

Protocol for Administering Continuous Positive Airway Pressure in Neonates

M. Jeeva Sankar, Jhuma Sankar, Ramesh Agarwal, Vinod K. Paul and Ashok K. Deorari

Division of Neonatology, Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India

ABSTRACT

Continuous positive airway pressure (CPAP) is a simple, inexpensive and gentle mode of respiratory support in preterm very low birth weight (VLBW) infants. It helps by preventing the alveolar collapse and increasing the functional residual capacity of the lungs. Since it results in less ventilator induced lung injury than mechanical ventilation, it should theoretically reduce the incidence of chronic lung disease in VLBW infants. Various devices have been used for CPAP generation and delivery. The relative merits and demerits of these devices and the guidelines for CPAP therapy in neonates are discussed in this protocol. [Indian J Pediatr 2008; 75 (5) : 471-478] Email: ashokdeorari_56@hotmail.com

Key words: Continuous positive airway pressure; Devices, Fixation; Treatment; Protocol

Continuous positive airway pressure (CPAP), often thought to be the 'missing link' between supplemental oxygen and mechanical ventilation, is gaining immense popularity in neonatal intensive care units. Being technically simple, inexpensive and effective, it has become the primary mode of respiratory support in preterm very low birth weight (VLBW) infants. The evidence, clinical studies, and the controversies regarding its use have been extensively reviewed and are not discussed here.^{1,2} This protocol deals mainly with the practical aspects of CPAP administration in neonates.

DEFINITION AND BACKGROUND

CPAP refers to the application of positive pressure to the airway of a spontaneously breathing infant through out the respiratory cycle.

The first clinical use of CPAP was reported by Gregory *et al* in a landmark report in 1971. They described the use of CPAP *via* endotracheal tube or a head box in preterm infants with respiratory distress syndrome (RDS).³ Shortly after this, Kattwinkel reported

successful use of nasal prongs to provide CPAP in these infants.⁴ After the initial enthusiasm, it gradually fell out of favor in 1980s because of the advent of newer modes of ventilation (such as high frequency ventilation) and the perceived complications of CPAP (such as air leak). However, reports of significantly lower incidence of chronic lung disease (CLD) from Columbia University unit that used more CPAP (Hudson prongs) as compared to other North American Centers have led to a resurgence of interest in CPAP over the past 15 years.⁵

CPAP: HOW DOES IT WORK?

CPAP predominantly helps by preventing collapse of the alveoli with marginal stability. This results in better recruitment of alveoli thus increasing the functional residual capacity (FRC). The physiologic effects of CPAP are represented in fig. 1.

Components of CPAP system

The components of a CPAP system are:

- **Gas source:** To provide continuous supply of warm humidified and blended gases *i.e.*, air and oxygen
- **Pressure generator:** To create the positive pressure in the circuit
- **Patient interface/delivery system:** To connect the CPAP circuit to the infant's airway.

Correspondence and Reprint requests : Prof Ashok K Deorari, Professor, Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India.

[Received April 24, 2008; Accepted April 24, 2008]

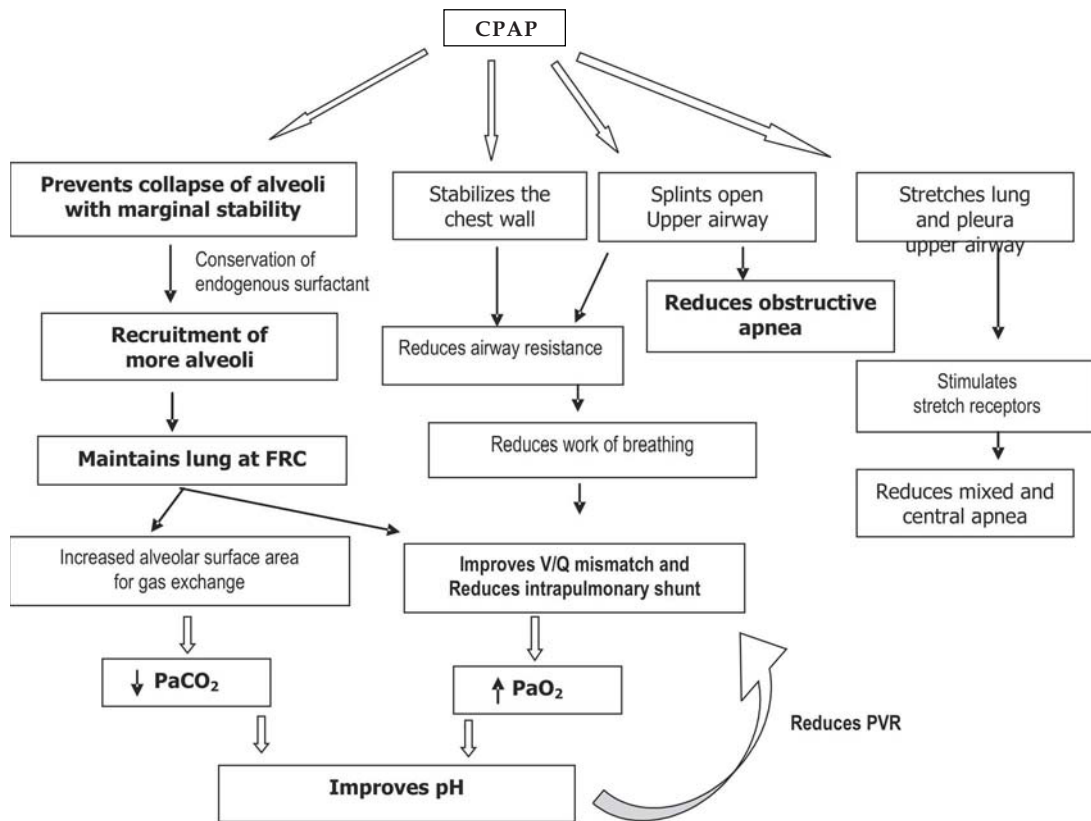


Fig. 1. Effects of CPAP

(FRC, functional residual capacity; V/Q, ventilation-perfusion ratio; PVR, pulmonary vascular resistance; PaCO₂ & PaO₂, partial pressure of carbon-di-oxide and oxygen respectively in the arterial blood)

Devices used for pressure generation

The pressure sources of CPAP can be broadly grouped into:⁶

- Continuous flow devices
- Variable flow devices (Fig. 2)

Bubble CPAP: A typical bubble CPAP setup is shown in Panel 2. One has to remember that though classified as a continuous flow device, flow may still need to be adjusted to maintain continuous bubbling in the water chamber and thus the required level of CPAP.

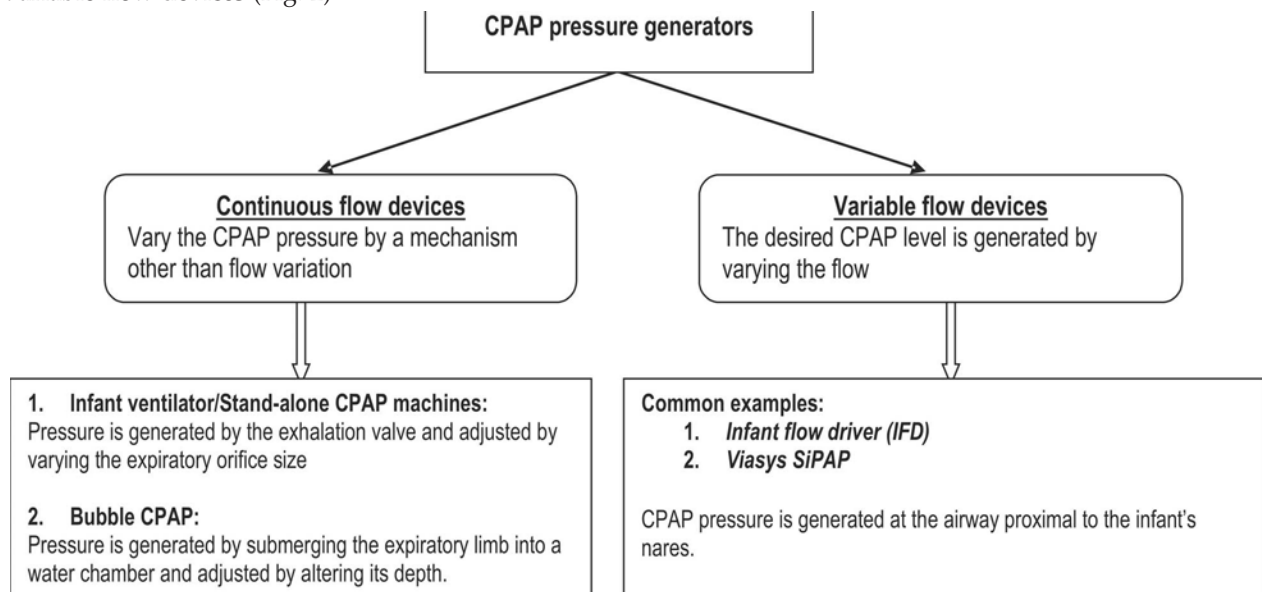


Fig. 2. Types of CPAP Devices

Protocol for Administering Continuous Positive Airway Pressure in Neonates

Variable flow CPAP: A typical example is the *Infant flow driver (IFD)*. It uses the *Bernoulli Effect* via dual injector jets directed towards each nasal prong to maintain a constant pressure. If the infant requires more inspiratory flow, the Venturi action of the injector jets entrains additional flow. When the infant makes a spontaneous expiratory effort, there is a 'fluidic flip' that causes the flow to flip around and to leave the generator chamber via the expiratory limb (*Coanda effect*). So, unlike in the other methods of CPAP where the infant has to exhale against the incoming gas flow, the 'fluidic flip' of the variable flow devices assist his exhalation thus reducing the work of breathing.

We use continuous flow CPAP by both conventional ventilators and bubble CPAP device in our unit.

The advantages and disadvantages of each of these methods are given in table 1.

Devices used for CPAP delivery (Patient interface)

Various devices used for CPAP delivery include:

- Nasal prongs (single/double or binasal)
- Long (or) nasopharyngeal prongs
- Nasal cannulae (Fig. 3)
- Nasal masks
- Face mask, endotracheal, and head box are no longer used for delivering CPAP in neonates.

Endotracheal CPAP is not recommended because it has been found to increase the work of breathing (infant has to breathe 'through a straw').

The advantages and disadvantages of each of these methods have been summarized in table 2.

TABLE 1. A Comparison of CPAP Devices Used for Pressure Generation⁷

Device	Examples	Approximate Cost (INR)	Advantages	Disadvantages	Remarks
Conventional ventilator derived CPAP	Bear Cub, Bird-VIP, Draeger Baby log, Newport, Sechrist, Siemens, SLE, etc.	5 – 10 lakhs	<ul style="list-style-type: none"> • No need of separate equipment • Can be easily switched over to mechanical ventilation, if CPAP fails 	<ul style="list-style-type: none"> • Expensive • Standard flow of 5-8L/min may be insufficient in the presence of high leak • Difficult to know if the set flow is sufficient or not (insufficient flow can lead to increased WOB) 	Of practical utility in units having ventilators but not so in a small hospital/nursing home without a neonatal ventilator.
Stand-alone CPAP machines ('Indigenous CPAP')	Lectromedik, Meditrin, Phoenix, Shreeyash, Zeal	25,000 to 80,000	<ul style="list-style-type: none"> • Economical • Useful for small hospitals • Can have bubble CPAP option 	<ul style="list-style-type: none"> • Most of them do not have proper blenders and/or pressure manometer 	Though inexpensive, they have not been tested adequately; niggling issues observed during daily use
Bubble CPAP	Indian: Mediserve, Meditrin Imported: Fisher & Paykel	50,000 to 80,000 1,60,000	<ul style="list-style-type: none"> • Simple and inexpensive • Oscillations produced by continuous bubbling might contribute to gas exchange (akin to HFV) • Can identify large leaks at the nares (bubbling stops) 	<ul style="list-style-type: none"> • Flow has to be altered to ensure proper bubbling • It is difficult to detect high flow which can lead to over distension of the lungs 	It seems unlikely that oscillations delivered at the nares are transmitted up to the alveoli; Still, the stand-alone option makes it an easy and cost effective proposition in developing countries
Variable flow devices	Arabella, IFD, Viasys SiPAP	3 lakhs	<ul style="list-style-type: none"> • Maintains more uniform pressure • Might decrease the WOB • Recruits lung volume more effectively 	<ul style="list-style-type: none"> • Expensive • Requires more technical expertise 	On theoretical grounds, this device scores more than the other two; However the prohibitive cost and the lack of evidence regarding its superiority preclude its widespread use

(WOB, work of breathing; HFV, high frequency ventilation; IFD, infant flow driver)

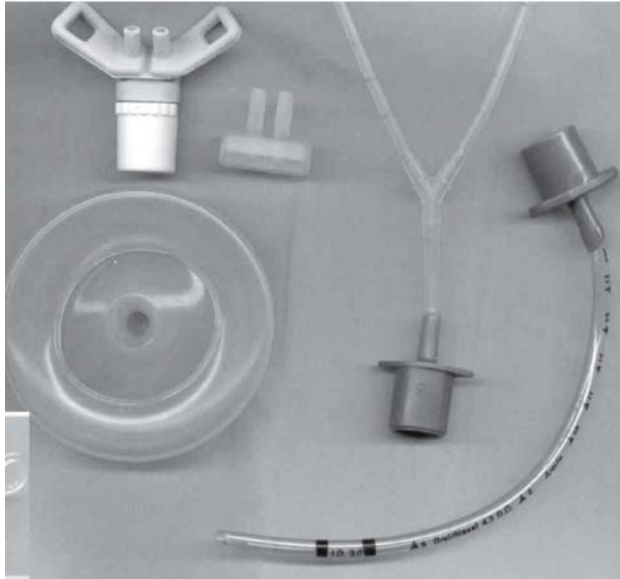


Fig. 3. CPAP Delivery Systems

listed in Panel 1.

Practically, CPAP is very useful in preterm (<35 weeks') infants with respiratory distress/failure of any etiology. Some of these indications have been briefly described below:

- **RDS:** The most common indication for CPAP is mild to moderate RDS. It helps in this condition by preventing collapse of alveoli with marginal stability. The recruitment of more alveoli helps to increase the FRC thus helping in better oxygenation (Fig. 1). Numerous studies have proved its efficacy in reducing the need for mechanical ventilation and probably the incidence of chronic lung disease in infants with RDS.^{10, 11}

CPAP and surfactant: The beneficial effect of CPAP in preterm infants (<29 to 30 weeks') could probably be enhanced by administering surfactant. In this approach, if respiratory distress progresses even after initiating CPAP, the baby is intubated, given

TABLE 2. Advantages and Disadvantages of Common CPAP delivery Systems

Delivery system	Advantages	Disadvantages	Remarks
Nasal prongs (single/binasal) Example: • Argyle • Hudson • IFD prongs	<ul style="list-style-type: none"> • Simple device • Lower resistance leads to greater transmission of pressure • Mouth leak acts like a 'pop-off' mechanism 	<ul style="list-style-type: none"> • Relatively difficult to fix • Risk of trauma to nasal septum and turbinates • Leak through mouth means end expiration pressure is variable 	Studies have shown that they are more effective than nasopharyngeal prongs (in post-extubation setting) ⁸
Nasopharyngeal prongs (e.g., using a cut endotracheal tube) Length is estimated by measuring the distance from the earlobe to the tip of the chin or nose; <i>Tube placement is confirmed by direct visualization of the tip behind the uvula</i>	<ul style="list-style-type: none"> • Easy availability • Economical • More secure fixation 	<ul style="list-style-type: none"> • More easily blocked by secretions • Likely to get kinked 	Though more economical and easily available, they are found to be inferior to short binasal prongs ⁸
Nasal cannulae (with an outer diameter of 3mm and flows up to 2 L/min)	Ease of application	<ul style="list-style-type: none"> • Unreliable pressure delivery • May need high flows to generate pressure if only oxygen is used (without air blender) • FiO₂ delivered may be high • Large leaks around the cannulae 	<ul style="list-style-type: none"> • Mainly tried in apnea of prematurity – paucity of data in other conditions⁹ • Still experimental
Nasal masks	Minimal nasal trauma	Difficulty in obtaining an adequate seal	New generation masks are yet to be studied in detail

(IFD, Infant flow driver)

In our unit, we use short bi-nasal prongs for delivering CPAP (both ventilator and bubble CPAP).

Indications for CPAP

The common clinical indications of CPAP have been

surfactant, and then extubated and put back on CPAP again. Known as INSURE (Intubation-Surfactant-Extubation), this approach might further reduce the need for subsequent ventilation and improve the outcome in extreme preterm infants.¹²

Protocol for Administering Continuous Positive Airway Pressure in Neonates

Panel 1. Indications for CPAP

Common indications

- Respiratory distress syndrome (RDS)
- Apnea of prematurity (especially obstructive apnea)
- Post-extubation in preterm VLBW infants
- Transient tachypnea of newborn (TTNB)/delayed adaptation

Other indications

- Pneumonia
- Meconium aspiration/ other aspiration syndromes
- Pulmonary edema/pulmonary hemorrhage
- Laryngomalacia/ tracheomalacia/ bronchomalacia

However, clinical trials have not shown any reduction in the incidence of CLD so far. More studies are needed to confirm or refute its possible beneficial effects. *We do not routinely employ INSURE technique at present.*

- **Apnea of prematurity:** The mechanism by which CPAP helps in apnea of prematurity has been explained before (Fig. 1). It is typically used when clinically significant episodes persist despite optimal methylxanthine therapy.
- **Post-extubation in VLBW infants:** CPAP reduces the incidence of apnea, respiratory acidosis, and increased oxygen requirement in VLBW infants extubated after a brief period of mechanical ventilation.
- **Delayed adaptation/TTNB:** In these conditions associated with excess lung fluid, CPAP helps by maintaining the lung expansion. Though useful in premature infants, term and near-term neonates with TTNB often do not tolerate this mode of respiratory support.
- **Pneumonia:** CPAP can be tried in stable infants with mild to moderate respiratory distress due to pneumonia. It helps in this condition by maintaining the lung expansion preventing any collapse due to fluids and secretions.
- **Meconium aspiration syndrome:** Use of CPAP is a contentious issue in this condition as most of the infants would already have hyperexpanded lung fields and CPAP might further aggravate it. Moreover, these term infants are unlikely to tolerate CPAP well. It is only indicated in a rare infant with predominant collapse/atelectasis (preferably proven by chest X-ray).

We use CPAP predominantly in preterm infants (<35 weeks' and birth weight <1800g) with respiratory distress, apnea of prematurity, delayed adaptation, and pneumonia; also we extubate VLBW infants to CPAP routinely. We occasionally use CPAP in near-term and term infants with transient tachypnea and pneumonia.

CONTRAINDICATIONS OF CPAP

The important contraindications for CPAP include:

- Progressive respiratory failure with PaCO₂ levels >60 mmHg and/or inability to maintain oxygenation (PaO₂ <50 mmHg)
- Certain congenital malformations of the airway (choanal atresia, cleft palate, tracheo esophageal fistula, congenital diaphragmatic hernia, etc.)
- Severe cardiovascular instability (hypotension)
- Poor respiratory drive (frequent apnea and bradycardia) that is not improved by CPAP.

GUIDELINES FOR INITIATION OF CPAP THERAPY

When to initiate CPAP?

The timing of initiation of CPAP in preterm infants with respiratory distress needs further elaboration.

Early CPAP: It is important to note that CPAP helps mainly by preventing the alveolar collapse in infants with surfactant deficiency. Once atelectasis and collapse have occurred, CPAP might not help much. Therefore, all preterm infants (<35 weeks') with any sign of respiratory distress (tachypnea/chest in drawing/grunting) should be started immediately on CPAP.

Prophylactic CPAP: Extending this logic, some have advocated use of prophylactic CPAP (before the onset of respiratory distress) in preterm VLBW infants as majority of them would eventually develop respiratory distress. However, there is no evidence for any additional benefit with this approach; indeed, there are concerns regarding increased adverse effects such as intraventricular hemorrhage. Hence, prophylactic CPAP is NOT recommended at present.¹³

How to set up a CPAP apparatus?

The steps in setting-up a bubble CPAP are summarized in Panel 2.

How to fix the CPAP delivery system (nasal cannula)

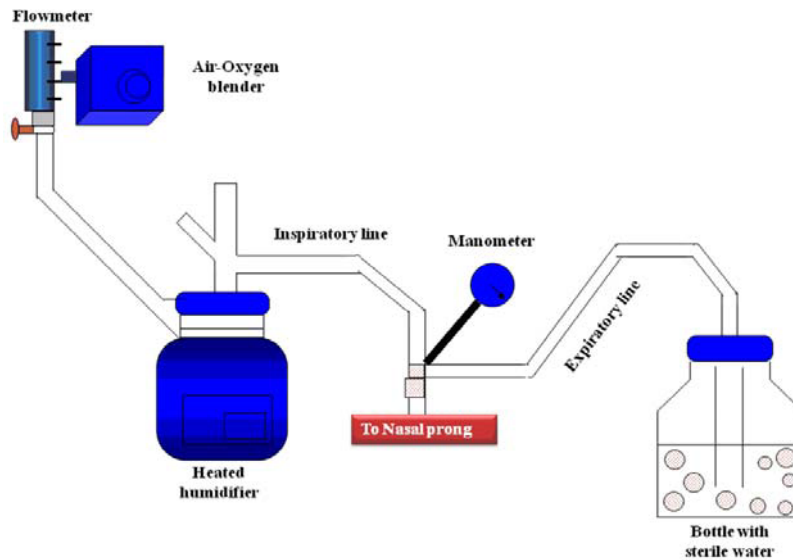
The most difficult aspect of using nasal CPAP is the positioning and fixation of the patient interface. The optimal technique of fixation depends on the type of delivery system used; the exact technique used does not matter as long as the device is secure and not traumatizing.

Short binasal prongs: It is important to choose the appropriate sized prong that snugly fits in the nasal cavity to avoid a significant leak. However, to avoid causing any injury, it should be fixed straight and not pressed hard against the nasal septum.

We use a modified cap (made from adult cotton socks) and

Panel 2. Steps of Initiation and Nursing Care during CPAP⁷**A. How to set-up a bubble CPAP?**

1. Connect the air and oxygen tubing (pressurized gases from either central manifold or from compressor and oxygen cylinder respectively)
2. Attach both to the air-oxygen blender
3. Set the flow using flow meter (usually at 5-8 L/min)
4. Set up the inspiratory limb:
 - a. From the flow meter to the humidifier and
 - b. From the humidifier to the patient end (e.g., nasal cannula); fill water in the humidifier and humidify the gases to 34-37°C.
5. Set up the expiratory limb - from the patient end to a chamber filled with sterile water. Immerse it under the water up to the required depth (which is determined by the intended pressure - e.g., to deliver 5 cm H₂O, immerse up to 5 cm mark in the tube).
6. Attach a pressure manometer at the patient end



7. Set required pressure and FiO₂, low pressure alarm and apnea alarm
8. Occlude the patient end of the ventilator circuit with your palm and observe if:
 - a. Bubbling occurs in the water chamber - If there are no bubbles, look for any leak in the circuit; if no leak is found, increase the flow by 1 L/min and recheck.
 - b. The set pressure is delivered (see the manometer reading) - If it is less than the set pressure, look for any leaks in the circuit/ around the cannula. If no leak is found, increase the flow and recheck.

B. Initiation of CPAP

1. Place a roll under infants' shoulder to slightly extend the neck
2. Application of prongs:
 - a. Choose the correct size prong (the prongs should fill the nasal opening without stretching the skin)
 - b. Apply a thin strip of *Tegaderm* on overlying skin of septum
 - c. Place the prongs with the curve downwards and fix as shown in Fig. 4.
3. Attach the patient end of the ventilator circuit to the cannula
4. Attach a pulse-oximeter to the infant

C. Nursing Care

1. Monitor the infant frequently (see text); observe if the baby is comfortable
2. Pass an orogastric tube. Keep the proximal end of tube open. If the infant is being fed while on CPAP, close the tube for half an hour after giving feeds and keep it open for the next 90 minutes (if fed 2 hourly).
3. Do regular but gentle nasal suction to clear the mucus 4 hourly or as and when required.
4. Clean the nasal cannula and check its patency once per shift.
5. Change the infant's position regularly every 2-4 hours and check the skin condition frequently for redness and sores.

Protocol for Administering Continuous Positive Airway Pressure in Neonates

TABLE 3. Protocol for CPAP Therapy in Three Common Neonatal Conditions

	Indications		
	RDS	Apnea of prematurity	Post extubation
How to initiate ?			
Pressure	<ul style="list-style-type: none"> Start at 5cm H₂O 	<ul style="list-style-type: none"> Start at 4cm H₂O 	<ul style="list-style-type: none"> Start at 4-5cm H₂O
FiO ₂	<ul style="list-style-type: none"> 0.5 (titrate based on SpO₂) 	<ul style="list-style-type: none"> 0.21-0.4 (as decided by SpO₂) 	<ul style="list-style-type: none"> 0.05 to 0.1 above the pre-extubation FiO₂
What to do if there is no improvement?			
Pressure	<ul style="list-style-type: none"> Increase in steps of 1-2cm H₂O to reach a maximum of 7-8 cm H₂O 	<ul style="list-style-type: none"> Increase up to 5cm H₂O (further increase is not warranted usually in this condition - may lead to hyperinflation) 	<ul style="list-style-type: none"> Increased in steps of 1-2cm H₂O to reach a maximum of 7-8cm H₂O
FiO ₂	<ul style="list-style-type: none"> Increase in steps of 0.05 (if oxygenation is still compromised) up to a maximum of 0.8 	<ul style="list-style-type: none"> FiO₂ increase does not help much 	<ul style="list-style-type: none"> Increase in steps of 0.05 to a maximum of 0.8
Failure of CPAP			
	Worsening respiratory distress (as indicated by Silverman scoring) and/or hypoxemia (PaO ₂ <50mmHg) / hypercarbia (PaCO ₂ >60mmHg) despite CPAP pressure of 7-8 cm H ₂ O and FiO ₂ of 0.8 <i>(Likely to occur in infants with severe RDS, associated sepsis, and in ELBW infants who have not received ANS)</i> Same as for RDS	Recurrent episodes of apnea requiring PPV <i>(Likely to occur in infants with central apnea's sepsis)</i>	<i>(Likely to occur in ELBW infants and in sepsis / pneumonia, PDA, metabolic acidosis, and collapse)</i>
Weaning from CPAP			
• When to wean	<ul style="list-style-type: none"> When there is no respiratory distress and SpO₂ / blood gases are normal 	<ul style="list-style-type: none"> No episodes of apnea/ desaturation / bradycardia for atleast 12-24 hrs 	<ul style="list-style-type: none"> Same as for RDS
• How to wean	<ul style="list-style-type: none"> Reduce FiO₂ in steps of 0.05 to 0.4, then decrease pressure in steps of 1-2cm H₂O until 3-4 cm H₂O (infants clinical condition will guide the speed of weaning) 	<ul style="list-style-type: none"> Same as for RDS 	

tapes to secure the binasal prongs (Fig. 4).

Steps of initiation and nursing care before and during CPAP

The steps of initiation and nursing care during CPAP therapy are given in Panel 2.

PROTOCOL FOR CPAP THERAPY

Protocol for CPAP therapy in the three most common clinical indications is given in table 3.

Monitoring while on CPAP

The following parameters need to be monitored while the infant is on CPAP:

- Continuous monitoring of respiratory rate, heart rate, SpO₂
- Serial monitoring of
 - a. Severity of respiratory distress by using Downe's or Silverman score
 - b. Arterial blood gases (ABGs)
 - c. Perfusion - CFT, BP, peripheral pulses, urine output

d. Abdominal girth

Hazards/Complications of CPAP

CPAP though less invasive and generally safer than IMV, is not free of side effects.

- Pulmonary air leaks are probably the most important clinically significant adverse effect of CPAP.¹⁴ It occurs following over distension of the lungs caused by inappropriately high pressures. They tend to occur when the lung compliance starts improving and the oxygen requirements also show a reduction. One has to note that the two recent trials on CPAP for RDS have shown either a trend or a definite increase in the incidence of pneumothorax.^{15, 16} Therefore, extra vigilance is required during CPAP therapy.
- Decreased cardiac output due to reduction in the venous return, decreased right ventricular stroke volume, and altered dispensability of left ventricle.¹⁷ This effect can be minimized by using optimal CPAP and achieving adequate intravascular volume.
- Impedance of pulmonary blood flow with increased

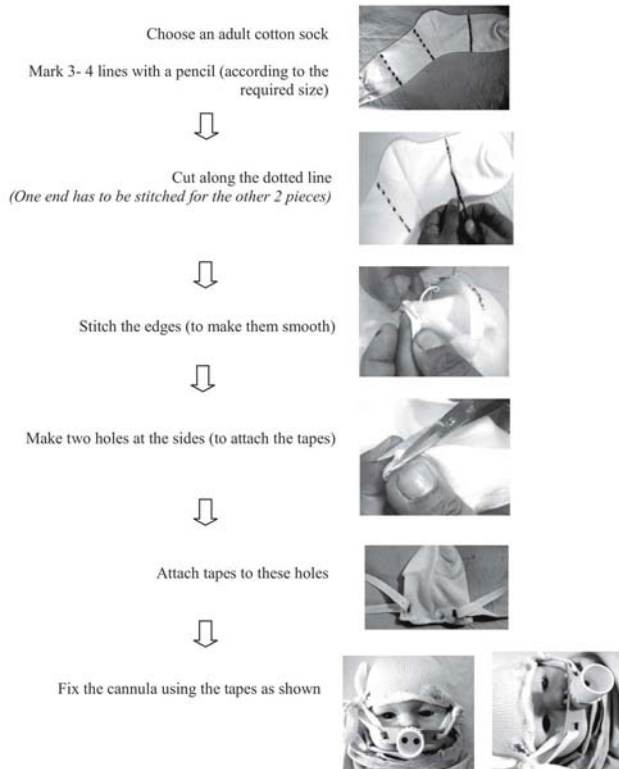


Fig. 4. Steps in Fixation of CPAP Nasal Cannula

pulmonary vascular resistance (with inappropriately high CPAP pressure)

- Gastric distension and 'CPAP belly syndrome'. These complications are rarely seen nowadays. The risk is further minimized by routine use of orogastric tube.
- Nasal irritation, damage to the septal mucosa, or skin damage and necrosis from the fixing devices.

CONCLUSION

CPAP has been well established as the first line therapy in the management of respiratory distress in preterm VLBW infants. It helps by preventing alveolar collapse, maintaining airway stability and stabilizing the chest wall. Various devices, both for pressure generation and for delivery of CPAP, are available for use in neonates. The advantages and disadvantages of each device, method of fixation of short binasal prongs, and a protocol for initiation of CPAP have been discussed in this protocol.

REFERENCES

1. Sankar MJ, Deorari AK. CPAP – A gentler mode of ventilation. *J Neonatol* 2007; 21 : 160-165.
2. Upadhyay A, Deorari AK. Continuous positive airway pressure - a gentler approach to ventilation. *Indian Pediatr* 2004; 41 : 459-469.
3. Gregory GA, Kitterman JA, Phibbs RH *et al*. Treatment of idiopathic respiratory distress syndrome with continuous positive airway pressure. *N Engl J Med* 1971; 284 : 333-340.
4. Kattwinkel J, Nearman HS, Fanaroff AA, Katona PG, Klaus MH. Apnea of prematurity. Comparative therapeutic effects of cutaneous stimulation and nasal continuous positive airway pressure. *J Pediatr* 1975; 86 : 588-592.
5. Avery ME, Tooley WH, Keller JP *et al*. Is chronic lung disease in low birth weight infants preventable? A survey of eight centers. *Pediatrics* 1987; 79 : 26-30.
6. Courtney SE, Barrington KJ. Continuous positive airway pressure and noninvasive ventilation. *Clin Perinatol* 2007; 34: 73-92.
7. Anonymous. Continuous Positive Airway Pressure Machines. In Deorari AK, Paul VK, eds. *Neonatal Equipment*. 3rd ed. New Delhi, Sagar Publications; 2006, 129-137.
8. De Paoli AG, Davis PG, Faber B, Morley CJ. Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates. *Cochrane Database of Syst Rev* 2002: CD002977.
9. Sreenan C, Lemke RP, Hudson-Mason A *et al*. High-flow nasal cannulae in the management of apnea of prematurity: a comparison with conventional nasal continuous positive airway pressure. *Pediatrics* 2001; 107 : 1081-1083.
10. Gittermann MK, Fusch C, Gittermann AR, Regazzoni BM, Moessinger AC. Early nasal continuous positive airway pressure treatment reduces need for intubation in very low birth infants. *Eur J Pediatr* 1997; 156: 384-388.
11. Poets CF, Sens B. Changes in intubation rates and outcome of VLBW -a population based study. *Pediatrics* 1996; 98: 24-27.
12. Verder H, Robertson B, Greisen G, Ebbesen F, Albertsen P, Lundstron JT. Surfactant therapy and nasal continuous positive airway pressure for newborns with respiratory distress syndrome. Danish-Swedish Multicentre Study Group. *N Engl J Med* 1994; 331: 1051-1055.
13. Subramaniam P, Henderson-Smart DJ, Davis PG. Prophylactic nasal continuous positive airways pressure for preventing morbidity and mortality in very preterm infants. *Cochrane Database of SystRev* 2005: CD001243.
14. Hall RT, Rhodes PG. Pneumothorax and pneumomediastinum in infants with idiopathic respiratory distress syndrome receiving CPAP. *Pediatrics* 1975; 55: 493.
15. Buckmaster AG, Arnolda G, Wright IM, Foster JP, Henderson-Smart DJ. Continuous positive airway pressure therapy for infants with respiratory distress in non tertiary care centers: a randomized, controlled trial. *Pediatrics* 2007; 120 : 509-518.
16. Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet JM, Carlin JB; COIN Trial Investigators. Nasal CPAP or intubation at birth for very preterm infants. *N Engl J Med* 2008; 358 : 700-708.
17. Tittley JG, Femes SE, Weisel RD, Christakis GT, Evans PJ, Madonik MM *et al*. Hemo-dynamic and myocardial metabolic consequences of PEEP. *Chest* 1985; 88: 496-502.