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EDITORIAL COMMENTARY

Continuous Positive Airway Pressure: Method of Discontinuing in Neonates, Unresolved

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The use of continuous positive airway pressure (CPAP), first described by George Gregory in 1971 for the management of respiratory distress syndrome [1] and now used for a variety of respiratory diseases in infants remains one of the most actively investigated interventions for neonatal intensive care. Nasal CPAP (NCPAP) provides continuous distending pressure to stabilize the lung volume to prevent alveolar collapse, splint the upper airway to reduce obstructive apnea, attenuates distortion of chest wall during inspiration and increases the efficiency of the diaphragm. Several important large scale clinical trials evaluating the role of NCPAP in early respiratory management in preterm infants have been published in recent years [2–5]. Treatment with early NCPAP rather than intubation/surfactant may be associated with less respiratory morbidity by 18–22 mo corrected age [6]. NCPAP has become the primary mode of respiratory support in preterm infants to avoid intubation and mechanical ventilation and to facilitate weaning from the ventilator [7–9].

There are risks associated with NCPAP use, including pneumothorax, nasal trauma, increased abdominal distension and impeded systemic and pulmonary venous return [3, 10]. Therefore, its weaning is important when infants' respiratory status shows improvement. However, the optimal methods and factors associated with successful wean are not well defined. A survey involving 124 Australian tertiary neonatal units showed that at least 48 % of neonatologists used grade-time-off CPAP and at least 50 % weaned the airway pressure prior to coming off NCPAP despite the paucity of evidence to support either strategy [11]. Another survey of all 58 neonatal units with intensive care cots in the Northern Region of England revealed that 66 % of the units weaned by "time off", while the others indicated no set method [12]. Thus, an expert have commented that weaning babies from CPAP is "a matter of trial and error to see how they manage" [13]. The wide variation in practice undoubtedly reflects the lack of sufficient evidence from existing trials to direct neonatologists in the weaning of preterm infants from NCPAP.

In this issue, Nair et al. report a pilot, feasibility study (NCT02114112) to compare the effectiveness of nasal CPAP (NCPAP) cycling with continuous NCPAP in the successful weaning of preterm infants of 25°–28^{6} wk gestation to nasal prongs [14]. A total of 30 infants ventilated for respiratory distress syndrome (RDS) and extubated to NCPAP were randomized to NCPAP cycling or to continuous NCPAP at 4 cm of H_2O. After 72 h of intervention, both groups were weaned to 1 Liter per minute (LPM) nasal prong (NP), per their neonatal intensive care unit standard practice. Successful weaning was defined when an infant continued to be on 1LPM NP for at least 72 h. The authors did not find any significant difference in rates of successful weaning between the two groups.

We appreciate the efforts of the authors to study this important question of "how to wean" in the most vulnerable group of extremely low gestational age neonates (ELGAN). They planned to recruit 40 subjects, but unfortunately the study was terminated early due to the introduction of a respiratory bundle quality initiative in authors' unit to reduce the bronchopulmonary dysplasia rate. As a consequence only 30 subjects were recruited into this one-year study with 13

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subjects randomized to the Cycling NCPAP arm and 17 in the Continuous NCPAP arm. Interestingly, the number of male infants, the median age of entry into study and the median duration of ventilation prior to the intervention were higher in the continuous NCPAP group. One could argue that the NCPAP cycling group represented infants with lower severity of respiratory illness; that explained why they were ventilated for less hours and could enter the study earlier in life. Such differences in the baseline factors in the two groups renders the interpretation of any outcomes on shaky grounds.

Significant variations in the inclusion criteria of infants (like gestational age), intervention strategies (like use of nasal cannula), duration of weaning and criteria for failed tried "off" NCPAP renders comparison difficult [15–21]. For instance, while Nair included only ELGAN, other studies included infants of more advanced gestational age (even up to 33 wk) [15, 16, 18, 22] and weaned infants off CPAP either abruptly or gradually (pressure or time) [15, 18]. Moreover, the primary outcomes of interest ranged from "length of time to wean off CPAP", "duration of CPAP treatment" to "success rate of first trial to wean from NCPAP" [15, 16, 20]. Most studies were of relatively small sample size and under-powered, while only Rastogi, Abdel-Hady and Todd outlined their rationale of sample size calculations [16–18, 20]. Thus it is difficult to compare and contrast these studies and their heterogeneity renders high quality meta-analysis virtually impossible.

Nair's study adds to the literature by using a totally different set of outcome and success criteria of NCPAP weaning among infants born at 25–28 wk gestation. However, the criteria and method of weaning is still unsettled and begs for an adequately powered prospective trial to evaluate different weaning strategies.

Conflict of Interest None.

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