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Review

# Continuous positive airway pressure: Physiology and comparison of devices

Samir Gupta [a, *], Steven M. Donn [b]

[a] Department of Paediatrics, University Hospital of North Tees and University of Durham, Stockton-on-Tees, UK
[b] Department of Pediatrics, Division of Neonatal–Perinatal Medicine, C.S. Mott Children's Hospital, University of Michigan Health System, Ann Arbor, MI, USA

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S U M M A R Y

Nasal continuous positive airway pressure (CPAP) is increasingly used for respiratory support in preterm babies at birth and after extubation from mechanical ventilation. Various CPAP devices are available for use that can be broadly grouped into continuous flow and variable flow. There are potential physiologic differences between these CPAP systems and the choice of a CPAP device is too often guided by individual expertise and experience rather than by evidence. When interpreting the evidence clinicians should take into account the pressure generation sources, nasal interface, and the factors affecting the delivery of pressure, such as mouth position and respiratory drive. With increasing use of these devices, better monitoring techniques are required to assess the efficacy and early recognition of babies who are failing and in need of escalated support.



## 1. Introduction

Continuous positive airway pressure (CPAP) is the most extensively studied non- invasive respiratory support technique in preterm babies. It has been tested as a primary form of respiratory support and as continuing support after extubation from mechanical ventilation. The rationale for the use of CPAP is to stent the airways and to maintain functional residual capacity (FRC). The mechanism of action is multifactorial and includes an increase in the pharyngeal cross-sectional area, improvement in diaphragmatic activity, enhanced pulmonary compliance, and decreased airway resistance. The end result is a reduction in the work of breathing and conservation of surfactant on the alveolar surface.

CPAP works by delivering continuous distending pressure (CDP) using an air/oxygen mixture and a device to generate the CDP. The method of generating nasal CPAP (nCPAP) differs among devices but may be broadly grouped into two main types: "variable flow" or "continuous flow." For example, the Infant Flow® driver (IFD) is a variable-flow device and bubble CPAP (bCPAP) is a continuous-flow device [1]. In this article we discuss the physiologic effects of CPAP, factors affecting delivery of CPAP, and the evidence comparing various types of CPAP devices.

## 2. Respiratory physiology and CPAP

The full physiologic mechanism by which CPAP improves respiratory function in newborns is incompletely understood. During spontaneous breathing, CPAP augments the driving pressure required to overcome the elastic, flow-resistive, and inertial properties of the respiratory system. This is achieved by changes in intra-pleural pressure normally generated by the respiratory muscles that help to maintain FRC [2].

The very compliant chest wall and paradoxical inward rib-cage motion in very premature newborn infants result in lowered FRC that may result in airway closure, alveolar atelectasis, and ventilation–perfusion mismatch. In response, the infant tries to elevate the FRC above the relaxation volume by generation of intrinsic end-expiratory pressure through an increase in the tonic activity of the diaphragm, a higher than normal respiratory rate, and laryngeal braking or glottic closure during expiration. Positive pressure applied to the airway helps to support the infant's own effort to increase FRC. Physiologic studies suggest that CPAP, by increasing end-expiratory lung volume, stabilizes the highly compliant chest wall, thereby improving pulmonary mechanics and thoraco-abdominal synchrony [3].

* Corresponding author. Address: Research & Development, University Hospital of North Tees, Stockton-on-Tees, Cleveland TS19 8PE, UK. Tel.: +44 1642 624232.
*E-mail address:* Samir.gupta@durham.ac.uk (S. Gupta).

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The upper airway also plays an important role in the respiratory mechanics of the premature infant. The increased flexibility of the epiglottis and the laryngeal cartilage, and the decreased connective tissue support of the upper airway structures predispose the infant to partial or complete airway obstruction during regular breathing. The more cephalad position of the larynx further exacerbates upper airway resistance. CPAP may produce mechanical splinting of the upper airway by increasing its cross-sectional area and preventing collapse of the lateral pharyngeal walls. This, in turn, decreases the resistance to gas flow (Box 1).

Respiratory inductance plethysmography (RIP) has been used to study the effects of various CPAP systems by measuring the thoraco-abdominal synchrony, tidal volume, and FRC. Evidence from RIP studies suggests that the application of CDP from CPAP results in increased end-expiratory lung volume. However, RIP has some limitations, as it does not equate to an absolute level of FRC, and the validity of the changes in FRC apply only when the body posture is maintained during measurements. The level of CPAP also dictates the FRC. Excessive CPAP may be deleterious by increasing work of breathing, causing a fall in tidal volume, and by producing adverse cardiovascular effects.

### 2.1. CPAP and the upper airway

nCPAP of $\geq$5 cm$H_2O$ is effective in abolishing mixed or obstructive apnea, but has little or no effect on central apnea [4]. Miller et al. studied the manner in which CPAP exerts this selective effect on apnea accompanied by supraglottic airway obstruction. They studied 10 infants with a history of apnea at a postconceptional age of 34 $\pm$ 2 weeks (birth weight 1321 $\pm$ 310 g) post extubation. The CPAP was applied by nasal mask and pressures were recorded in the mask, oropharynx and esophagus. nCPAP between 0 and 5 cm$H_2O$ correlated with the oropharyngeal pressure ($r = 0.94$). The supraglottic resistance decreased from 46 $\pm$ 29 to 17 $\pm$ 16 cm$H_2O$/L/s ($P < 0.005$) during uptitration of CPAP from 0 to 5 cm$H_2O$. The decrease in supraglottic resistance was observed both during inspiration and expiration, accounting for 60% of the change in total pulmonary resistance at CPAP of 5 cm$H_2O$ [5]. The supraglottic airway of apneic infants thus appears to be a potential site of high resistance during sleep, as simple flexion of the neck may produce airway obstruction.

### 2.2. Effect of mouth position

The effect of mouth position on pharyngeal pressure was shown by DePaoli et al. in preterm infants receiving bubble CPAP (bCPAP) with the mouth open and closed. They studied 11 infants at a median postnatal age (interquartile range) of 14 (12–46) days and at a mean (SD) corrected gestation of 30.6 (1.9) weeks. bCPAP with binasal Hudson prongs at CPAP 3–8 cm$H_2O$ was utilized. They reported a mean (95% confidence interval (CI)) pressure fall from prongs to pharynx of 3.2 (2.6–3.7) cm$H_2O$ with the mouth open, and 2.2 (1.6–2.8) cm$H_2O$ with the mouth closed. The mean difference in pharyngeal pressure between open and closed mouth positions was 1.1 (0.7–1.4) cm$H_2O$ ($P < 0.05$) [6].

**Box 1**

Physiologic effects of continuous positive airway pressure.

- Abolition of upper airway occlusion and decrease in upper airway resistance
- Increased diaphragmatic tone and contractility
- Improvement in lung compliance and reduction in airway resistance
- Increased tidal volume of the stiff lung with low functional residual capacity
- Improved ventilation/perfusion and reduction in oxygen requirement
- Conservation of surfactant on alveolar surface and reduction of alveolar edema

### 2.3. Effect of CPAP on breathing pattern

The high chest wall:lung compliance ratio of premature newborns tends to reduce the passive resting volume of the respiratory system to a level that is close to airway closing volume. The end-expiratory lung volume of premature newborns is maintained above passive resting lung volume during active breathing through the combination of an increased time constant and a high respiratory rate. This is achieved by the persistence of inspiratory muscle activity during the expiratory phase and adduction of the vocal cords during expiration, which prolong the time constant of the respiratory system by decreasing inspiratory resistance. In addition, the high breathing rate decreases the expiratory time with incomplete emptying of the lungs. These two mechanisms dynamically elevate the end-expiratory lung volume [7]. The dynamic elevation of FRC occurs when the expiratory time is <3 time constants.

nCPAP is believed to benefit preterm infants with respiratory distress. It improves respiratory function by splinting the upper airway, improving the synchrony of thoracic and abdominal motion [8], and increasing end-expiratory lung volume [9].

### 2.4. Effect of different levels of CPAP

Elgellab et al. studied different levels of CPAP (0, 2, 4, 6, and 8 cm$H_2O$) to determine its effect on breathing patterns and changes in lung volumes, using RIP. They observed an increase in end-expiratory lung volume (EELV) by 2.1 $\pm$ 0.3 $\times$ tidal volume ($V_t$) as the CPAP level was increased from 0 to 8 cm$H_2O$ ($P < 0.01$). Tidal volume also increased by 43% ($P < 0.01$), and the phase angle decreased from 76% to 30% ($P < 0.01$) when CPAP was increased from 0 to 8 cm$H_2O$ (Fig. 1). They concluded that nCPAP improves the breathing of premature infants with respiratory failure through improved thoraco-abdominal synchrony, increased tidal volume, and a reduced labored breathing index [10].

Magnannent et al. reported a dynamic elevation of FRC with nCPAP, and the spontaneous volume-preserving expiratory flow-


| NCPAP (cm $H_2O$) | 0 | 2 | 4 | 6 | 8 |
|---|---|---|---|---|---|
| Phase angle | 66° | 71° | 25° | 6° | 4° |

**Fig. 1.** Lissagous figures and phase angles (degree) at various nasal continuous positive airway pressure (NCPAP) levels. As the nasal CPAP level increased there was improvement in rib cage (chest) movement and decrease in phase angle, i.e. thoraco-abdominal asynchrony. RC, rib cage; AB, abdominal wall. (Adapted from Elgalleb et al. [10].)

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braking mechanisms normally present in preterm infants with respiratory distress were not required during CPAP therapy. This conclusion was based on the decreased phase angle changes between the abdominal and thoracic compartments and increased tidal volume during nCPAP [11].

As there is a direct relationship between the nCPAP the EELV, a theoretical risk of overdistension exists in preterm infants at higher CPAP levels. If high nCPAP levels result in hyperinflation of the lung, this may have deleterious effects by causing a decrease in compliance, thoraco-abdominal asynchrony, and placing the diaphragm at a mechanical disadvantage. Interestingly, in the study by Elgalleb et al. [10] using IFD CPAP, one infant exhibited worsening respiratory failure at a CPAP of 8 cm$H_2O$. This raises the question of what is the optimum nCPAP level and suggests variability between continuous and variable flow devices.

The outcome of different levels of CPAP in clinical situations depends not only upon the type of CPAP used, but also upon the severity of underlying lung disease [12].

## 3. Methods of generating CPAP

CPAP is derived from either continuous or variable gas flow. Continuous-flow CPAP consists of gas flow directed against the resistance of the expiratory limb of the breathing circuit. Ventilator-derived CPAP and bubble or water-seal CPAP are examples of continuous-flow devices. In variable-flow CPAP, pressure is generated at the airway proximal to the infant's nares and uses the Bernoulli effect to alter the gas flow to maintain constant pressure.

### 3.1. Variable-flow CPAP

#### 3.1.1. Infant Flow Driver (IFD)

The Infant Flow CPAP system™ (Electro Medical Equipment Ltd, Brighton, UK; Infant Flow® SiPAP System, CareFusion®, San Diego, USA) is an example of variable-flow CPAP. It uses a dedicated flow driver and gas generator with a fluidic-flip mechanism to deliver variable flow (Fig. 2). The principle of IFD CPAP is the Bernoulli effect, which directs gas flow towards each naris, and the Coanda effect to cause the inspiratory flow to flip and exit the generator chamber via the expiratory limb. This may assist spontaneous breathing and reduce the work of breathing by decreasing expiratory resistance and maintaining stable airway pressure throughout respiration [13]. CPAP may be delivered with binasal prongs or a nasal mask.

#### 3.1.2. Benveniste gas-jet valve CPAP

This is an alternative variable-flow system. The device consists of two coaxially positioned tubes connected by a ring. It works via the Venturi principle to generate pressure. It is connected to a blended gas source and then to the patient via nasal prongs, generating variable-flow CPAP [14].

### 3.2. Continuous-flow CPAP

#### 3.2.1. Bubble CPAP

Underwater or bCPAP or water-seal CPAP is a continuous-flow system. It was first described in 1914 and has been in use since the early 1970s (Fig. 3) [15]. Blended gas is heated and humidified and delivered to the infant through a secured low-resistance nasal-prong cannula. The distal end of the expiratory tubing is submersed and the CPAP generated is equal to the depth of submersion of the expiratory limb. Chest vibrations produced by bCPAP may contribute to gas exchange [16].

#### 3.2.2. Ventilator-derived CPAP (conventional CPAP)

Ventilator-derived CPAP is another way of providing continuous flow CPAP. The CPAP is increased or decreased, in general, by varying the ventilator's expiratory orifice size. The exhalation valve works in conjunction with other controls, such as flow and pressure, to maintain the desired CPAP.

#### 3.2.3. CPAP interface

The interfaces currently used for the delivery of nCPAP include single and binasal prongs in short (6–15 mm) and long (40–90 mm) versions. Short binasal prongs include Hudson, Argyle, INCA, and those used with IFD and Bubble CPAP (Fisher & Paykel, Auckland, New Zealand), and examples of long CPAP prongs are nasopharyngeal tubes, endotracheal tubes, and Duotube.

In addition, nasal masks are available for use with CPAP systems. The older CPAP interfaces such as endotracheal tubes, head chambers (head boxes), face chambers, and full face masks are now obsolete. Nasal cannulas are also used to deliver air/oxygen and at high flows can provide CDP.

Evidence comparing nasal interfaces is sparse. Davis et al. compared binasal short Hudson prongs with a single long prong (Portex size: 2.5 or 3.0 mm, inserted to 2.5 cm). They randomized 87 infants before extubation to one of the two CPAP interfaces connected to the ventilator to provide nasal CPAP. This trial was stopped early before achieving the target sample size of 130. There was a significantly lower incidence of respiratory failure within seven days post extubation with short binasal prong use, but no differences in other outcomes [17]. Roukema et al. also compared short binasal prongs with nasopharyngeal prongs and reported a lower rate of reintubation with the use of short prongs [18]. This trial used different CPAP devices, thus making the interpretation difficult. In the trial by Mazzela et al., short binasal

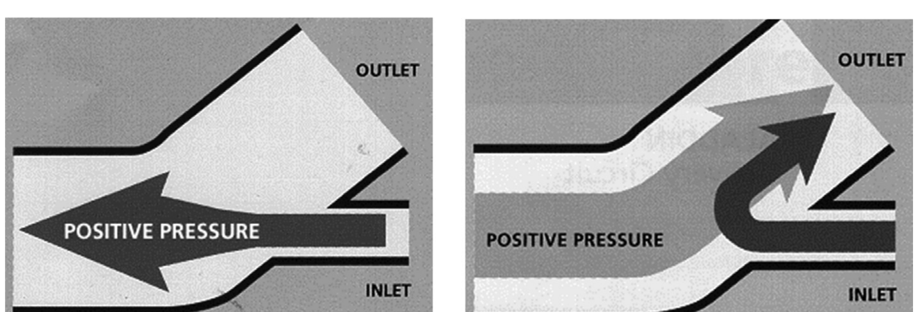


**Fig. 2.** Infant Flow Driver pressure generator. The variable-flow generator uses the Bernoulli principle via injector jets directed toward each naris; Venturi action allows the infant to draw additional gas flow through the injector jets from either the gas supply or exhalation tube reservoir. The dual-jet variable flow generator utilizes fluidic technology to deliver a constant continuous positive airway pressure.

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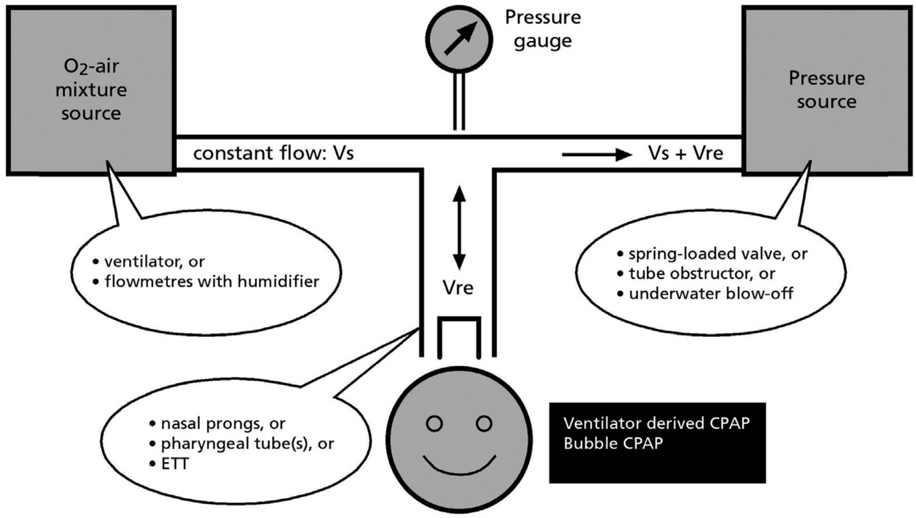


**Fig. 3.** Continuous-flow positive airway pressure (CPAP) system. ETT, endotracheal tube.

prongs and nasopharyngeal prongs were used, but the outcomes were not assessed beyond 48 h, and again the CPAP devices were different [19]. In the meta-analysis of the studies, De Paoli et al. concluded that short binasal prongs are more effective in reducing the rate of reintubation [20]. Another trial compared nasal prongs and nasal masks for delivering IFD CPAP in 120 babies <31 weeks of gestation. Mask nCPAP was more effective than nasal prong CPAP for preventing intubation within 72 h of starting therapy [21].

The pressure fall through various CPAP devices may differ according to the design, length, and the physical principle used for CPAP generation. De Paoli et al. compared resistances of different devices in vitro for delivery of nCPAP in neonates. They studied different devices at a flow of 4–8 L/min, and measured the resultant fall in pressure using a calibrated pressure transducer. They concluded that devices with short binasal prongs had the lowest resistance to flow, and suggested that a large variation in pressure could occur in the clinical setting [22].

## 4. Effect of bubbling on CPAP

The gas flow rate during bCPAP has been observed to affect the degree of bubbling. Bubbling may enhance gas exchange by delivering low-amplitude, high-frequency oscillations to the lungs.

Lee et al. observed vibrations of the chest secondary to vigorous bubbling while babies were receiving bCPAP. They tested this in a crossover design in 10 preterm babies ready for extubation to determine whether bCPAP results in better gas exchange than ventilator-derived CPAP. They measured tidal volume, minute volume, respiratory rate, pulse oximetry, and transcutaneous carbon dioxide. They reported a 39% reduction in minute volume ($P < 0.001$) and a 7% reduction in respiratory rate ($P = 0.004$) with no change in oxygenation or ventilation. They concluded that the chest vibrations produced by bCPAP might have contributed to gas exchange [16]. This study has been widely cited, but was done in the group of babies who had recovered from acute lung disease nearing extubation and in larger babies with a mean corrected gestational age of 30.7 ± 1.8 weeks and mean weight of 1350 ± 390 g. In addition, there appears to be an arithmetic error in the calculation of minute ventilation, inadvertently favoring ventilator-derived CPAP.

Morley et al. further studied the physiologic effects of bubble CPAP. They enrolled 26 babies at a median gestational age of 27 weeks (range 24–32) and a birth weight of 1033 g (range 604–1980). The nCPAP was used at 6 $cmH_2O$ (range 5–9). The baseline gas-flow rate was kept at 6 L/min (range 5–9), and the inspired oxygen at 0.21 (range 0.21–0.30). The median (interquartile range) pressure amplitude was 2.7 $cmH_2O$ (2.5–4.0) for slow bubbling (at 3 L/min) and 6 $cmH_2O$ (4.6–7.1) for vigorous, high-amplitude bubbling (at 6 L/min). They also reported slightly lower (effective CPAP) pressure with slow bubbling compared to vigorous (5.28 vs 5.98 $cmH_2O$; $P < 0.001$). They did not observe any effect of bubbling on transcutaneous carbon dioxide, oxygen saturation, respiratory rate, or minute ventilation [23].

Pillow and Travadi hypothesized that superimposing noise on the underlying constant pressure in bCPAP may promote lung volume recruitment and reduce intrinsic work of breathing. In an in-vitro model, they examined how lung compliance and applied flow altered the frequency and magnitude of the oscillatory component of bCPAP. They concluded that in a closed system, increasing flow increased both the mean pressure and the range of pressure oscillations, whereas decreasing compliance increased the frequency and magnitude of the transmitted oscillations. They suggested that the use of bCPAP in a poorly compliant lung may promote lung volume recruitment through stochastic resonance and augment the efficiency of gas mixing [24]. This study has limitations of an in-vitro model with no leak and the amplitude of transmitted oscillations may be greater than that observed in a clinical situation. However, some reports of visible chest vibrations have been reported in vivo with bCPAP.

In another study, Pillow et al. compared constant-pressure CPAP with bCPAP in a lamb model. They hypothesized that bCPAP enhances volume recruitment in the newborn preterm lung. They compared various physiologic parameters among three study groups in 32 lambs; bCPAP at 8 L/min flow ($n = 10$), constant-pressure CPAP ($n = 12$), and bCPAP at a flow of 12 L/min ($n = 10$). Flow did not influence 3 h outcomes in the bCPAP groups. The bubble technique was also associated with a higher $PaO_2$, oxygen uptake, and area under the flow-volume curve, and a decreased alveolar protein, respiratory quotient, $PaCO_2$, and ventilation homogeneity compared to the constant-pressure group. They concluded that bCPAP promotes airway patency and may offer protection against lung injury [25].

Kahn et al. compared delivered to intended intra-prong, proximal-airway, and distal-airway pressures using ventilator CPAP and bCPAP devices. They repeated measurements at five flow rates (4, 6, 8, 10, and 12 L/min) and three nasal CPAP pressure levels (4, 6, and 8 $cmH_2O$) under no, small, and large leak conditions. The authors concluded that the self-adjusting capability of ventilators allows closely matched actual versus intended ventilator CPAP levels. For bCPAP, at the range of flows used clinically, there were higher intra-prong and intra-airway bCPAP pressures at increasing flows than operator-intended levels, even when an appreciable leak was present [26].

The conflicting results discussed above highlight the need for standardization of clinical practices. These pressure, flow, and bubbling dynamics are very complex, and the in-vivo delivery of CPAP is dependent upon many other factors, including the severity of lung disease and the individual patient–device interaction.

## 5. Work of breathing and choice of CPAP

Although the initial use of nasal CPAP in preterm infants utilized the continuous-flow underwater device promoted by Gregory et al. in 1971 [15], there has been a wide variation in the choice of devices, especially since the introduction of variable flow first described by Moa et al. in 1988 [13].

Although the advantages of nCPAP on decreasing the work of breathing are well established, efforts to optimize CPAP delivery continue. Recent studies compared the work of breathing using variable versus continuous flow CPAP. The initial study of Moa et al. on a lung model claimed that despite a virtually constant pressure within the traditional CPAP system, variations in mean airway pressure and external workload were considerably less with the variable-flow device, which was also reported to be less sensitive to airway leakage [13].

Klausner et al. compared work of breathing between a variable and continuous flow device. They observed an imposed work of breathing with IFD CPAP of 0.135 mJ/breath (95% C $\pm$0.004) compared to 0.510 mJ/breath (95% CI $\pm$0.004) with conventional CPAP (difference $P < 0.01$) and concluded that imposed work of breathing with variable flow was approximately one-fourth that of the continuous-flow system [27].

## 6. Studies comparing variable-flow and continuous-flow devices

Multiple studies compared variable and continuous flow devices, albeit with different nasal interfaces. Measurements reported in these studies included changes in lung volume, thoraco-abdominal synchrony, resistance to breathing, and changes in pleural pressure measured with an esophageal balloon. Together, these studies reported advantages of the variable-flow device over the continuous-flow device at varying CPAP levels of 0, 4, 6, and 8 $cmH_2O$ water.

Courtney et al. compared three CPAP devices: continuous-flow nCPAP via prongs, continuous nCPAP via modified nasal cannula, and variable-flow nCPAP. The continuous-flow CPAP was generated using the CPAP mode on a conventional ventilator. The study was carried out in 32 premature infants with mild respiratory failure at a mean gestational age of 29 weeks, and the age at study was 13 days. After initial lung recruitment at 8 $cmH_2O$, they tested the breathing parameters at 8, 6, and 4 cm and compared with 0 $cmH_2O$ CPAP. Lung recruitment was better with the variable-flow device than with both the continuous flow devices. The breathing synchrony obtained with the continuous flow was similar to that with variable flow. They suggested that better lung recruitment with the variable-flow system could have resulted from decreased variability of the mean airway pressure as reported by Moa et al. [13] and Klausner et al. [27]. These differences could also be affected by the variations in the flow rates and the nasal interfaces. They also observed comparable lung volume recruitment with continuous flow and a modified nasal cannula compared to continuous-flow nasal prongs, but this was at the cost of higher thoraco-abdominal asynchrony, higher respiratory rates and higher $FiO_2$ requirements. They discouraged the use of nasal cannula CPAP [9].

In another study by Pandit et al., constant flow nCPAP was delivered by connecting INCA nasal prongs to an infant ventilator set on the CPAP mode, and compared to variable flow nCPAP using the Aladdin/IFD CPAP. They evaluated the work of breathing between the two systems using a crossover design at CPAP of 0, 4, 6, and 8 $cmH_2O$ in 24 preterm infants with mild respiratory distress born at a mean gestation of 28 weeks and at a mean postnatal age of 14 days. They calculated the inspiratory work of breathing and lung compliance using esophageal pressure measurements and standardized the results by dividing work of breathing by tidal volume. They reported decreased work of breathing at all CPAP levels with the variable-flow device, the greatest reduction being at a CPAP of 4 $cmH_2O$. Lung compliance increased with variable flow and decreased with continuous flow, except at 8 $cmH_2O$ when compliance decreased with variable flow and increased with continuous flow. The findings of this study, however, cannot be extrapolated to infants with moderate-to-severe lung disease requiring higher pressure [28].

Courtney et al. compared two variable-flow nasal CPAP devices: Infant Flow™ (EME, Brighton, UK) and Arabella® (Hamilton Medical™, USA). They assessed lung recruitment and work of breathing between the two devices in very low birth weight babies requiring nasal CPAP. In 18 infants at a mean (SD) birth weight of 1107 (218) g and a gestational age of 27.9 (2.0) weeks, there were no differences in lung volume recruitment at any nCPAP level ($P = 0.943$), inspiratory work of breathing ($P = 0.468$), or resistive work of breathing ($P = 0.610$) between devices [29].

The investigators also compared the work of breathing using bCPAP with Hudson prongs versus variable-flow nCPAP using the Viasys (CareFusion) system. They studied seven very low birth weight infants with mild respiratory distress on each device at a mean (SD) age of 8 (8.7) days. They reported a significantly lower inspiratory and resistive work of breathing with variable-flow CPAP at 6 and 4 $cmH_2O$ pressure [30].

As many of the previously reported studies advocated the use of a ventilator to deliver continuous-flow nasal CPAP, the study by Lipsten et al. compared work of breathing and breathing asynchrony during bCPAP versus variable-flow nCPAP in 18 premature infants with a mean gestation of 28 weeks and a birth weight of 1042 g at a mean postnatal age of 9.4 days. Their findings were consistent with the previously reported studies, showing an increased respiratory rate, phase angle, and resistive work of breathing with bCPAP. Interestingly, the inspiratory work of breathing, minute ventilation, and tidal volume were similar between the two groups. They explained the observed differences in resistive work of breathing and asynchrony as relevant during expiration only, not during inspiration. The total work of breathing with bCPAP was also not as markedly increased as reported in the other studies with continuous flow, ventilator-derived CPAP. They speculated that bCPAP may provide an advantage [31].

Kahn et al. compared the work of breathing between bCPAP and ventilator-derived CPAP. They studied 10 preterm babies with mild respiratory distress at a mean gestation of 28.8 $\pm$ 1.9 weeks and a postnatal age of 11 $\pm$ 7 days. Each infant was studied on both devices in a randomized crossover design and the nCPAP pressure was varied as 3, 5, 7, 4, and 2 cm $H_2O$ (in that order). They observed identical intra-prong pressures and similar inspiratory work of breathing between the two devices. They concluded that when intra-prong pressures were controlled, the inspiratory work of breathing was no different between the devices [26].

The available data on the work of breathing and the choice of nCPAP device address the important issue of the intended and the actual airway-distending pressure. The data also highlight the differences in the inspiratory and resistive work of breathing across the available devices. It is important to recognize these differences, but it will be more pertinent to relate these findings to clinically relevant outcomes in clinical trials.

### 6.1. Cardiovascular effects of CPAP

There are limited data on the hemodynamic effects of CPAP in preterm newborns. An animal study by Adams et al. reported the hemodynamic effects produced by CPAP and continuous negative extrathoracic pressure (CNEP). CPAP and CNEP of 4 and 8 $cmH_2O$ were compared in eight normal, spontaneously breathing piglets. Arterial blood gases and hemodynamic measurements were obtained before and during CPAP and CNEP. At 8 $cmH_2O$, CPAP and CNEP produced significant increases ($P < 0.01$) in $PaO_2$ from baseline. No significant changes occurred in $PaCO_2$ or cardiac index, except during CPAP of 8 $cmH_2O$, the $PaCO_2$ increased significantly ($P < 0.05$), and cardiac index decreased ($P < 0.05$). During CPAP of 4 $cmH_2O$, there were significant increases in mean right atrial pressure ($P_{ra}$), left ventricular end-diastolic pressure (LVEDP), and mean pulmonary artery pressure ($P_{pa}$). CPAP of 8 $cmH_2O$ produced marked increases in $P_{ra}$, LVEDP, and $P_{pa}$ [32].

## 7. Comparison of CPAP devices

nCPAP has been used immediately after birth for the management of RDS and after extubation for providing respiratory support to preterm babies. Investigators have compared ventilator-derived CPAP, bCPAP, and IFD CPAP in observational studies and clinical trials.

### 7.1. Cohort and observational studies

The cohort study by Narendran et al. incorporated the introduction of bCPAP in one hospital and conventional nCPAP at another for the management of preterm babies with RDS (birth weights 401–1000 g). The data were collected on all extremely low birth weight babies and compared to historical controls and between the hospitals. They reported a reduction in delivery room intubations with the use of both bCPAP and conventional nCPAP compared to historical controls ($P < 0.001$). There was also a significant reduction in the use of postnatal steroids with bCPAP, but not with conventional nCPAP ($P < 0.001$), and a trend towards a reduction in chronic lung disease with bCPAP [33].

In an observational study from Canada, Pelligra et al. reported a comparison of two time-periods; the first used ventilator-derived CPAP with a nasopharyngeal tube, and the second used bCPAP. Data from 821 babies <32 weeks (397 babies in period 1, and 424 babies in period 2) were analyzed. There was a significant reduction in the use of exogenous surfactant, postnatal steroids, and in the duration of mechanical ventilation with the use of bCPAP [34].

In another observational study, Massaro et al. collected data on 36 preterm babies <2000 g who were solely managed on nCPAP over a period of 16 months. They grouped the babies into those who received bCPAP support and those who received ventilator-derived CPAP at the same pressures. The groups were demographically equivalent. The authors reported no differences in the duration of nCPAP support and other clinical outcomes, except that babies managed on bCPAP required oxygen for a shorter duration [35].

Although these observational studies suggest advantages with bCPAP, the heterogeneity of the data warrants further evidence from well-designed randomized trials. There were no observational studies comparing IFD CPAP and continuous-flow CPAP devices.

### 7.2. Randomized trials

#### 7.2.1. Randomized controlled trials at birth

Mazzela et al. compared IFD CPAP with binasal prongs and bCPAP through a single nasopharyngeal prong. They randomized 36 preterm infants <36 weeks of gestation at <12 h of age to receive one of the CPAP modes. They reported a significant beneficial effect on both oxygen requirement and respiratory rate ($P < 0.0001$) with IFD CPAP, compared to bCPAP, and a trend towards a decreased need for mechanical ventilation. This study, however, was limited by a small sample size and the use of different nasal interfaces [19].

McEvoy et al. randomized 53 spontaneously breathing preterm babies between 25 and 32 weeks of gestation to receive either bCPAP or ventilator-derived CPAP using Hudson prongs after initial stabilization. The respiratory measurements (FRC and compliance) and CPAP failure through seven days were compared. They observed no differences in the respiratory measurements, CPAP failures, surfactant use, days on CPAP, and oxygen need and BPD at 36 weeks between groups [36].

Tagare et al. compared the efficacy and safety of bCPAP with ventilator-derived CPAP in preterm neonates with respiratory distress. Preterm neonates with a Silverman–Anderson score ≥4 and oxygen requirement >30% within first 6 h of life were randomly allocated to bCPAP or ventilator-derived CPAP and the proportion of neonates succeeding was compared. In all, 47 of 57 (82.5%) neonates receiving bCPAP and 36 of 57 (63.2%) receiving ventilator-derived CPAP did not require mechanical ventilation ($P = 0.03$), suggesting superiority of bCPAP for managing preterm neonates with early onset respiratory distress [37].

Mazmanyan et al. randomized 125 infants <37 weeks of gestation to bCPAP or IFD CPAP after stabilization at birth in a resource-limited setting. bCPAP was equivalent to IFD CPAP in the total number of days needing CPAP within a margin of 2 days. The median days (range) for the primary outcome (days on CPAP) were 0.8 days (0.04–17.5) on bCPAP, and 0.5 days (0.04–5.3) on IFD CPAP [38]. It is difficult to determine whether study infants required CPAP support or were put on CPAP as part of the trial, as the duration of support is less than a day in both study arms. The results of this trial should be interpreted with caution in extremely and moderately premature babies, as the study group was more mature, but it is a reassuring finding for a population of larger babies in a developing country [38].

The trial by Bhatti et al. compared Jet-CPAP (variable flow) and bCPAP in 170 preterm newborns <34 weeks of gestation with respiratory distress within 6 h of birth. CPAP failure rates within 72 h were similar in infants who received Jet-CPAP and in those who received bCPAP (29% versus 21%; relative risk 1.4 (95% CI 0.8–2.3), $P = 0.25$). Mean (95% CI) time to CPAP failure was 59 h (54–64) in the Jet-CPAP group compared to 65 h (62–68) in the bCPAP group. In this well-designed trial, no difference was reported between the two study devices; however, the investigators did not stratify babies by severity of respiratory illness or gestational age [39].

#### 7.2.2. Randomized trials after extubation

The initial studies compared IFD CPAP with ventilator-derived CPAP, using either binasal prongs or nasopharyngeal prongs with ventilator-derived CPAP.

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Sun et al. randomized 73 premature babies >30 weeks of gestation and birth weight >1250 g to IFD CPAP or ventilator-derived CPAP with binasal prongs. They reported that 19/35 (54%) babies receiving ventilator-derived CPAP met failure criteria versus 6/38 (16%) on IFD CPAP ($P < 0.001$). The results favored IFD CPAP over ventilator-derived CPAP in this population [40]. Stefanescu et al. randomized 162 extremely low birth weight infants after extubation from mechanical ventilation to receive either IFD CPAP or conventional CPAP through a ventilator using INCA prongs. The primary outcome for this study was the need for reintubation in the first seven days after extubation. The investigators found no difference in the extubation success rate between the two study groups [41].

The trials by Sun et al. and Stefanescu et al. did not stratify babies by duration of ventilation. The demographic differences in the trials also make it difficult to draw concrete conclusions but the results suggest that IFD CPAP is either superior to or has similar efficacy to ventilator-derived CPAP when used after extubation.

Roukema et al. randomized 93 very low birth weight infants to IFD CPAP or nasopharyngeal CPAP. In their trial, 27/45 (60%) failed extubation on nasopharyngeal CPAP versus 18/48 (38%) on IFD CPAP ($P = 0.0006$). These results should be interpreted with caution, as there is heterogeneity in the nasal interface used in the study. They used short binasal prongs with IFD CPAP but a nasopharyngeal prong for the delivery of ventilator-derived CPAP [18]. De Paoli et al. stressed in their meta-analysis that a comparable nasal interface is needed to allow comparison of CPAP pressure generation systems in randomized trials, and thus the results of Roukema et al. have limited usefulness [20].

In a subsequent trial Gupta et al. randomized 140 preterm infants 24–29 weeks of gestation or 600–1500 g at birth to receive bCPAP or IFD CPAP at the first attempt at extubation [42]. Infants were stratified according to duration of initial ventilation (≤14 days or >14 days). Babies were extubated when they passed a minute ventilation test used to assess objectively readiness for extubation [43]. The primary outcome of the study was the need for reintubation within 72 h. If an infant required reintubation, then the same CPAP device to which the infant was initially randomized was used at subsequent extubation until the infant was no longer requiring respiratory support. Although there was no statistically significant difference in extubation failure rates (16.9% on bCPAP, 27.5% on IFD CPAP), the median duration of CPAP support was 50% shorter in the infants on bCPAP (median 2 days, 95% CI 1–3) compared to IFD CPAP (4 days, 95% CI 2–6) ($P = 0.031$). In infants ventilated for ≤14 days ($n = 127$), the extubation failure rate was significantly lower with bCPAP (14.1%; 9/64) compared to IFD CPAP (28.6%l 18/63) ($P = 0.046$) [42].

This well-designed clinical trial suggests the superiority of post-extubation bCPAP over IFD CPAP in preterm babies at <30 weeks who are initially ventilated for <2 weeks. In this trial, similar nasal interfaces were used, stratification by duration of ventilation was performed, a similar weaning approach was utilized, and enrollment occurred after an objective assessment for readiness for extubation.

## 8. Nasal septal injury

Nasal septal injury is recognized as an important complication of nCPAP therapy. It may cause destruction of the nasal septum requiring surgery. The success or failure of a CPAP device depends to a large extent upon the nasal interface, the experience of the staff, and the ease of use. Among very low birth weight babies, the incidence of significant nasal trauma with the use of nasal prongs has been reported to be 35% with a mean age of onset of 8 days [44]. In study by Gupta et al. [42], a prospectively validated nasal scoring was used for all babies. In the study population, nine babies (17%) on IFD CPAP and 13 babies (25%) on bCPAP developed nasal septal injury (defined as indentation of the septum with or without skin breakdown). Moreover, the median age at nasal injury was 14 days in this study [45]. The lower incidence and higher age at onset could relate to better nursing practices and/or the use of Cannulaide® and Lyofoam® dressings between the prongs and the nose. Although the incidence of nasal injury with nasal mask and nasal prong on IFD CPAP has been reported to be similar [44], all babies with nasal septum injuries in Gupta et al.'s study were managed with a nasal mask using IFD CPAP [45]. In a cross-sectional study by Jatana et al. nasal complications were reported in 12 of the 91 patients (13.2%) with at least seven days of nasal CPAP exposure, whereas no complications were seen in the nine patients with nasal cannula use alone [46]. The nasal cannula interface is used with a humidified high-flow system and fewer nasal injuries are reported with its use. These differences need to be studied further in well-designed trials.

## 9. Conclusion

There seems to be only a slight difference between continuous- or variable-flow CPAP devices but there is a trend in favor of bCPAP for post-extubation support, especially in babies ventilated for ≤2 weeks. The nasal interface is important for optimal delivery of pressure and CPAP delivery, while limiting untoward effects, which also requires close monitoring and good nursing care. With increasing use of CPAP devices it is important that units use the evidence to select an appropriate CPAP device and minimize complications.

**Practice points**

- CPAP devices are either continuous-flow or variable-flow systems.
- Efficacy of CPAP depends on CPAP generation, the nasal interface, and good nursing care.
- Currently available CPAP devices have comparable efficacy when used for respiratory support after birth.
- In babies ventilated for less than two weeks, bubble CPAP seems to reduce extubation failures.

**Research directions**

- Better respiratory monitoring techniques to detect early decompensation on CPAP.
- Optimum CPAP pressure during acute and recovery phases of RDS.
- Effect of different levels of CPAP on hemodynamics.
- Techniques for minimizing nasal injury on CPAP.

## Conflict of interest statement

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