Seminars in Fetal & Neonatal Medicine 21 (2016) 189–195

Contents lists available at ScienceDirect

Seminars in Fetal & Neonatal Medicine

journal homepage: www.elsevier.com/locate/siny

Review

Duration of continuous positive airway pressure in premature infants

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Keywords:
Premature infant
Respiratory distress syndrome
Non-invasive ventilation
Continuous positive airway pressure
Oxygen inhalation therapy
Bronchopulmonary dysplasia

SUMMARY

Continuous positive airway pressure (CPAP) has been used for respiratory support in premature infants for more than 40 years and is now a cornerstone of modern neonatal care. Clinical research on CPAP has primarily focused on understanding which devices and pressure sources best implement this therapy. In contrast, less research has examined the optimal duration over which CPAP is administered. We review this aspect of CPAP therapy.

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1. Introduction

In 1968, Harrison and colleagues reported cessation of grunting and progressive hypoxemia following endotracheal intubation in infants with respiratory distress syndrome (RDS) [1]. This observation led to the use of continuous distending airway pressure to counteract lungs prone to collapse [2]. Nasal continuous positive airway pressure (CPAP) is the most widely used non-invasive continuous distending airway pressure modality and a cornerstone of modern neonatal care. Whereas there has been emphasis on understanding which devices and pressure sources best implement CPAP [3,4], the optimal duration of this therapy is less well studied. At birth, premature infants have life-threatening anatomic and physiologic immaturities of the respiratory system. CPAP attenuates this pathophysiology until sufficient stability develops and continuous distending pressure is no longer needed. But when does this occur? In this review, we summarize the benefits and harms associated with CPAP and describe the clinical considerations that determine CPAP duration. We then describe and synthesize the published evidence on this topic.

2. Benefits and harms of CPAP

Gregory proposed that the primary benefit of CPAP is "inflation of the atelectatic lung [2]." CPAP splints the upper airways, decreasing both supraglottic and total pulmonary resistance [5]. The distending pressure increases lung volumes and establishes functional residual capacity while preventing further alveolar collapse and promoting surfactant release [6–8]. Oxygenation is improved through enhanced diffusion, increased ventilation/perfusion matching and decreased shunt [7,9,10]. CPAP may improve respiratory mechanics [11] by improving compliance and stabilizing the compliant chest wall, improving thoracoabdominal synchrony and reducing work of breathing [10]. Upper airway splinting reduces obstructive apnea [12] and may also decrease central apnea by promoting a regular breathing pattern [13].

However, CPAP can also result in harm. Airway distending pressure is a risk factor for air leak syndromes [14,15]. High lung volumes can impair ventilation with resulting hypercarbia [16]. Excessive intrathoracic pressure can decrease venous return and impair cardiac output [17]. Sufficient compromise of pulmonary blood flow may actually worsen ventilation/perfusion mismatch and impair oxygenation [17–19]. Gastric distension [20] – so-called "CPAP belly" – may aggravate feeding intolerance and provoke gastroesophageal reflux, itself a risk factor for ongoing lung injury [21,22]. Prolonged CPAP use may delay initiation of oral feeds, prolong hospitalization, limit infant holding, and constrain developmental therapies [23]. Nasal septum breakdown [24] and perceived infant agitation cause distress in parents and caregivers alike [25,26].

3. Clinical considerations determining CPAP duration

CPAP duration is typically influenced by three clinical considerations:

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http://dx.doi.org/10.1016/j.siny.2016.02.005
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Table 1
Surveys on duration of CPAP practice highlight practice variation.

Survey	Findings
Bowe et al. [31] 58 English neonatal units	Weaning methods used: time cycling (66%), pressure weaning (4%) Adherence to specified weaning protocols: 6%
Jardine et al. [29] All level 3 Australian neonatal units	Weaning methods used: time cycling (70%), pressure weaning (74%) Range of responses for selected CPAP duration parameters: (i) minimum CPAP prior to discontinuation: 3–6 cmH_2O (ii) time allowed between pressure weans: 0–5 days (iii) time off CPAP before full discontinuation (with time cycling): 6–18 h (iv) increase in FiO_2 required to meet failure criteria: 5–60%

CPAP, continuous positive airway pressure; FiO_2, fraction of inspired oxygen.

Table 2
Randomized trials on duration of CPAP support: key characteristics and findings.

Study; population	Randomized intervention	Stability criteria	Failure criteria	Selected outcomes	Comments
Abdel-Hady et al. [20] $n = 88$ GA, cohort: 29 (2) weeks BW, cohort: 1264 (332) g Age at intervention, median (IQR): 7.0 (3–18) vs 7.5 (4–18) days	Group A: continued CPAP support Group B: pressure weaning over 1 h to CPAP 3 cmH_2O then off	No supplemental O_2, no frequent/severe apnea	Incubator FiO_2 >0.40; frequent/severe apnea; resulted in return to baseline CPAP support and study termination	(i) CPAP duration: 9.5 vs 0 days** (ii) Retractions: 0 vs 26%** (iii) Change in respiratory rate: +2 vs +7 breaths/min* (iv) Arterial to alveolar pO_2 ratio change at 6 h: (−0.01) vs (−0.04)* (v) Change in abdominal circumference: +0.5 vs −0.5**	Outcomes at 6 h post intervention; 1/44 in Group B met failure criteria within 6 h but 18/44 ultimately returned to CPAP
Singh et al. [34] $n = 112$; GA (range): 27 (24–32) vs 28 (24–31) weeks BW (range): 940 (614–1400) vs 1080 (520–1496) g Age at intervention, cohort (range): 29 (28–31) weeks PMA	Group A: pressure weaning Group B: time cycling	Supplemental FiO_2 <0.30	Not detailed	(i) Weaning duration: 1.5 vs 8.9 days** (ii) Successful weaning (defined as stable off of CPAP for 7 days): 65% vs 37%** (iii) Total CPAP duration: 6 vs 13.2 days**	Abstract only; weaning duration difference between groups demonstrates wean-time lag; difference in total CPAP duration largely explained by weaning duration difference.
Soe et al. [35] $n = 98$ GA, cohort (range): (24–31) weeks BW: not reported Age at intervention: not detailed	Group A: pressure weaning over 6 days Group B: time cycling over 6 days	Not detailed	Not detailed	(i) Successful weaning (not defined); 24–27 weeks GA: 82% vs 55%* 27–31 weeks GA: NS (ii) CPAP duration; 24–27 weeks GA: 10 vs 15 days* 27–31 weeks GA: NS	Abstract only
Abdel-Hady et al. [36] $n = 60$ GA: 31 (2.6) vs 31 (2.4) weeks BW: 1600 (390) vs 1600 (380) g Age at intervention: not reported	Group A: CPAP discontinuation to RA Group B: CPAP transitioned to 2 L/min NC with $FiO_2 = 0.30$; when $FiO_2 = 0.21$, NC flow weaned from 2 L/min by 0.5 L/min every 6 h	Supplemental FiO_2 0.21 (Group A) or <0.30 (Group B) and CPAP 5 cmH_2O for 24 h, no frequent/severe apnea, no respiratory distress, no abnormal blood gas	FiO_2 >0.60; frequent/severe apnea, respiratory distress, abnormal blood gas; resulted in return to CPAP, 24 h of stability criteria prior to repeat weans	(i) CPAP duration: 11.2 vs 7.6 days* (ii) Oxygen duration: 5 vs 14 days** (iii) Respiratory support duration: 10.5 vs 18 days* (iv) Length of hospitalization: 36 vs 36.7 days (NS)	Stability criteria unequal between groups, PMA at intervention between groups not reported
Todd et al. [38], Broom et al. [42] (secondary analysis) $n = 177$ Groups A vs B vs C	Group A: CPAP discontinuation to RA Group B: time cycling between RA and 6 h CPAP with increasing time off by 2	Supplemental FiO_2 <0.25 and down-trending, CPAP 4–6 cmH_2O for 24 h, no frequent/severe apnea, no respiratory distress; no sepsis or patent	Two of: FiO_2 >0.25; frequent/severe apnea, respiratory distress, abnormal blood gas; for Group A resulted in return to CPAP for minimum of 48 h; for Groups B and C	Groups A vs B vs C (i) CPAP duration: 11 vs 17 vs 19 days** (ii) Oxygen duration: 24 vs 49 vs 34** (iii) PMA at discharge: 35.8	Randomization chance imbalance on covariates of gender and Apgar score adjusted through multivariate analysis. Authors speculate that

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