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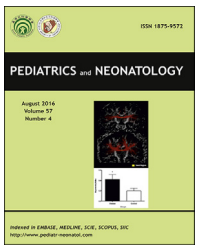

Original Article

A randomized pilot study comparing the role of PEEP, O_2 flow, and high-flow air for weaning of ventilatory support in very low birth weight infants

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Key Words
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nasal air flow

Background: There is a lack of evidence to guide step-wise weaning of positive pressure respiratory support for premature infants. This study sought to compare the efficacy of three weaning protocols we designed to facilitate weaning of very low birth weight (VLBW, less than 1500 g) preterm infants from nasal continuous positive airway pressure (NCPAP) support.
Methods: This was a prospective, randomized, controlled trial of VLBW preterm infants who received positive pressure ventilatory support in our neonatal intensive care unit (NICU) from April 2008 through March 2009. When these infants were weaned to CPAP as their last step of respiratory support, they would be randomly assigned to one of the following three groups as their further weaning methods (M): (M1) CPAP group, (M2) O_2 flow group, and (M3) air flow group. The time period they needed to wean off any kind of respiratory support, as well as the likelihood of developing relevant prematurity related morbidities, were compared among patients using different weaning modalities.
Results: 181 patients were enrolled in the study. Their gestational age (GA) and birth weight (BW) were 29.1 ± 2.5, 28.7 ± 2.4, 28.7 ± 2.4 (mean ± SD) weeks and 1142 ± 232, 1099 ± 234, 1083 ± 219 g, in M1, M2 and M3, respectively. The time (period) needed to wean off support was 16.0 ± 10.0 days (M1), 11.6 ± 6.4 days (M2), and 15.0 ± 8.9 days (M3), respectively ($p = .033$). Incidence of retinopathy of prematurity (ROP) and bronchopulmonary dysplasia (BPD) were both significantly higher in the O_2 flow group ($p = .048$).
Conclusions: Although using low oxygen flow significantly shortens CPAP weaning time, it may increase risks of BPD and ROP, both known to be related to oxygen toxicity. Unless the infant has BPD

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and is O_2-dependent, clinicians should consider using air flow or just splinting with no support at all when weaning NCPAP.

1. Introduction

Respiratory support has become the mainstay of successful care for the premature infants. We also made significant progress in the understanding and management of neonatal respiratory disorders. Nasal continuous positive airway pressure (NCPAP) therapy is used as a primary support modality for infants with respiratory distress syndrome and apnea of prematurity. It is also used as the key post-extubation respiratory support.[1–3] Multiple studies have demonstrated that NCPAP is a safe treatment modality with no increase in short-term[4–9] or long-term morbidities.[10,11] It also has other beneficial effects, including the induction of lung growth.[12]

In contrast to the variable but well-examined strategies in the initial management of respiratory distress in premature infants, there has been a lack of evidence-based guidelines for the step-wise weaning of these patients. This is especially true when the weaning process reaches the last part of pressure support, which often is NCPAP, either with low fraction of inspiratory oxygen (FiO_2) or room air. Further weaning techniques differ considerably from one clinician to another. At this point, drastic weaning may lead to hypoxemia or a rebound of respiratory distress, whereas sluggish weaning may be the cause of a prolonged hospital stay or even pose a risk of nosocomial infection.

After weaning from CPAP therapy, oxygen is often delivered through a nasal cannula (NC) at low-flow rate (up to 0.5–1 L/min). However, the preterm infant would more often have been in 21% FiO_2 with CPAP prior to this step, in which case they were being treated for apnea of prematurity.

Previous studies have demonstrated that high-flow nasal cannula can deliver positive distending pressure equivalent to conventional forms of nasal CPAP.[13,14] High flow was considered as a gas flow greater than 1 L/min in these studies. HF-CPAP has also been shown to be as effective as conventional CPAP in managing apnea of prematurity. Furthermore, it has been well illustrated in immature mammals that stimulation of the trigeminal afferent can trigger control of respiration.[15] Moreover, researchers also found that electrical stimulation of the sensory root of trigeminal nerve can induce significant responses on the pontine respiratory neurons in newborn rats, a finding indicating presence of respiratory neurons in the rostral pons approximately overlapping with the Kölliker-fuse nucleus receiving trigeminal input.[16] Based on the neuroanatomical distribution and pathophysiology of apnea of prematurity, tactile stimulation by an air flow to the nostrils, even in a moderate flow rate, could also be used as a modality in this circumstance.

Therefore, we performed this prospective, randomized controlled trial to compare the efficacy of the three weaning protocols we designed for the weaning of VLBW preterm infants from positive airway pressure support. With this study, we also aimed to set forth a standardized weaning practice.

2. Methods

2.1. Subjects

This study was conducted in the NICU of Chang Gung Medical Center in Lin Kou, Taiwan between August 2008 and September 2009. All VLBW preterm infants (BW $\leq$ 1500 g and GA $<$ 34 weeks) admitted to our NICU who also required positive pressure ventilation support were eligible for this study. The study population was comprised of 189 patients (106 males and 83 females), with a mean ($\pm$SD) gestational age of 28.8 $\pm$ 2.4 weeks, and BW of 1108 $\pm$ 228 gms. The exclusion criteria included the following: (1) CPAP use for $<$24 h; (2) no parental consent for the study; (3) weaning interrupted by a need for surgery; (4) transfer of the patient to other hospital; (5) FiO_2 use $>$25% at the time of CPAP weaning; (6) body weight less than 750 g at the time of randomization; (7) congenital abnormalities affecting cardiopulmonary performance; (8) intraventricular hemorrhage (IVH) Gr. III or above. Patient enrollment was started when these preterm infants' ventilator support was decreasing down to CPAP and they were ready for further weaning. This study was reviewed and approved by the Institutional Review Board (IRB) of Human Investigation Committee at the Chang Gung Memorial Hospital, and a signed informed consent was obtained from the parent(s) or guardian(s) of each participant before the study.

2.2. Measurements and protocol

Once the infant was stable and achieved target oxygen saturation of 88%–93% on a CPAP pressure of 5–7 cm H_2O and an FiO_2 no greater than 0.21 for 24 h, then the infant would be checked to meet the following criteria before starting weaning of CPAP: a body weight of 1250 g or larger; a hemoglobin level of at least 10 gm/dL; no use of vasoactive or sedative agents. In addition, the attending physician agreed with the patient's weaning. Once started, the enrolled premature infants would be randomly assigned to one of the three weaning protocols (Fig. 1).

(A) Method 1 (M1): The CPAP was continued at 4–6 cm H_2O for another five days, then the CPAP was taken "OFF" and the premature infant remained in the crib on oxygen by nasal cannula as needed or in room air with a plan to remain off CPAP. If the infant failed

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