing is absent or insufficient.[2,3] However, as PPV can deliver tidal volumes (V_T) that are variable[2,4] and inadvertently high, avoiding PPV whenever possible is likely to reduce the potential for lung injury.[5,6]

The question remains whether CPAP alone is capable of providing sufficient respiratory support for most preterm infants, thereby avoiding the use of PPV. O'Donnell et al showed that the majority of preterm infants breathe and cry at birth.[7] Schilleman et al also reported that most infants receiving PPV breathe during or between inflations, which is often missed by the caregiver.[2] Assessing spontaneous breathing and the adequacy of breathing can be difficult in preterm infants,[8,9] because breathing can be subtle and easily missed, particularly when infants are wrapped for the prevention of heat loss.

Several studies have described the respiratory effort of preterm infants breathing on CPAP[4,10,11]; however, less is known about the breathing effort while PPV is given. It is possible that the respiratory effort of infants receiving PPV is underestimated and that potentially harmful V_T are delivered by PPV when inflations coincide with breaths.

CPAP	Continuous positive airway pressure
FiO_2	Oxygen requirement
FRC	Functional residual capacity
HR	Heart rate
MV	Minute ventilation
PPV	Positive pressure ventilation
RFM	Respiratory function monitoring
RR	Respiratory rate
SpO_2	Oxygen saturation
V_T	Tidal volume
V_{Te}	Expiratory V_T
V_{Ti}	Inspiratory V_T

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The aim of this study was to determine the respiratory effort in the first minutes after birth of very preterm infants receiving PPV vs CPAP.

Methods

A retrospective, observational study was performed at the Neonatal Intensive Care Unit of the Leiden University Medical Center, The Netherlands. The local institutional review boards approved physiological and video recordings at birth in the delivery room when respiratory support was necessary. Written parental consent to use these recordings for research was obtained after birth. Recordings of all infants <32 weeks of gestation from April 2008 until June 2013 were reviewed. Infants were included for analysis when they received noninvasive respiratory support (PPV and/or CPAP).

Respiratory support was delivered with a T-piece infant resuscitator (Neopuff; Fisher & Paykel Healthcare, Auckland, New Zealand) combined with a Laerdal silicone round mask (Laerdal, Stavanger, Norway). Initial settings were a gas flow rate of 8 L/minute to give an inflation pressure of 20 and a positive end-expiratory pressure of 5 cm H_2O for PPV and a positive end-expiratory pressure of 5-8 cm H_2O for CPAP.[12] Respiratory function monitoring (RFM), heart rate (HR), oxygen saturation (SpO_2), and oxygen requirement (FiO_2) were recorded, starting as soon as the infants' shoulder was delivered. Respiratory measures were recorded with either a Florian RFM (Acutronic Medical Systems AG, Hirzel, Switzerland), or a New Life Box (Applied Biosignals, Weener, Germany) connected to an MRT-A RFM (Applied Biosignals). The Florian RFM used a hot wire anemometer and the MRT-A RFM a variable orifice pneumometer (Avea Varflex Flow transducer; Carefusion, Yorba Linda, California). The SpO_2 and HR were recorded using a Masimo SET pulse oximeter (Masimo Radical, Masimo Corporation, Irvine, California) with the pulse oximetry probe placed around the infant's right wrist. Gas flow, pressures given, V_T, SpO_2, HR, and breathing signals were digitized using Spectra physiological software (Grove Medical Limited, Hampton, United Kingdom) for the Florian RFM, and Polybench software for the New Life Box (Applied Biosignals).[12,13] We reported in 2013 that most caregivers did not use the parameters of the respiratory function monitor for evaluation of resuscitation.[2] We conducted training in 2013, but it is likely that RFM was not used to adjust the respiratory support in most infants recorded between 2008 and 2013.

For this study, the respiratory rate (RR) of spontaneous breathing, minute ventilation (MV), V_T, HR, SpO_2, and FiO_2 were analyzed in 2 time periods: the first 2 minutes after the infant was placed on the resuscitation table and the fifth minute of stabilization. For analysis, the infants were divided into 2 groups: a PPV group (infants receiving PPV at any time during the resuscitation) and a CPAP group (infants receiving only CPAP). Infants receiving PPV in the first 2 minutes remained in the PPV group even if breathing on CPAP at 5 minutes.

In the time period the recordings were obtained, the local resuscitation guidelines recommended to start with initial sustained inflation(s). Depending on the time period, the guidelines recommended an initial 5 sustained inflations each lasting 2-3 seconds or a single sustained inflation lasting 10 seconds. When sustained inflation(s) were followed by consecutive inflations, the infants were included in the PPV group. When no consecutive inflations were given and only CPAP followed, infants were included in the CPAP group.

Normal values of V_T and MV of preterm infants breathing on CPAP at birth have been published.[4,10,11] However, there is no clear definition of when breathing is adequate. For the purposes of this study, to compare the respiratory effort we calculated how often the MV in the PPV group was >25th percentile of the MV of the infants in the CPAP group, and how often recruitment breaths of >8 mL/kg per minute occurred.[14]

Because we were interested in the respiratory effort, inspiratory V_T (V_{Ti}) was used for the analysis of volume. Most of the mask leak arises from pressurization of the mask when inflations are given; leak rarely occurs during spontaneous breaths. Signals were only analyzed when there was no mask leak. V_{Ti} and expiratory V_T (V_{Te}) were determined, percent leak was calculated by the difference between the V_{Ti} and the V_{Te} using the formula $([V_{Ti} - V_{Te}]/V_{Ti}) \times 100\%$. However, a discrepancy between V_{Ti} and V_{Te} could also reflect a relative increase in FRC.[15] To differentiate between mask leak and increase in FRC, the following rules were maintained: when inspiratory flow did not return to zero before the end of inflation, this was considered to be leak. When inspiratory flow wave did return to zero, the difference between V_{Ti} and V_{Te} was most likely a change in FRC.

The characteristic flow patterns created by spontaneous breaths have been described in detail in a previous publication.[2] Spontaneous breaths were identified during CPAP (**Figure 1**, A), in between inflations (**Figure 1**, B), and coinciding with inflations (**Figure 1**, C and D). Because the inflation can contribute to the V_T, the V_T of breaths coinciding with an inflation were only included in the V_{Ti} and MV analyses when the flow signal of the spontaneous breath returned to baseline, resulting in 2 separate flow peaks (**Figure 1**, D). However, when the flow signal did not return to baseline before a second flow peak was formed (**Figure 1**, C), V_T could not be differentiated from the volume of the inflation. These breaths were excluded from the V_{Ti} analysis, but were still counted as a breath for the RR. MV was then calculated using the average V_{Ti}.

SPSS (IBM SPSS Statistics for Windows, Version 20.0, IBM Corp, Armonk, New York) was used for the statistical analysis. Descriptive statistics are presented as median (IQR) for non-normally distributed values and number (%) for categorical parameters. Homogeneity between groups was tested with Mann-Whitney *U* tests or with χ^2 tests when the data was categorized. Reported *P* values are 2-sided and considered as statistical significant when $P < .05$. The outcome parameters of the groups were compared using a Mann-Whitney *U* test when non-normally distributed, and a χ^2 test when the data was categorized.

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