Continuous Positive Airway Pressure Therapy: Neonates & Infants

Clinical Evidence Summary

Fisher & Paykel HEALTHCARE

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Reviews: Overview of Continuous Positive Airway Pressure Literature

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INTRODUCTION

Respiratory support is critical for the survival of some neonates, especially those with respiratory problems or who were born prematurely.[1] Up to and including the 1970s, mechanical ventilation with endotracheal intubation was the primary strategy for infants requiring respiratory support.[2,3] However, invasive mechanical ventilation in preterm neonates presents a major risk factor for the development for bronchopulmonary dysplasia (BPD) and ventilator-induced lung injury (VILI), which has prompted the use of noninvasive alternatives of providing respiratory support.[2,3]

Noninvasive respiratory support (NIRS) and noninvasive ventilation (NIV) refer to the administration of respiratory support without the use of an artificial airway such as an endotracheal tube or tracheostomy tube using a noninvasive interface.[1,4] NIV includes therapies such as nasal intermittent positive airway pressure (NIPPV) and nasal high frequency oscillatory ventilation (nHFOV). NIRS includes flow-based therapies (nasal high flow – NHF) or continuous positive airway pressure (CPAP).[1]

CPAP is a modality of noninvasive respiratory support that is being increasingly used in neonatal intensive care units (NICU). It is an accepted alternative to routine intubation and mechanical ventilation in preterm infants with respiratory distress syndrome (RDS) and is the gold standard of care in providing noninvasive respiratory support.[1,3,5] CPAP is effective in reducing respiratory distress, preventing intubation, and decreasing the risk of post-extubation failure.[1]

SYSTEM OVERVIEW OR METHODS OF DELIVERING CPAP

There are different devices that can be used to deliver CPAP – broadly classified as constant-flow and variable-flow devices (Figure 1). The interface connects to a range of positive airway pressure systems via a humidifier (Figure 2). Positive airway pressure systems typically include an air/oxygen source, humidifier, breathing circuit and a positive airway pressure generator. The table below shows the different components for continuous and variable-flow devices.

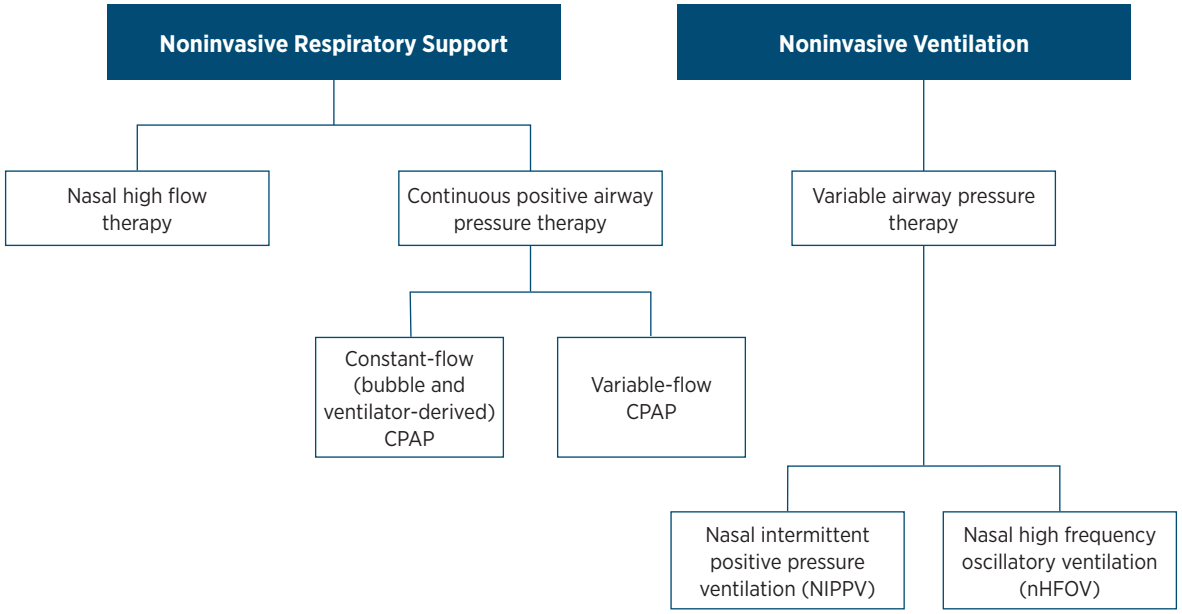

Figure 1: Different modes on noninvasive respiratory support and noninvasive ventilation.

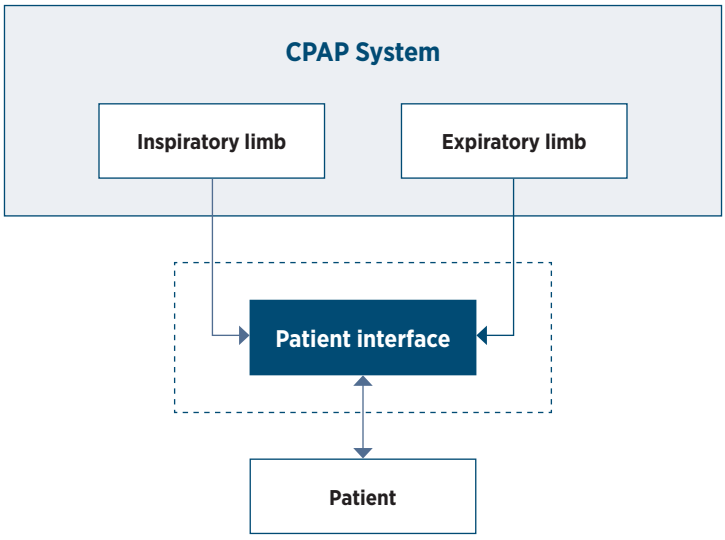

Figure 2: The dual-limb CPAP system comprises of the inspiratory and expiratory limb; these are connected to the patient interface.

Components of continuous-flow devices (bubble CPAP and ventilator CPAP) and variable-flow devices			
	Continuous flow devices		Variable-flow devices
	Bubble CPAP	Ventilator CPAP	
Flow/gas source	Generates a blended flow of air and/or oxygen and delivers it to the humidifier via a tube	Ventilator supplies a blended flow of air and/or oxygen and delivers it to the humidifier via a tube	Flow driver supplies a blended flow of air and/or oxygen and delivers it to the humidifier via a tube
Humidifier	Heats and humidifies the air and/or oxygen mixture and delivers it to the inspiratory circuit tubing		
Inspiratory circuit tube	Transfers the humidified air and/or oxygen mixture from the humidifier to the Interface		
Interface	Nasal prongs or mask that transfers the air and/or oxygen mixture from the circuit tube into the patient's upper airway via the nose		
Expiratory circuit tube	Transfers any humidified air and/or oxygen mixture that bypasses the patient as well as expired air to the CPAP generator	Transfers any humidified air and/or oxygen mixture that bypasses the interface as well as expired air to the ventilator	Transfers any humidified air and/or oxygen mixture that bypasses the interface as well as expired air to the atmosphere
Positive pressure generator	**Bubbler:** All flow is vented from the expiratory circuit tube to atmosphere via a tube submerged in water. Immersion of the tube in water provides a back pressure which generates CPAP	**Ventilator:** Receives flow from the expiratory circuit tube and provides a back pressure to generate CPAP	**Interface:** The jet of blended air and/or oxygen flows to the interface where pressure in generated. Level of pressure is controlled by adjusting the flow

BUBBLE CPAP

CPAP has been used since the 1970s after it was first prescribed for use in preterm infants with RDS by Gregory et al. (1971), who found that CPAP and grunting achieved similar physiologic effects with CPAP providing an additional benefit of reduced work of breathing in neonates. In addition, Dr. Jen-Tien Wung first prescribed a nasal route for therapy delivery, which is still considered to be the standard of care for neonates with respiratory diseases.[7]

Bubble CPAP is accepted as a safe and effective mode of respiratory support for managing neonates with RDS in high-income countries. There is now increasing evidence to support the use of bubble CPAP in low- to middle-income countries. Its use in these countries is recommended by the World Health Organization and supported by evidence from randomized clinical trials (RCTs) and systematic reviews.[8–10]

In bubble CPAP, the depth to which the tube is immersed equals the set pressure. An underwater seal is created by submerging the expiratory tube in a variable depth of water. The gas that exits the expiratory tube produces bubbles that then generate pressure oscillations.[11]

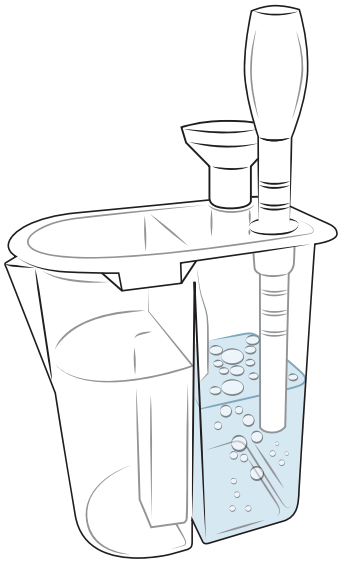

Figure 3: Bubbler – positive pressure generator for bubble CPAP.

CPAP INTERFACES

Interfaces are important components in ensuring optimal delivery of CPAP therapy as they are designed to create a seal for pressure-based therapies. Additional characteristics of a CPAP interface include larger tubes to lower the resistance to flow (Figure 4). The interfaces used to deliver CPAP include nasal masks, single nasal prongs, bi-nasal prongs, nasopharyngeal prongs (or long nasal prongs), nasal cannula and head box enclosures.[12,13] Of these, bi-nasal prongs and nasal masks are the most common interfaces used to deliver CPAP.[13]

Figure 4: Key characteristics of a CPAP interface.

INTRODUCTION

CPAP has been regarded as the gold standard for noninvasive support in neonates and infants for many applications. As early as the 1970s, CPAP was shown to restore functional residual capacity (FRC),[14] improve hypoxemia,[6] reduce pulmonary vasculature resistance, and preserve surfactant.[15] CPAP is also associated with several other mechanisms of action.

MECHANISMS OF ACTION

Maintains functional residual capacity

- FRC is the volume of the respiratory system when the respiratory muscles are relaxed, and no external forces are applied.[16] It is the volume of the lung at the end of a normal expiration. This volume is important for keeping the lungs open after exhalation.[4,17]
- In very premature neonates, the compliant chest wall and paradoxical inward ribcage motion may result in a lowered FRC, and lead to airway closure and alveolar atelectasis.[11] The neonate attempts to raise the FRC by increasing the tonic activity of the diaphragm, increasing the respiratory rate, and laryngeal braking or glottic closure during expiration.[11]
- In the lower airways, the constant distending pressure provided by CPAP helps maintain adequate FRC within the alveoli and prevents end-expiratory alveolar collapse.[4,17]
- Improved lung volumes and compliance lead to improved inspiratory tidal volumes and a secondary improvement in alveolar minute ventilation. This results in lower ventilation rates and improved partial pressures of carbon dioxide (CO_2) levels.[17,18]

Figure 5: Image illustrating the effect of CPAP on an infant lung under respiratory distress. In the absence of any positive airway pressure (left), FRC is decreased, resistance is high, resulting in alveolar collapse. With the application of positive airway pressure (right), FRC is effectively maintained effectively, thus reducing atelectasis.

Reduces work of breathing

- The work of breathing is the force generated to overcome the frictional resistance and static elastic forces that oppose lung expansion and gas flow into and out of the lungs.[19]
- CPAP therapy can improve the work of breathing by reducing the energy required to expand the lungs for breathing.[17,20] CPAP has been shown to elevate end-expiratory lung volume, which helps to unload the inspiratory muscles and reduce the work of breathing.[17,20] This improvement in ventilation efficiency provides comfort for the infant and allows them to continue to spontaneously support ventilation.[17]

Improves heating and humidifying of respiratory gases

- The major roles of the nasopharynx and the epithelium lining the upper airway are to provide moisture and remove debris while heating and humidifying the inspiratory gas.[17]
- CPAP delivers heated (34 to 37 °C) and humidified gas to the lungs, assisting with natural defense mechanisms, maintaining airway mucosa and mucociliary function, and promoting conservation of energy for growth and development.[17]

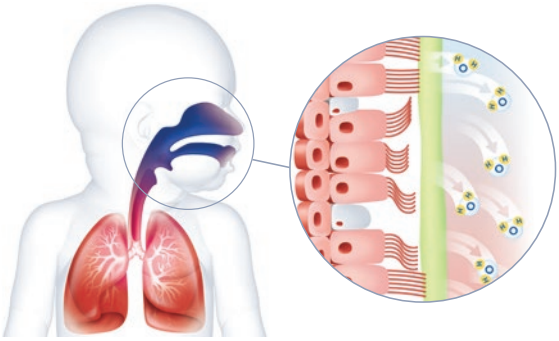

Figure 6: Delivery of heated and humidified gas during respiratory support facilitates mucociliary transport.

Bubble CPAP generates pressure oscillations

- The flow that is delivered is vented from the expiratory circuit tube to the atmosphere via a tube submerged in water. The immersion of the tube in the water provides a back pressure which generates CPAP. The bubbling action of the vented flow provides pressure oscillations that are considered to have a therapeutic effect.[11]
- The pressure oscillations that are generated via the submerged expiratory limb are transmitted down the airways into the lung. It is suggested that the oscillations superimposed on the airway pressure provide a plausible mechanism to improve gas exchange and CO_2 elimination.[21,22]

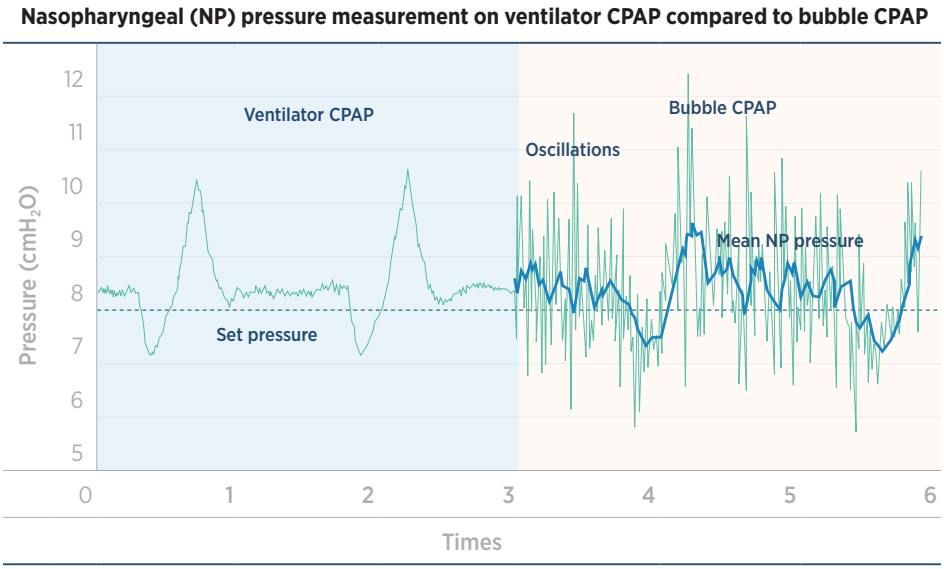

Figure 7: Graphical representation of bubble CPAP generated pressure oscillations. Pressure vs. time plot shows how pressure oscillations vary over time (green line) and the resulting mean airway/nasopharyngeal pressure (solid blue line).

INTRODUCTION

There is a large body of evidence from RCTs, systematic reviews and guidelines supporting the use of CPAP for the neonatal and infant population.

COMMON MEDICAL CONDITIONS

There are many medical conditions in which CPAP is an established modality, such as:

Respiratory distress syndrome (RDS)

- RDS primarily occurs due to surfactant deficiency and presents with tachypnea, retractions, nasal flaring, diminished breath sounds, inspiratory crackles, cyanosis and pallor. Risk factors associated with RDS are prematurity, gestational diabetes, perinatal asphyxia and multiple gestation.[23]
- Current European guidelines recommend that CPAP should be started from birth in all neonates at risk of RDS, such as those at < 30 weeks' gestational age (GA) who do not need intubation for stabilization, with a starting pressure of about 6 to 8 cmH_2O. Positive end-expiratory pressure can then be individualized depending on the clinical condition, oxygenation and perfusion.[1,17]

Apnea of prematurity

- Apnea of prematurity is commonly diagnosed in the NICU. Apnea has been defined as cessation of breathing for 20 seconds or longer, or a shorter pause accompanied by bradycardia (< 100 beats per minute), cyanosis or pallor. The incidence of apnea of prematurity is inversely correlated with GA and birth weight.[23]
- CPAP is effective in reducing the frequency and severity of apnea in preterm infants. It appears to work by splinting open the upper airway and decreasing the risk of obstructive apnea.[23,24]

Low birth weight infants

- Very low birth weight (VLBW) infants are those born with a birth weight of < 1500 g and extremely low birth weight are those with a birth weight of < 1000 g. Low-birth-weight infants are at an increased risk of BPD.[25]
- CPAP may also decrease the depth and duration of oxygen desaturation during central apnea by helping maintain a higher end-expiratory lung volume.
- Bubble CPAP has been commonly used in low-birth-weight infants as studies have shown the reduced need for intubation and mechanical ventilation as well as a decrease in mortality.[25]

Infants with bronchiolitis

- Bronchiolitis is caused by a respiratory virus, commonly the respiratory syncytial virus, and is the leading cause of hospitalization in those under two years old. The clinical features are primarily due to airway obstruction and diminished lung compliance with symptoms of tachypnea, chest wall retractions and wheezing.[26]
- Evidence from RCTs and systematic review supports the use of CPAP in infants with bronchiolitis. A systematic review concluded that breathing improved (a decreased respiratory rate) in infants with bronchiolitis who received CPAP.[27]
- However, CPAP may not be as well tolerated as other modes of NIRS such as NHF, particularly by older infants, and choosing an optimal interface can be problematic.[27]

CPAP APPLICATIONS

There is a significant body of evidence comparing CPAP with different respiratory management strategies in the following range of applications:

Alternative to invasive mechanical ventilation

- There is a large body of evidence supporting the use of CPAP as an alternative to mechanical ventilation, especially in the management of RDS.[3,5]
- CPAP has been shown to reduce the incidence of BPD and ventilator-induced lung injury.

Primary respiratory support

- CPAP initiated early or following initial resuscitation at birth in a spontaneously breathing infant provides effective respiratory support for infants with respiratory distress/failure, even for those infants born at < 28 weeks' GA.[28]
- CPAP, compared with routine initial intubation and ventilation, reduced the need for mechanical ventilation and surfactant, according to data from RCTs. These outcomes were supported by results of systematic reviews/meta-analyses which also found that CPAP reduced the incidence of BPD and death, or BPD.[28]

Post-extubation support

- CPAP is effective in preventing failure of extubation in preterm infants following a period of endotracheal intubation, according to data from RCTs, systematic reviews and meta-analyses.[29–31]

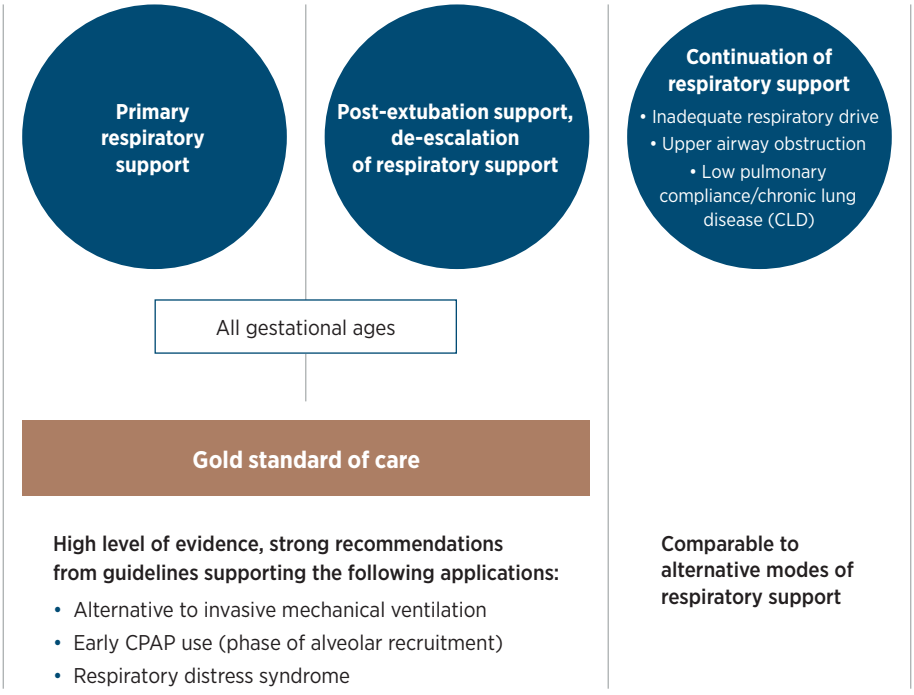

Figure 8: Applications of CPAP therapy.

INTRODUCTION

- Mechanical ventilation was first introduced for use in neonates in the 1960s, with widespread use improving survival rates of VLBW infants. However, mechanical ventilation is associated with lung injury.[32,33]
- With the known complications associated with mechanical ventilation, there is an increasing trend towards the implementation of more noninvasive ventilation strategies. Reducing the need for intubation and mechanical ventilation is particularly advantageous in low resource settings.[34]
- Despite the physiological and clinical benefits of the therapy becoming evident in the early 1970s, it is only in the last 20 years that a re-emergence of interest in CPAP is leading to further progress in the development of different CPAP applications and platforms.

CLINICAL EVIDENCE

SUPPORTING THE EARLY USE OF CPAP

- Three pivotal RCTs (COIN, SUPPORT and VON-DRM) investigated early prophylactic use of CPAP compared with routine intubation and ventilation.[35–37]

	Dunn et al. 2011 VON-DRM	Finer et al. 2010 SUPPORT	Morley et al. 2008 COIN
Patient Population	648 neonates, 26–30 weeks' GA	1316 neonates, < 28 weeks' GA	610 neonates, 25–28 weeks' GA
Intervention	Bubble CPAP (5–7 cmH_2O)	Bubble, ventilator and variable-flow CPAP (5 cmH_2O)	CPAP (8 cmH_2O)
Comparator	Surfactant + MV	Surfactant + MV	MV
Primary Outcome	Death or BPD at 36 weeks' postnatal age	Death or BPD at 36 weeks' GA	Death or BPD at 36 weeks' GA

MV: mechanical ventilation

Results

- These studies showed that early prophylactic use of CPAP reduced the need for mechanical ventilation and surfactant use in premature infants, compared with routine intubation and ventilation.
- A significant reduction in the rate of death or BPD in the CPAP group was reported in these studies. Morley et al. (2008) also found that at 28 days there was a lower risk of death or BPD in the CPAP group (p = 0.006).

Death or BPD at 36 weeks postnatal age (%)		
Dunn et al. 2011		
Bubble CPAP (n=223)	Surfactant + MV (n=209)	Relative Risk
30.5	36.5	0.83 (0.64 to 1.09)
Finer et al. 2010		
Bubble, ventilator and variable-flow CPAP (n=663)	Surfactant + MV (n=653)	Relative Risk
48.7	54.1	0.91 (0.83 to 1.01), p=0.07
Morley et al. 2008		
CPAP (n=307)	MV (n=303)	Relative Risk
35.2	40.3	0.81 (0.58 to 1.12), p=0.19

MV: mechanical ventilation

- These RCTs have also been included in a Cochrane Review meta-analysis by Subramaniam et al. (2016) which determined whether prophylactic CPAP initiated soon after birth reduces the incidence of BPD and need for mechanical ventilation in very preterm or VLBW infants.[38]
  - The authors concluded that CPAP compared to assisted ventilation reduces the combined outcome of BPD and death or BPD and reduces the need for MV (typical RR 0.50, 95% CI 0.42 to 0.59; typical RD –0.49, 95% CI –0.59 to –0.39).

CPAP REDUCES THE NEED FOR INTUBATION AND MV

- In addition to the RCTs above, further studies have shown that CPAP may reduce the need for intubation and mechanical ventilation when used as the primary support and decrease the rate of extubation failure when used post-extubation.[39–42]

	Tooley et al. 2003	Dani et al. 2004	Tapia et al. 2012	Verder et al. 1994
Patient Population	42 neonates, 25–28 weeks' GA	27 neonates, < 30 weeks' GA	256 neonates, 800–1500 g	68 neonates, 25–35 weeks' GA
Intervention	Variable-flow CPAP (5–9 cmH_2O)	Variable-flow CPAP + surfactant	Bubble CPAP + surfactant (5 cmH_2O)	CPAP + surfactant (8 cmH_2O)
Comparator	MV	MV + surfactant	MV + surfactant	CPAP
Primary Outcome	Need for MV at 72 h	Need for MV at 7 days	Need for MV	Need for MV at 7 days
Secondary Outcomes†	Duration of CPAP and ventilation and adverse events	Duration of oxygen, CPAP and MV, mortality and adverse events	Death, surfactant use and adverse events	Duration of oxygen, CPAP and MV, mortality and adverse events

MV: mechanical ventilation

† Adverse events include rates of any of the following: pneumothoraces/air leaks, BPD/CLD, necrotising enterocolitis (NEC), retinopathy of prematurity (ROP) and/or intraventricular hemorrhage (IVH).

Results

- Both Tooley et al. (2003) and Dani et al. (2004) studies demonstrated that the CPAP group reduced the need for MV at 72 hours of life and at 7 days of life. Neither study reported significant differences in the outcomes of death, BPD and pneumothoraces.
- Verder et al. (1994) found that CPAP with surfactant administration significantly reduced the need for MV.
- Tapia et al. (2012) found that the need for MV was significantly lower in the bubble CPAP group.

Need for mechanical ventilation at 72 h (%)		
Tooley et al. 2003		
Variable-flow CPAP (n=21)	MV (n=21)	p-value
62	100	0.003
Need for mechanical ventilation at 7 days (%)		
Dani et al. 2004		
Variable-flow CPAP + surfactant (n=13)	MV + surfactant (n=14)	p-value
0	43	0.027
Verder et al. 1994		
CPAP + surfactant (n=33)	CPAP (n=27)	p-value
43	85	0.003
Need for mechanical ventilation (%)		
Tapia et al. 2012		
Bubble CPAP + surfactant (n=131)	MV + surfactant (n=125)	p-value
29.8	50.4	0.001

MV: mechanical ventilation

KEY POINTS

- To avoid the complications associated with MV, the use of CPAP is an accepted alternative mode of respiratory support.
- Clinical evidence has showed that:
  - CPAP can reduce the need for mechanical ventilation when used as post-extubation or primary support.
  - CPAP is a safe and effective mode of noninvasive respiratory support for those born preterm or with low birth weight.

INTRODUCTION

- A number of RCTs and systematic reviews have compared bubble CPAP to ventilator and variable-flow CPAP in terms of clinical and physiological outcomes in preterm neonates with respiratory distress.
- Physiological studies that have compared bubble CPAP to ventilator and variable-flow CPAP found no significant differences in respiratory parameters such as respiratory rate and work of breathing.[43–45]

CLINICAL EVIDENCE

BUBBLE CPAP COMPARED TO VENTILATOR CPAP

- Three RCTs investigating clinical outcomes between bubble CPAP and ventilator CPAP are:[46–48]

	Tagare et al. 2013	Yadav et al. 2012	Agarwal et al. 2016
Patient Population	114 preterm neonates, < 37 weeks' GA	32 preterm neonates, ≤ 32 weeks' GA/< 1500 g	63 neonates, < 1500 g
Intervention	Bubble CPAP (6 cmH_2O)	Bubble CPAP (4–6 cmH_2O)	Bubble CPAP (4–7 cmH_2O)
Comparator	Ventilator CPAP (6 cmH_2O),	Ventilator CPAP (4–6 cmH_2O)	Ventilator CPAP (4–7 cmH_2O)
Primary Outcome*	Proportion of therapy success	Extubation failure	Treatment failure
Secondary Outcomes†	Duration of CPAP support and adverse events	Time to extubation failure, duration of MV and adverse events	Adverse events

MV: mechanical ventilation

* Therapy/extubation failure was defined as, but not limited to, meeting one or more of the following criteria: (i) SpO_2 < 90%, (ii) FiO_2 > 0.6 and (iii) episodes of apneas and bradycardias.
† Adverse events include rates of any of the following: pneumothoraces/air leaks, nasal injury, CLD, NEC, ROP and/or IVH.

Results

- These studies show that the therapy success rate was significantly higher with bubble CPAP, while safety and reduction in extubation failure was comparable to ventilator CPAP.
- In addition, there were no significant differences in the secondary outcomes between bubble CPAP and ventilator CPAP in any of the studies.
- Similarly, a systematic review reported a lower failure rate (need for intubation) with bubble CPAP compared to ventilator CPAP (Odds ratio 0.32; 95% CI 0.16 to 0.67; p < 0.003).[49]

Treatment success (%)		
Tagare et al. 2013		
Bubble CPAP (n=57)	Ventilator CPAP (n=57)	p-value
82.5	63.2	0.03
Treatment failure (%)		
Yadav et al. 2012		
Bubble CPAP (n=16)	Ventilator CPAP (n=16)	p-value
25	56	0.14
Agarwal et al. 2016		
CPAP (n=307)	MV (n=303)	Relative Risk
35.2	40.3	0.81 (0.58 to 1.12), p=0.19

MV: mechanical ventilation

BUBBLE CPAP COMPARED TO VARIABLE-FLOW CPAP

- Several RCTs investigated clinical outcomes between bubble CPAP and variable-flow CPAP. Of particular interest are these three RCTs:[10,50,51]

	Bhatti et al. 2015	Gupta et al. 2009	Yagui et al. 2011
Patient Population	170 preterm neonates, < 34 weeks' GA	140 preterm neonates, 24–29 weeks' GA/600–1500 g	39 neonates, ≥ 1500 g
Intervention	Bubble CPAP	Bubble CPAP (4–6 cmH_2O)	Bubble CPAP (6 cmH_2O)
Comparator	Variable-flow CPAP	Variable-flow CPAP (4–6 cmH_2O)	Variable-flow CPAP (6 cmH_2O)
Primary Outcome*	Failure rate within 72 h	Extubation failure within 72 h	Treatment failure
Secondary Outcomes†	Failure of CPAP by 7 days, surfactant use, duration of CPAP, adverse events	Duration of CPAP support, successful extubation at 7 days, adverse events	Duration of oxygen/CPAP use, hospital length of stay, adverse events

* Therapy/extubation failure was defined as, but not limited to, meeting one or more of the following criteria: (i) SpO_2 < 90%, (ii) FiO_2 > 0.4, (iii) increasing PEEP and (iv) episodes of apneas and bradycardias.
† Adverse events include rates of any of the following: pneumothoraces/air leaks, nasal injury, CLD, NEC, ROP and/or IVH.

Results

- These studies have shown that there were no significant differences in failure rates within 72 hours of therapy initiation between bubble CPAP and variable-flow CPAP (Bhatti et al., Gupta et al., Yagui et al.).
- There were no significant differences in the other secondary outcomes between the two groups in any of the studies.

Treatment failure (%)		
Bhatti et al. 2015		
Bubble CPAP (n=90)	Variable-flow CPAP (n=80)	p-value
16	25	0.07
Gupta et al. 2009		
Bubble CPAP (n=71)	Variable-flow CPAP (n=69)	p-value
16.9	27.5	0.130
Yagui et al. 2011		
Bubble CPAP (n=20)	Variable-flow CPAP (n=19)	p-value
20	25	1.00

KEY POINTS

- Bubble CPAP is comparable to both ventilator CPAP and variable-flow CPAP by improving various respiratory parameters including work of breathing, tidal volume, respiratory rate, minute ventilation and lung compliance.
  - There were no significant differences also in secondary outcomes (adverse events, duration of CPAP support and hospital length of stay).

INTRODUCTION

Bubble CPAP is accepted as a safe and effective mode of respiratory support for managing neonates with RDS in high-income countries. There is now increasing evidence to support the use of bubble CPAP in low- to middle-income countries.

CLINICAL EVIDENCE

- A systematic review by Martin et al. (2014) analyzed data from 14 studies that evaluated the use of bubble CPAP in low- to middle-income countries. The authors concluded that bubble CPAP is a simple intervention that can be used for RDS and is becoming more economical and accessible in these settings.[52]
- In addition, the studies included in this meta-analysis have demonstrated that bubble CPAP in tertiary and non-tertiary hospitals in low- to middle-income countries is effective in reducing the need for mechanical ventilation (OR 0.32, 95% CI0.16 to 0.67, $p < 0.003$) without a corresponding increase in mortality.[52]
- Similarly, Thukral et al. conducted a meta-analysis of 21 studies in the same setting, of which two studies that were included for analysis reported costs associated with bubble CPAP equipment were lower than those associated with ventilators.[34]

KEY POINTS

- Bubble CPAP is a safe and effective therapy for use in the early management of preterm neonates with RDS, especially in low- to middle-income countries.

GLOSSARY

100% RELATIVE HUMIDITY (RH)

The maximum amount of water a gas can hold at a given temperature.

BRONCHOPULMONARY DYSPLASIA (BPD)

A form of lung disease that develops in premature neonates treated with oxygen and positive-pressure ventilation, characterized primarily by arrest of alveolar and vascular development. Also defined as supplemental oxygen dependency for at 36 weeks corrected gestational age.

CHRONIC LUNG DISEASE (CLD)

A form of lung disease that develops in premature neonates treated with oxygen and positive-pressure ventilation, characterised primarily by arrest of alveolar and vascular development. Also defined as supplemental oxygen dependency for at 36 weeks corrected gestational age. Also referred to as BPD.

COCHRANE REVIEW

An evidence-based systematic review of published healthcare research performed by an international group of academics who study the effectiveness of medical treatments.

CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

A technique of respiratory therapy in which airway pressure is maintained above atmospheric pressure throughput the respiratory cycle by pressurization of ventilatory circuit.

DISTENDING PRESSURE

Pressure applied to the lungs to expand them. Can be applied using continuous positive or negative airway pressure to create a partial vacuum.

ENDOTRACHEAL TUBE (ETT)

A tube inserted through the mouth or nose into the trachea to maintain an unobstructed airway.

EXTUBATION

Withdrawing an endotracheal tube (ETT) from a patient's airway.

FRACTION OF INSPIRED OXYGEN (FIO_2)

The proportion of oxygen in the air that is inspired.

HEATED, HUMIDIFIED GAS

Air that has been heated and humidified prior to delivery by noninvasive ventilation, typically to 37 °C and 100% relative humidity.

INFANT

Defined by the FDA as greater than 1 month to 2 years of age.

INTRAVENTRICULAR HEMORRHAGE (IVH)

Bleeding inside or around the ventricles in the brain. There are 4 grades of IVH: 1) bleeding in a small area of the ventricles, 2) bleeding inside the ventricles, 3) ventricles are enlarged by the blood and 4) bleeding occurs in the brain tissues around the ventricles.

INTUBATION

The insertion of an ETT or tracheostomy tube into the trachea.

LOW BIRTH WEIGHT (LBW)

Birth weight less than 2500 g.

LUNG COMPLIANCE

The ease of lung expansion.

MECHANICAL VENTILATION (MV)

The use of an invasive artificial airway to mechanically assist or replace spontaneous breathing, when patients cannot do so on their own.

NASAL HIGH FLOW (NHF)

A mode of noninvasive respiratory support that delivers high flows of heated and humidified blended air and oxygen through an unsealed interface.

NASAL INTERMITTENT POSITIVE PRESSURE VENTILATION (NIPPV)

A method of noninvasive ventilation that provides positive pressure to the back of the nose that is transferred to the lungs with intermittent breaths from a ventilator.

NECROTISING ENTEROCOLITIS (NEC)

An inflammatory intestinal disorder primarily seen in preterm infants, characterized by variable damage to the intestinal tract ranging from mucosal injury to perforation. Associated with presentations of abdominal distention and feeding intolerance.

NEONATE

Defined by the FDA as between 0 and 28 days postnatal age (time elapsed after birth).

NONINVASIVE VENTILATION (NIV)

The delivery of ventilatory support without the need for an invasive artificial airway.

OXYGEN SATURATION (SPO_2)

Oxygen saturation as measured by pulse oximetry.

PARTIAL PRESSURE OF CARBON DIOXIDE (PCO_2)

The part of total blood gas pressure exerted by CO_2 gas; a measure of how much CO_2 is dissolved in the blood and how well CO_2 is able to move out of the body.

PARTIAL PRESSURE OF OXYGEN (PO_2)

The part of total blood gas pressure exerted by oxygen gas; a measure of how much oxygen is dissolved in the blood and how well oxygen is able to move from the airspace of the lungs into the blood.

PRETERM

An infant born < 37 weeks gestation, regardless of weight. They may be further classified as:

Moderate-to-late preterm:
32 to < 37 weeks gestation.

Very preterm
28 to < 32 weeks gestation.

Extremely preterm
< 28 weeks gestation.

RANDOMIZED CONTROLLED TRIAL (RCT)

Study design where participants are randomly allocated to receive or not receive clinical intervention(s) with the aim of comparing selected outcomes between these groups. Random allocation aims to reduce certain sources of bias.

RESPIRATORY DISTRESS SYNDROME (RDS)

A lung disease of the newborn, most frequently occurring in premature infants, that is caused by abnormally high alveolar surface tension as a result of a deficiency in lung surfactant; also called hyaline membrane disease.

RESPIRATORY RATE (RR)

The amount of breaths over a specified time period.

RETINOPATHY OF PREMATURITY (ROP)

Occurs from varying oxygen concentrations in blood that results in vasoconstriction and subsequent proliferation and abnormal vascular growth in the retina. Most commonly occurs in premature infants who receive oxygen therapy.

STATISTICAL SIGNIFICANCE

A statistical measure which helps to quantify whether a result is likely due to chance or a true relationship between variables. This can be represented by the p-value.

SURFACTANT

A substance produced in the lungs that tends to reduce the surface tension of the fluid in the lungs and helps make the small air sacs in the lung (alveoli) more stable.

VENTILATOR INDUCED LUNG INJURY (VILI)

A form of lung injury which occurs from mechanical ventilation, either from overdistention (barotrauma or volutrauma) or repetitive collapse and expansion of the alveoli (atelectrauma).

VERY LOW BIRTH WEIGHT (VLBW)

Birth weight less than 1500 g.

WORK OF BREATHING (WOB)

The force required to expand the lung against its elastic properties

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