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Newer experience with CPAP

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Progress in neonatal intensive care is closely linked to improvements in the management of respiratory failure in small infants. Current modalities of ventilatory assistance range from more benign continuous positive airway pressure (CPAP) to various modes of mechanical ventilation (including high frequency ventilation). The advent of less invasive methods of delivering CPAP has permitted earlier treatment of infants with respiratory distress syndrome and avoided the need for mechanical ventilation. Children's Hospital of New York (Columbia University) places all spontaneously breathing infants on nasal prong CPAP as the first mode of respiratory support. The early initiation of nasal prong CPAP in combination with a tolerance to elevated PCO_2 levels has reduced the incidence of chronic lung disease to <5% in infants weighing less than 1500 g. This report will present an historical review and summarize the experience with CPAP at Columbia and other centres. In addition, it reviews the clinical applications and physiological effects of CPAP in preterm infants with respiratory distress syndrome.

Key words: continuous positive airway pressure, CPAP, bronchopulmonary dysplasia, respiratory distress syndrome

Introduction

Bronchopulmonary dysplasia (BPD) is a complex pulmonary disorder characterized by lung inflammation and injury leading to abnormal repair mechanisms and arrested lung development (decreased alveolarization). While events in prenatal, intrapartum, and postnatal life are all believed to contribute to it occurrence, the use mechanical ventilation for prolonged periods of time is thought to be a major contributing factor. Unfortunately, once the inflammatory cascade is initiated within the lung (with release of proteases, free radicals, and cytokines), there is little that can be done to prevent the development of lung injury [1].

Attempts to decrease the incidence of chronic lung disease have for the most part been unsuccessful. Neither surfactant nor antenatal steroids have significantly decreased the incidence of BPD [2,3]. Similarly, interventions aimed at the primary mechanisms of lung injury (free radical scavengers, vitamin E, systemic and inhaled steroids) have shown little benefit [4–6]. Furthermore, postnatal steroid use has associated serious long-term problems, including an increased incidence of cerebral palsy [7]. Other strategies including those aimed at decreasing volutrauma (e.g., high frequency ventilation and synchronized ventilation) have met with limited success [8,9]. In contrast the years following the introduction use of continuous positive airway pressure (CPAP) were associated with a decrease in the risk of air leak and chronic lung disease in preterm infants with respiratory distress syndrome (RDS).

In 1987, Avery *et al.* [10] published a retrospective study designed to answer the question, 'Are there differences among centres in the incidence of chronic lung disease of prematurity when birth weight, race, and sex are taken into consideration?' In this retrospective study of 1625 infants at eight tertiary centres, Columbia University had the lowest incidence of chronic lung disease without any significant differences in mortality. Among the

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differences between centres, Columbia University physicians instituted CPAP with nasal prongs soon after birth in all weight groups of infants who showed signs of respiratory distress. In addition, hyperventilation was avoided and $PaCO_2$ values were allowed to go as high as 60 mm Hg without endotracheal intubation. Recently, Van Marter *et al.* [11] re-examined the role of NICU practices in the development of chronic lung disease using a case-cohort study design. Once again, the authors observed marked differences in the incidence of chronic lung disease (4% at Babies Hospital [Columbia University] vs, 22% at two Boston hospitals). Infants at Babies Hospital were less likely to be mechanically ventilated, and those who did were ventilated for significantly shorter time periods. In addition, mean $PaCO_2$ values were higher at Babies hospital than at the Boston centres. Importantly, there were no differences in short-term morbidities (periventricular leukomalacia and intraventricular haemorrhage) between centres. Although, CPAP was first described by Gregory in 1971 [12], it is somewhat disconcerting that no long-term data on infant development have been published from the Columbia group and no one has prospectively studied or compared the 'Columbia approach' with other gentle ventilation techniques.

Historical overview

Continuous positive airway pressure was applied to adults in the mid-1930s [13] to treat pulmonary oedema and asthma but was later abandoned when mechanical ventilation became feasible. In the 1960s, mechanical intermittent positive pressure ventilation became widely accepted as the standard treatment of respiratory distress of the newborn. Gregory *et al.* first reported the use of endotracheal tube CPAP in the treatment of respiratory distress of the newborn in 1971 [12]. Originally CPAP was administered via head box or endotracheal tube, because it was thought that a tight seal was essential to its therapeutic effects. However, in 1973, Agostino *et al.* reported a small series of low birth weight infants with RDS who were treated successfully with nasal CPAP [14]. This method took advantage of the fact that most infants were obligate nasal breathers and would spontaneously form a seal between the palate and the tongue. In cases of excessive pressure, the mouth would act as a natural pop-off valve. Over subsequent years a variety of different non-nasal CPAP devices were also developed including a pressurized plastic bag fitted over the infant's head [15], face chambers [16], and face masks [17,18]. The use of secured facial masks and devices requiring a neck seal declined with the growing realization that a tight seal was unnecessary and that nasal devices facilitated better access to the infants [19]. Earlier reports called for the discontinuation of CPAP devices utilizing a collar because of their link with an increased number of cases of post-haemorrhagic hydrocephalus [20]. Subsequently an association was found between tight fitting masks and an increased incidence of cerebellar haemorrhage [21]. More recently, CPAP has been delivered by nasopharyngeal tubes ending above the vocal cords. Several forms of these nasal tubes exist, some long enough to end just above the epiglottis and some extending only 1–2 cm inside the nose. The advantages and disadvantages of various CPAP delivering devices are summarized in Table 1.

Physiological effects

The physiological effects of CPAP will vary, depending on the underlying pulmonary pathology. CPAP is believed to result in progressive alveolar recruitment, inflating collapsed alveoli [12], and reducing intrapulmonary shunt [22,23]. These findings have never been clearly demonstrated. However, some of the effects of CPAP have been measured. CPAP increases lung volume [22]. Initially, as functional residual capacity increases, gas exchange improves, PaO_2 increases and $PaCO_2$ decreases. Improved oxygenation relieves hypoxic vasoconstriction in the pulmonary vascular bed and decreases pulmonary vascular resistance, resulting in increased pulmonary blood flow, decreased shunting, and further increases in PaO_2. With additional CPAP the volume of the lung may increase excessively. In such cases, PaO_2 remains high, but $PaCO_2$ also begins to increase as tidal volume diminishes. Excessive CPAP may ultimately lead to serious consequences, such as air leak syndromes and increased dead space ventilation, leading to a rise in $PaCO_2$. Furthermore, although low levels of CPAP may be useful in decreasing pulmonary oedema or left-to-right cardiac shunting, high levels of CPAP can lead to

Table 1. Advantages and disadvantages of various methods of delivering CPAP

Method	Advantages	Disadvantages
Endotracheal tube	Patent airway; easy attachment to the respirator; easily stabilized and controlled	Complications associated with intubation; higher airway resistance
Nasal prongs	Easy to apply; flexible and enable change in infant's position; low airway resistance, easily stabilized and controlled; eliminates need for intubation	Nasal septal erosion or necrosis; nasal obstruction from secretions or improper position of CPAP prongs; abdominal distension from swallowing air
Nasopharyngeal tube	Easily inserted; eliminates need for intubation	Loss of CPAP with crying or leaks; pressure necrosis; higher airway resistance; abdominal distension from swallowing air
Mask	Easily applied; eliminates need for intubation	Oral care difficult; leaks, CO_2 retention with inadequate flow; pressure necrosis; abdominal distension from swallowing air; danger of aspiration
Head box	Easily applied; eliminates need for intubation	Leaks; compression of neck vessels; difficult head and oral care; tissue necrosis; access for resuscitation difficult

reduction in cardiac output, reduced pulmonary perfusion, and enhanced ventilation-perfusion mismatch, resulting in a lower PaO_2 [24,25]. CPAP also increases intrathoracic pressure, which may further decrease venous return to the heart and cardiac output. The risk of cardiac compromise depends on the amount of pulmonary disease present. In RDS, when compliance is dramatically reduced, most of the pressure may be absorbed in the lung, with little or no negative effects on cardiac output [26].

CPAP has some nonspecific effects on neonatal ventilation as well. Application of CPAP appears to produce a more regular breathing pattern in preterm neonates [27], which has been thought to be mediated through chest wall stabilization and reduction of thoracic distortion. CPAP splints the airway and the diaphragm [28,29]. Obstructive apnea is also reduced with CPAP [30]. Furthermore, it has been shown that both inspiratory and expiratory times are increased with CPAP. Finally, it is thought that surfactant release may be enhanced by CPAP in RDS [31].

Some effects of CPAP on renal function have been documented. These include a decrease in glomerular filtration rate, reduction of urinary sodium excretion, and diminished urinary output [32,33]. These findings appear to be mediated through transmission of pressure to the cardiovascular system with reduction in renal blood flow. Aldosterone appears to increase with application of CPAP [34] and antidiuretic hormone secretion may increase as well [35]. Some of these physiologic effects of CPAP are summarized in Table 2.

CPAP delivery devices

The goal of any CPAP delivery device is to prevent atelectasis and airway closure. An ideal CPAP delivery system should include a patient-system that is easily and rapidly applicable, readily removable and re-connectable, non-traumatic to the neonate, capable of producing stable pressures at the desired levels, readily accepting of humidification and supplementary oxygen, associated with low resistance to breathing and minimal dead space, easily understood and maintained, readily sterilizable, safe, and cost effective. Given the infrequent use of non-nasal methods of CPAP in current clinical practice, this review will focus exclusively on nasal interfaces and modes of pressure generation utilized in nasal CPAP delivery systems.

Essentially, any CPAP delivery system consists of three components:

(i) Circuit for continuous flow of inspired gases: Oxygen and compressed air sources provide inspired gases at the appropriate FiO_2. The rate of flow of inspired gases is controlled by a flow meter. The minimal flow rate required should be sufficient to prevent rebreathing of carbon dioxide, i.e. two and half times the infant's minute ventilation. The

Table 2. Physiological effects of CPAP

Organ system	Beneficial effects	Risks
Pulmonary	Increased transpulmonary pressure and FRC Decreased PVR Decreased intrapulmonary shunt Increased static compliance Decreased work of breathing Increased PaO_2 Splinting of airways and diaphragm	Air leak syndrome (pneumothorax, pneumomediastinum, PIE) At high levels decreased compliance and increased work of breathing
Cardiovascular		Decreased venous return and consequent decrease in cardiac output
Renal		Reflex secretion of ADH and increased levels of aldosterone causing decreased urine output and renal clearance

flow should compensate for leaks around connectors and CPAP prongs. Usually flow rates of 5–10 LPM are sufficient in neonates. The gases are warmed and humidified by a heated humidifier prior to delivery to the infant.

(ii) Nasal interface to connect the CPAP circuit to the infant's airway: Nasal masks, nasal cannula, single and binasal tubes/prongs of varying lengths, ending in the nares or nasopharynx have been used as nasal interfaces. Nasal masks were an early means of applying CPAP to neonates [19,36]. They lost popularity because of the difficulty in maintaining an adequate seal and a tendency to cause nasal airway obstruction [37]. Nasal cannulas are most often used in neonates to deliver supplemental oxygen at low flows (<0.5 l/min) with no intention of generating CPAP. Binasal prongs, when first introduced to apply CPAP, were felt to be simple to use, effective and safe, but have the potential to cause nasal trauma [14,37]. A number of binasal devices are now in common use including Argyle prongs [38] and Hudson prongs [39,40]. With the realization that such binasal prongs might result in a significant increase in work of breathing [41], efforts were directed at designing a nasal interface that would lower this by reducing airway resistance and fluctuations in airway pressure [42]. The resultant short-pronged binasal devices, currently known as Infant Flow (EME Medical Inc.) and Arabella Generators (Hamilton Medical), are structured to allow the jet flow to flip between inspiratory and expiratory routes. They aim to provide sufficient demand flow on inspiration while minimizing expiratory resistance. Work with lung models [42,43] and a small study on preterm neonates with minimal lung disease [44] demonstrated reduced work of breathing when compared with conventional devices. Limited randomized crossover [45] and non-randomized [46] clinical studies, in preterm neonates, have compared the Infant Flow nasal CPAP system with single prong nasal CPAP. They found no significant difference in short-term measurement of physiological variables. Prongs inserted to the nasopharyngeal level have been shown to deliver effective CPAP [47,48]. They received early criticism because they were perceived to be poorly tolerated and difficult to insert when compared with short nasal tube insertion [49]. Despite this shortcoming, the use of nasopharyngeal tubes became established in clinical practice and were featured in several trials that examined both binasal [50] and single [51] forms. Single prong CPAP, (nasopharyngeal or short nasal), a relatively simple and inexpensive technique [45], continues to be widely used despite criticism of inefficiency [52]. In common with naso-endotracheal tubes, nasal CPAP interfaces have the potential to cause nasal excoriation and scarring if inappropriately applied or infrequently monitored [53,54]. It is not clear which NCPAP device is least likely to cause nasal trauma.

(iii) Modes of positive pressure generation in the CPAP circuit: Nasal CPAP is usually provided by varying the resistance to exhalation, using a threshold resistor exhalation valve, while constant gas flow is delivered via nasal prongs connected to a neonatal ventilator. Underwater bubble CPAP has provided an alternative to pressure derived from conventional ventilators and remains in use since first devised in the early 1970's [12]. The bubble CPAP uses a column of water to provide the positive airway pressure rather than a variable resistor. In addition to providing positive airway pressure, bubble CPAP results in small vibrations in

the infant's chest at the frequency of 15–30 Hz. These vibrations when transmitted to the lung produce marked changes in the amplitude of pressure oscillations as well as of the frequency of oscillations [55]. A comparison of underwater bubble endotracheal CPAP with conventional ventilator derived endotracheal CPAP in preterm neonates suggested that the bubbling contributed to gas exchange and reduced respiratory rate and minute ventilation significantly without increasing $PaCO_2$ [56].

In contrast, the variable flow nasal CPAP device generates CPAP in the vicinity of the nasal airways by converting kinetic energy from a jet of fresh humidified gas. The theory behind this device is that the direction of the high-pressure supply jet responds to pressures exerted in the nasal cavity by the patient's efforts. On inspiration the low pressure in the nasal cavity gives a positive pressure gradient between the jet supply and the nasal cavity, and the jet flows towards the patient, aiding the respiratory effort. On exhalation the build up of pressure in the nasal cavity alters the detailed structure of the jet mixture and the fluid from the jet flows down the expiratory outlet rather than continue towards the nares. By these changes in the flow, the device follows the breathing requirements of the infant allowing spontaneous inhalation and exhalation with only minimal variations in CPAP during the breathing cycle. The Benveniste pediatric gas jet device generates pressure at the level of the nasal interface. It was initially used in conjunction with facemask or endotracheal tube to deliver CPAP in neonates [57]. A study of the subsequent use of the device to deliver nasal CPAP demonstrated that a high gas flow of 14 LPM was required to create a pressure of between 3 and 10.5 cm H_2O in the oropharynx. No significant difference was evident in oropharyngeal pressure whether the flow was delivered by single or binasal tube [58]. The Benveniste jet device, in conjunction with a binasal tube (Argyle), has been described as a simple and effective nasal CPAP system for the treatment of respiratory distress in the preterm neonate [38]. Recently, greater lung recruitment, better breathing patterns, and lower inspiratory work of breathing have been demonstrated during variable versus constant flow nasal CPAP [44,59].

The modes of pressure generation can be varied independently of nasal interfaces; however, the manufacturers of the Infant Flow and Arabella Generators nasal devices recommend exclusive use of the Infant Flow Driver as the flow source for their devices. As evident from the above description there exists a multiplicity of nasal CPAP delivery systems. Not all devices are similar and success with nasal CPAP may be device specific. Further studies need to focus on the most effective nasal CPAP interface and the best mode of pressure generation for the delivery of nasal CPAP.

Experience with CPAP at other centres

In 1968, Harrison demonstrated that insertion of an endotracheal tube in an infant with RDS eliminated the ability to grunt and was associated with a fall in arterial oxygenation [60]. That observation was the basis for the study by Gregory *et al.* [12], which demonstrated that application of CPAP through an endotracheal tube ($n=18$) or plastic chamber ($n=2$) resulted in an increase in arterial oxygen tension of almost 80 mm Hg. There was no significant change in $PaCO_2$ or respiratory rate. Positive airway pressure in this system was generated by varying the degree of occlusion of the tail of a respiratory bag. It is noteworthy that 10 infants had apnea before application of CPAP that resolved with placement of the device. It is remarkable that CPAP has been used for more than 30 years, yet there are still many unanswered questions regarding its clinical use (see below). Most fundamentally, it is still unknown whether use of nasal prong CPAP (as practiced at Columbia University) is associated with a reduction in the incidence of BPD *and* acceptable neurological outcomes.

The Cochrane Library has multiple entries for CPAP including meta-analyses for infants with respiratory distress (treated with or without surfactant), preterm infants with apnea, and in preterm infants following extubation. While the data suggest that nasal CPAP following intermittent positive pressure ventilation reduces the incidence of 'extubation failure', other analyses are not as definitive. Ho, Subramaniam, Henderson-Smart, and Davis concluded that continuous distending pressure in spontaneously breathing infants with RDS was effective in decreasing the incidences of respiratory failure and mortality [61]. However, the four trials included for review [17,62–64] were conducted in the 'pre-surfactant and antenatal steroid era' and used techniques for generating continuous

Table 3. Need for mechanical ventilation and incidence of BPD during two time periods: early CPAP used or not used routinely

	Need for ventilation			Incidence of BPD	
	CPAP used	No CPAP	CPAP type	CPAP used	No CPAP
Lindner	40%†	84%†	NP	12%*	35%*
Gitterman	30%	53%	IFD	32%	30%
Joris	31%	72%	IFD	8%	15%
De Klerk	14%*	65%*	BCPAP	0%*	11%*
Aly	—	—	BCPAP	27%*	56%*
Jacobsen	35%*	76%*	IFD	42%	42%

†Need for intubation in the DR.
*$P<0.05$.
NP=Nasal prongs; IFO, infant flow driver; BCPAP, bubble CPAP.

distending pressure that are not commonly employed including a negative pressure chamber [62], face mask CPAP [17,63], and endotracheal CPAP [64]. Furthermore, most of the improvement in mortality was in infants >1500 grams. CPAP was associated with an increased rate of pneumothorax. In a second meta-analysis by Subramanian *et al.* [65], the benefits of prophylactic nasal continuous positive airway pressure were evaluated. Only a single study was considered suitable [66], and in that study naso-pharyngeal CPAP did not improve the outcome of infants with RDS. The authors concluded that there were insufficient data to make clinical recommendations. A number of investigators [67–72] have examined outcomes in their nurseries during a time period when CPAP was not used prophylactically with a later period in which infants were placed on CPAP shortly after birth (Table 3). While these were not prospective randomized trials, most demonstrated a reduction in the need for mechanical ventilation and half of them noted a significant reduction in the incidence of BPD.

The optimal time for the application of CPAP was addressed in five controlled trials [73–77]. Each evaluated early vs late initiation of CPAP ($n=129$). In these studies, early application of CPAP was associated with a significant reduction in the subsequent need for mechanical ventilation (absolute reduction 20.6%) and in the duration of ventilatory assistance (mean difference 33.7 h). The incidence of air leaks and the mortality rate failed to reach statistical significance. Once again however, these studies were performed during a time period when surfactant and antenatal steroids were uncommonly used.

One of the concerns with the use of nasal CPAP in very low birth weight infants with surfactant deficiency is that respiratory failure may occur over hours to days, and delay the administration of surfactant until intubation/ventilation is needed. Therefore, some centres have recommended that surfactant be administered shortly after birth, followed quickly by extubation. This hypothesis has been addressed in two large trials. Verder *et al.* [78] randomized preterm infants with RDS ($n=60$) to receive a single dose of Curosurf either immediately after randomization or when the arterial-to-alveolar oxygen tension fell below 0.22. Nasal CPAP was begun at a median age of 17 min after birth and randomization occurred at a median age of 4.3 h. The need for mechanical ventilation was reduced from 68% in the late-treated infants to 25% in the early-treated infants. Among infants born to women receiving antenatal steroids the outcome was even better. In a recent multicenter IFDAS trial [79], infants were randomized to one of four groups: (1) early nasal CPAP (infant flow driver) and prophylactic surfactant (Curosurf administered within 15 min and extubation occurred within 2 h), (2) early nasal CPAP ± early rescue surfactant (extubation within 2 h), (3) early IPPV and prophylactic surfactant and (4) early IPPV ± rescue surfactant. Randomization included 241 infants at 14 centres. In infants who received at least one-dose antenatal steroids, nasal CPAP reduced the need for mechanical ventilation in the first 5 days of life. However, none of the strategies reduced the total duration of respiratory support or oxygen dependency at 28 days or 36 weeks post-conceptional age.

Table 4. Clinical characteristics of infants <1500 g in Children's Hospital of New York and Vermont Oxford Network

	Children's Hospital of New York			Vermont Oxford		
	2000 (%)	1999 (%)	1998 (%)	2000 (%)	1999 (%)	1998 (%)
Nasal CPAP	87	88	87	56	52	51
Conventional ventilation	42	46	32	68	68	69
High frequency ventilation	8	6	2	23	23	22
Surfactant	27	19	15	61	61	60
Steroids for CLD	4	1	1	22	26	27
Oxygen@36 weeks	10	7	7	36	33	31
Died	16	14	19	16	16	16

Table 5. Experience with CPAP at Columbia University (1999–2001)

Weight (gm)	CPAP (*N*)	CPAP %*	CPAP/IMV (*N*)	CPAP/IMV %*	Expired
1251–1500	123	(83%)	25	(17%)	(7%)
1001–1250	61	(70%)	26	(30%)	(3%)
751–1000	47	(47%)	27	(53%)	(9%)
501–750	20	(26%)	57	(74%)	(39%)

*% of infants managed with CPAP or CPAP and ventilation.

Experience with nasal CPAP at Columbia University

Nasal CPAP has been used for more than 25 years at the Children's Hospital of New York, and despite anecdotal reports that the incidence of chronic lung disease is less at Columbia University [80], there has been little interest by other centres in evaluating this technology. All spontaneously breathing infants with respiratory distress and a supplemental oxygen requirement are placed on nasal CPAP by our nursing staff. CPAP is usually initiated between 5 and 10 min of life. Table 4 summarizes our experience with nasal CPAP for the years 1998–2000 and compares outcomes with the hospitals in the Vermont Oxford Network.

As noted above, the intensive care nursery at Columbia, uses CPAP more liberally, ventilates fewer infants, uses less sedation, postnatal steroids, and surfactant, and has a much lower incidence of chronic lung disease (defined as a need for supplemental oxygen at 36 weeks' gestation). Our success with nasal CPAP results from a number of variables which extend far beyond the cognitive decision to initiate it in an infant with respiratory distress. Table 5 summarizes our experience with nasal CPAP in different birth weight categories at Columbia University. About 80% of infants with RDS weighing 1251–1500 g, can be successfully managed with nasal CPAP alone. However, three-quarters of our tiniest infants (501–750 g), ultimately require mechanical ventilation.

To determine, why nasal CPAP is effective in some infants and not in others, we analysed the clinical course of 24 infants admitted to our NICU in 2001 weighing <1000 g. Twelve of the infants remained on CPAP and never required mechanical ventilation, and 12 others failed CPAP and required intubation and ventilation (Tables 6–8). All of the mothers received antenatal steroids. In infants with RDS, our guideline is to intubate if ventilation is inadequate ($PaCO_2$>65 torr and pH<7.2) or oxygenation is worsening or inadequate with a $FiO_2 \geq 0.6$. The infants successfully managed with nasal CPAP weighed significantly more than those requiring ventilation ($P=0.049$), and there was a trend to increased disease severity (lower PaO_2/FiO_2 ratio) among infants failing CPAP ($P=0.09$). Failure occurred at a mean age of 29.7 ± 18 h. The

Table 6. Comparison of infants ≤1000 g with RDS managed successfully with CPAP or requiring intubation after a trial of CPAP

	N	Weight (gm)	Gestational age (weeks)	pH†	$PaCO_2$†	PaO_2/FiO_2†
CPAP	12	758 ± 152*	25.9 ± 2.0	7.31 ± 0.06	44 ± 9	229 ± 96**
CPAP/vent	12	646 ± 110	25.0 ± 1.4	7.32 ± 0.05	42 ± 6	156 ± 84

†First postnatal arterial blood gas.
*P=0.049, CPAP vs CPAP/vent.
**P=0.09, CPAP vs CPAP/vent.

Table 7. Infants ≤1000 g with RDS requiring intubation after a trial of CPAP

Time of intubation (h)	pH*	$PaCO_2$* (mmHg)	PaO_2/FiO_2*	Duration vent (PCA-wks)	Duration O_2 (PCA-wks)
29.7 ± 18	7.19 ± 0.09	63 ± 16	133 ± 86	27.1 ± 1.8	32.1 ± 4.6

*Blood gases at time of intubation.
PCA=Post-conceptional age.

Table 8. Infants ≤1000 g with RDS managed successfully with CPAP

Duration CPAP (PCA-wks)	Duration O_2 (PCA-wks)
34.5 ± 2.2	30.0 ± 3.3

PCA=Post-conceptional age.

group of infants requiring ventilation no longer required supplemental oxygen by a post-conceptional age of 32.1 ± 4.6 weeks. That compares with 30.0 ± 3.3 weeks in infants who only required CPAP. Nasal CPAP is generally continued for long periods of time at our hospital (34.5 ± 2.2 weeks M ± SD post-conceptional age). However, efforts to wean CPAP are often not made until 32 weeks' gestation or beyond.

Unanswered questions

Despite clinical evidence of effectiveness of nasal CPAP and technological advances in its delivery the optimal way of utilizing CPAP in the management of infants with respiratory support requirements, especially in the era of widespread use of antenatal steroids and exogenous surfactant, remains unclear. Some of the issues that need to be addressed in well-designed, prospective, and randomized control trials include: What constitutes good or effective CPAP? Which mode of pressure generation for the delivery of nasal CPAP and which type of nasal CPAP interface most effectively reduce the need for additional respiratory support? What are the optimum pressure levels? What is the best timing, duration of treatment, and weaning strategy with CPAP use? Does ongoing CPAP support for relatively prolonged periods without supplemental oxygen enhance lung growth and aid in recovery of the injured lung? Are there increases in adverse non-respiratory outcomes with nasal CPAP based-approaches of respiratory care? What are the long-term outcomes, especially neurodevelopmental, associated with use of CPAP? Is the reported success with nasal CPAP reproducible at other centres? No single study could adequately address all or even many of these issues simultaneously, and it may be necessary to test individual components and strategies in a series of controlled studies to determine the overall best approach. Long-term neurodevelopmental follow-up needs to be a priority of any such trials.

Recommendations

Based on the available information and our experience, nasal CPAP seems to have a central role in

management of infants with RDS. Spontaneously breathing preterm infants with RDS weighing <1500 g should be allowed time on nasal CPAP to determine if they can achieve acceptable ventilation and oxygenation. During that time period, these infants must be monitored very closely. If ventilation is not improving or oxygenation is worsening or inadequate with FiO_2>0.6 these infants should be intubated and exogenous surfactant should be given. Even in developing countries, where resources are limited, CPAP should significantly improve morbidity and mortality associated with RDS in preterm infants. There is a learning curve to the implementation of nasal CPAP-based respiratory approach, and a team effort is required for success. It is our strong belief that a CPAP-based strategy similar to that practised at Columbia can and will produce a consistent, reliable, and reproducible decrease in adverse respiratory and perhaps some non-respiratory outcomes, if applied and maintained meticulously. However, further prospective research is required to validate this belief.

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