Continuous Positive Airway Pressure - A Gentler Approach to Ventilation

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Continuous positive airway pressure (CPAP) has become a useful modality in management of respiratory distress, especially in preterm babies. Main indications for use of CPAP are respiratory distress syndrome (RDS) and apnea of prematurity. It decreases the need of invasive and costly mechanical ventilation. This review details the physiological effects of CPAP, its methods of delivery, and its need in a country like India. It also describes the guidelines for initiating and weaning CPAP. The review concludes that use of CPAP in respiratory distress syndrome is associated with lower rates of failed treatment, decreased incidence of chronic lung disease and lower overall mortality, specially in infants with birth weight above 1500 grams. Early use of CPAP is more beneficial, Surfactant and CPAP act in conjunction for babies with RDS. CPAP is a low-cost, simple and noninvasive option for a country like India, where most places lack facilities of mechanical ventilation. Systematic reviews, randomized and quasi-randomized trials by searching MEDLINE and the Cochrane Library formed the basis of this update.

Continuous positive airway pressure (CPAP) is a continuously applied distending pressure (CDP) used for maintenance of an increased transpulmonary pressure during expiratory phase of respiration, in a spontaneously breathing patient. It is distinct from intermittent positive pressure ventilation (IPPV) or intermittent mandatory ventilation (IMV) in which breathing is taken over by the machine completely and the increase in pulmonary pressure occurs during both inspiratory as well as expiratory phases. This review details the physiological effects, modes of delivery of CPAP and emphasizes the need of CPAP in a country like India, where assisted ventilation for babies may be very costly and invasive option(1,2).

Historical Overview

Positive pressure therapy was first used by Poulton, and Oxan in 1936(3) who used facemask to treat acute ventilatory insufficiency. Harrison(4) is credited to first recognize the benefit of an increased alveolar pressure during expiration in infants with respiratory distress syndrome (RDS). He observed that grunt appears in cases of RDS, which increases progressively with increasing severity of disease and abolition of this grunt by use of endotracheal tube led to decrease in partial arterial pressure of oxygen (PaO_2) and further worsening of the disease. In 1971, Gregory, *et al.*(5) used CPAP for the first time in spontaneously breathing neonates with idiopathic RDS. Over the last 3 decades, several methods of applying CPAP have become routinely available. In recent years, newer modes of delivery systems are available such as Bubble CPAP and Dual Flow System (Infant Flow Drive).

Physiologic Considerations

The main application of CPAP is in

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treatment of hypoxemia. It does this by complex but integrated mechanisms. In doing so, it has some desirable and some undesirable effects on other body systems as well.

Respiratory system

CPAP causes increase in thoracic lung volume and functional residual capacity (FRC), decrease in total airway resistance(6), decrease in lung compliance(7), improvement in respiratory rate(8), tidal volume(9) and minute volume, regularisation of respiration(8,9) improvement in surfactant metabolism(10), splinting of chest wall, airways and the pharynx (pneumatic splinting) and reduced work of breathing(7).

Improvement in oxygenation occurs because of reopening of collapsed and/or unstable alveoli(11). This increases alveolar surface area for gas exchange, decreases intrapulmonary shunting(6) and improves surfactant metabolism(10,11). Reduction in compliance occurs, which suggests that over distension of normal air spaces is more prominent than recruitment of collapsed alveoli(7). The beneficial effect of CPAP is due to prevention of progressive alveolar collapse with marginal stability of alveoli. By preventing collapse of alveoli, CPAP also conserves surfactant. This is why CPAP is more effective early in disease when most alveoli are still open(11).

In extremely low birth weight babies, the chest wall is very compliant and tends to collapse with descent of diaphragm (paradoxical respiration). This results in small and ineffective tidal volumes. CPAP helps by splinting the chest wall and the airways, which increase in caliber. This decreases the airway resistance and improves the ventilation of lung segments supplied by airways(11,12). Thus permitting a larger tidal volume for a given pressure, thus reducing the work of breathing. The work of breathing is further reduced by constant flow of gas directed to the patient does part of the work.

Cardiovascular effects

CPAP increases intrathoracic pressure which can decrease venous return ultimately leading to decrease in cardiac output(13). This results in poor perfusion as oxygen availability to tissues decrease(14). This change in cardiac output results in decline in arterial blood pressures. These effects are enhanced in hypovolemic patients. These cardiovascular effects occur only at supraoptimal CPAP pressures. Giving optimal CPAP should improve metabolic acidosis and cardiac output.

Renal system

CPAP can result in decrease in glomerular filtration rate and thus the urine output(15). Renal effects are directly proportional to compliance of the chest wall.

Gastrointestinal tract

Abdominal distension can occur in babies on CPAP(16). It is compounded by presence of immature gut in preterms and some decrease in blood flow to the gut. All these together lead to what is called as ‘CPAP belly syndrome’. Clinically the baby develops increased abdominal girth and dilated bowel loops, which may cause upward pressure on diaphragm and respiratory compromise.

Central nervous system

There is increase in intracranial pressure (ICP) with application of CPAP. This, in combination with decrease in arterial pressure, results in decrease in cerebral perfusion pressure (CPP). Increase in ICP is seen more with head box CPAP than with endotracheal CPAP or nasal prongs(17,18). High ICP is instrumental in pathogenesis of intraventricular hemorrhage in low birth weight babies ventilated for RDS.

Modes of Delivery of CPAP

Gregory, *et al.*(5) first described two methods of delivery of CPAP in 1971 for treatment of RDS: through endotracheal tube and by pressure chamber around infants' head. Subsequently facemask and naso-pharyngeal tube have been used(19). Currently, the most commonly used method is delivery of CPAP by nasal prongs(1,2). These are useful and effective as neonates are obligate nasal breathers. The prongs can be sterilized and reused making them very cost-effective. Mouth leak provides pressure pop off; there is no benefit of forcible mouth closure as the transient benefit is outweighed by occurrence of gastric distension and rupture. Prongs can cause trauma to nasal turbinates and septum. They are not universally beneficial in infants less than 1000 to 1250 grams. Single prong nasal CPAP has been used by cutting short an endotracheal tube. It can be used to deliver both nasal and nasopharyngeal CPAP. However, double nasal prongs have been shown to be better than single nasal prongs for CPAP delivery(20). What should be the optimal length of nasal prongs has yet not been researched thoroughly.

Endotracheal CPAP should preferably not be used due to its invasiveness and increased risk of infection. It increases the work of breathing by increasing the resistance and baby can tire out. Cochrane review(21) prohibits the use of ET CPAP even before extubation as it offers no help and decreases the chance of successful extubation.

Recently, certain units in US have stated use of soft 'CPAP masks'. They offer the advantage of causing lesser damage to nasal septum, being more comfortable to the baby and better fixation. However, there are no trials to support the use of these new generation masks. Though nasal canulae used to deliver oxygen to the babies do provide some CPAP when the outer diameter is more than 3mm, it should not be used to do so routinely, as pressure delivered cannot be regulated and properly monitored.

Newer CPAP Systems

Bubble CPAP is CPAP delivered by CPAP system with underwater seal. It has been shown that CPAP delivered by underwater seal causes vibration of the chest due to gas flow under water, which is transmitted to infant's airway. These vibrations simulate waveforms produced by high frequency ventilation(22). Bubble CPAP has also been shown to reduce need for intubation and mechanical ventilation(23), postnatal steroids and trend towards decreased incidence of chronic lung disease(24). If proven by subsequent studies, it would offer an effective and inexpensive option for delivering CPAP.

Another new mode of CPAP delivery is use of dual flow CPAP, or Infant Flow Drive CPAP. In contrast to other binasal systems, it uses 'fluidic flip' mechanism, which is claimed to provide a more stable CPAP throughout the respiratory cycle (both inspiration and expiration) so that there is less variation in airway pressure(25). Mazzella, *et al*.(26) have shown superiority of IFD over nasal CPAP in terms of decreased oxygen requirement and respiratory rates and lesser need for mechanical ventilation. Babies who failed nasal CPAP could be rescued by IFD and mechanical ventilation could be avoided. IFD treated patients also had higher extubation rates, shorter duration of ventilation(26) and fewer extubation failures(20). However, this superiority of IFD over NCPAP has not been observed by others (27,28).

Indications for Initiating CPAP

CPAP is shown to be beneficial in preterms especially very low birth weight babies (<1500 grams) and can be used for respiratory distress after birth, irrespective of etiology, radiology and blood gas criteria. In general, criteria to initiate CPAP are moderate to severe respiratory distress, PaO_2 less than 50 to 60 mm Hg while patient is breathing 60% oxygen and recurrent apnea.

Guidelines

The CPAP is started at pressure of 5 cm of water with FiO_2 of 0.4 to 0.5. If respiratory distress does not improve with this, or worsens further or oxygenation is impaired, pressure is increased in steps of 1 to 2 cm of H_2O to reach a maximum of 8-10 cm of H_2O on nasal CPAP. If still the oxygenation is compromised, FiO_2 is then increased in steps of 0.05 to reach a maximum of 0.80. While starting CPAP, it is important to resist the temptation of raising FiO_2 before pressures for hypoxemia–this can be a fatal. Certain ventilators like SLE 2000 can adjust the flow rates to provide desired pressures. In others, optimal flow rate should be provided. It should be 6-8 Lit/min in preterm and 8-10 Lit/min in full term infants.

Monitoring of a Baby on CPAP

Continuous monitoring of respiratory rate, respiratory distress by Downe's or Silverman score, capillary refill time, blood pressure, peripheral pulses, temperature, abdominal girth and urine output, oxygen saturation monitoring and blood gas analysis should be done as and when required. Aim is to maintain saturation between 90-93%, PaO_2 between 60-80 mm Hg and $PaCO_2$ between 35 to 45 mm Hg of water. Permissive hypercapnia with upper limit of CO_2 up to 55 mm Hg can be allowed, provided the pH is maintained above 7.25(29,30). However this approach of permissive hypercapnia has its own adverse effects(31) and more randomized controlled trials are needed before this later strategy can be routinely recommended.

Optimal CPAP

It is that setting of CPAP which results in stabilized respiratory rate, no respiratory distress, pink color and normal capillary refill time and blood pressures. The saturation should be between 90 to 93%, PaO_2 of 60-80 mm Hg and $PaCO_2$ of 35 to 45 mm Hg and pH of 7.3 to 7.4. Physiologically speaking, optimal CPAP is the level of distending pressure that results in maximum PaO_2 on lowest FiO_2 without increase in $PaCO_2$ or any adverse effect on circulatory status. An easy bedside method is to look at X-ray chest. On optimal settings, number of posterior intercostal spaces above the diaphragm will be between 7-8. If lungs are low volume (£5 spaces), increase the CPAP, if lungs are hyperinflated (>8 spaces), or the dome of diaphragm appears to be flattened, decrease the CPAP.

Failure of CPAP

CPAP may not work in all patients. CPAP failure is defined as $PaCO_2$ of more than 60 mmHg and/or PaO_2 less than 50 mmHg at pressure of 8 cm H_2O at a FiO_2 of 0.8. CPAP failure can occur due to recurrent apnea, increased work of breathing due to worsening disease, or intracranial hemorrhage. Progressive metabolic acidosis, pulmonary edema and lack of nutrition with respiratory muscle fatigue may lead to initiation of CPAP to mechanical ventilation. Other remediable causes which should be looked into are: improper fixation of CPAP device and frequent dislodgement, excessive secretions obstructing the airways or nasal prongs, low flow rates in the circuit and faulty machine delivering lower pressures or FiO_2 than displayed on screen. CPAP failure is more likely to occur in extremely low birth weight babies (<1000 grams), and in babies with severe HMD or pneumonia. A delay in initiating CPAP is more likely to be associated with failure.

Weaning from CPAP

The patient should be weaned from CPAP after the natural course of disease is expected to be improving. There should be no respiratory distress on this setting, minimal or no need for vasopressor support, normal blood gas and an improving *X*-ray chest. Once it is decided to wean off CPAP, FiO_2 should be decreased in steps of 0.05 to FiO_2 of 0.40. Then pressures should be decreased in steps of 1-2 cm H_2O until a pressure of 3-4 cm H_2O is reached. Pressure should not be decreased beyond this as this may increase the work of breathing. The infant should then be transferred to oxygen hood at a slightly higher FiO_2 (by 0.10 to 0.20). The patients' condition will guide the speed of weaning. One should not be in unusual haste as 'fast weaning' is commonly associated with failure of weaning. A preterm may not tolerate removal of CPAP. Indications of restarting CPAP in such a baby are same as those when CPAP is started for first time.

Clinical Applications of CPAP

Respiratory distress syndrome (RDS)

RDS is a state of surfactant deficiency, which results in collapse of alveoli, resulting in loss of functional residual capacity and low volume lungs. RDS is an excellent indication for CPAP. The key for successful management of RDS is early initiation of CPAP, which means, starting CPAP immediately after the onset of respiratory distress. The aim is to intervene as early as possible, so as to (*i*) prevent progressive atelectasis, (*ii*) avoid need for intubation, which carries a risk of mucosal injury and secondary infection, and (*iii*) to minimize barotrauma and volutrauma to airways and lung parenchyma. The guidelines given earlier apply primarily to babies with hyaline membrane disease.

Use of early CPAP establishes and maintains an adequate functional residual capacity (FRC) by preventing collapse of unstable alveoli and opening up some already collapsed alveoli. This is crucial for gas exchange, stabilization of air spaces and promotion of release of surfactant stores. Numerous studies have shown the fact that early use of CPAP reduces the need for subsequent intubation and mechanical ventilation in RDS(32-34). In those who require it later, ventilation is successful at lower pressure(35). According to the Cochrane review(36), use of CPAP was associated with lower rates of failed treatment by about 30%, overall mortality by 50%, and mortality in infants with birth weight above 1500 grams by as much as 75%. However, the risk of pneumothorax is almost doubled. However, according to another Cochrane review(34), early use of CPAP (at onset of respiratory distress) was associated with decreased need for intermittent positive pressure ventilation (IPPV) by about 50%, but it had no effect on mortality, or chronic lung disease at 28 days of life, when compared to late initiation of CPAP *i.e.*, when FiO_2 requirement of baby is more than 60%. This is clinically important, as IPPV is associated with considerable increase in cost to the family. However, most studies in the meta-analysis are very old, and its generalisability in the era of surfactant and antenatal steroid needs to be reevaluated.

By employing the strategy of CPAP and

permissive hypercapnia ($PaCO_2$ upto 55 mm Hg), the need for mechanical ventilation can be reduced and hence decrease the risk for barotraum(33). By decreasing need for intubation, it decreases the risk of airway damage and secondary infection(37,38). This would also considerably reduce the cost of neonatal intensive care. The risk of development of CLD is also possibly reduced with early institution of CPAP(35,39).

Prophylactic CPAP

This refers to starting CPAP in VLBW babies as soon as they are brought to NICU even if they do not have any respiratory distress. This cannot be recommended because the Cochrane meta-analysis shows that there is no role of prophylactic CPAP in VLBW babies; it is not only not helpful, but is also associated with trend for increased incidence of CLD, IVH and even mortality(40).

CPAP in an era of surfactant

There is evidence that beneficial effect of early CPAP in preterms can be enhanced by giving surfactant to the patient after brief intubation(39,41,42). In this approach, the preterm is started on CPAP as soon as he develops respiratory distress. When respiratory distress on CPAP progresses beyond a predetermined point (ratio of arterial to alveolar oxygen tension (a/A) of less than 0.36), the baby is intubated, given surfactant, and then extubated and put back on CPAP again. This is known as Intubation - Surfactant-Extubation(INSURE) approach(42). This further reduces the need for subsequent ventilation by halting the progress of RDS and improves the outcome in newborns.

Surfactant and CPAP act in conjunction in fulfilling the aim of increasing lung volume and the functional residual capacity.

However, the ideal therapy for RDS would be the use of early nasal CPAP combined with surfactant inhalation via CPAP apparatus itself, obviating the need for even short-term intubation. With steadily decreasing cost of surfactant such an approach could probably be adopted in future in small NICUs of our country. Then the preterms referred to higher centers will be in much stable and healthier shape. However, extensive research is still required before it can be advocated or practiced.

Apnea of prematurity

CPAP has been shown to reduce the incidence and severity of mixed and obstructive apneas(43) by preventing collapse of pharynx and upper airways and splinting of diaphragm, a mechanism responsible for most of apnea of prematurity(44). It thus helps selectively in mixed and obstructive apnea(8). CPAP should be started at 3-5 cm H_2O by single or double nasal prongs, if life threatening or recurrent apnea occur despite drug treatment.

Patent ductus arteriosus (PDA)

CPAP relieves signs of cardiac decompensation associated with left-to-right shunt and reduces the left atrium to aortic root ratio(45). The mechanism by which CPAP helps in PDA in preterms with RDS is by preventing alveolar collapse and improving oxygenation. The high PaO_2 initiates ductal constriction. Also, it helps in pulmonary edema by reducing pulmonary vascular resistance and pulmonary artery pressure.

CPAP after extubation from ventilation

Nasal CPAP is effective in preventing failure of extubation in perterm infants following a period of endotracheal intubation and IMV as it reduces the incidence of apnea, respiratory acidosis and increased oxygen requirement(46-49). However, trial of short duration endotracheal CPAP prior to extubation from IMV is not recommended(20). Evidence is emerging that Synchronized Nasal Intermittent Positive Pressure Ventilation (SNIPPV) is better than nasal CPAP in preventing failure of extubation(50-52).

Meconium aspiration syndrome (MAS)

Application of CPAP can be beneficial in MAS, probably through resolution of atelectasis and stabilization of collapsing terminal airways. Those cases of MAS in which *X*-ray chest reveals low lung volumes respond best to CPAP therapy, because CPAP then helps in opening up atelectatic areas of the lung. CPAP will not have much benefit if lung is already overinflated. However, MAS is a disease of term babies and sometimes they do not tolerate the irritation of nasal CPAP devise. If infant is quite restless, it would be better to switch over to intermittent mandatory ventilation (IMV).

Nursing care of a baby on CPAP

Minimal handling of baby is recommended while the baby is on CPAP(53) (this does not mean that the baby should not be adequately examined). Air-oxygen mixture should be warmed and humidified. Keeping the nasal prongs in place is a big challenge, especially in larger babies. It should be firmly secured with the indigenous means available. Orogastric tube should be left *in situ* with its end open to prevent gaseous distension of stomach. Regular but gentle nasal suction to clear the mucus should be done 4 hourly or as and when required. Nasal cannula should be cleaned and its patency should be tested at least once a day. Periodic massage of the nares should be done to improve the blood circulation. The prongs should not press hard against the baby's face. Regular change in posture every 2-4 hours should be done and the skin checked frequently for sores. No attempt should be made to keep the mouth closed while the baby is on CPAP. This has no added advantage and can result in local trauma and gastric distension. Intermittent opening of mouth prevents excessive build up of pressure in the stomach. Some fluctuation in CPAP pressure is acceptable and reflects baby's efforts. Periodic change in posture of the baby should be done. With prone posture, fixation of nasal prong can be a practical problem, so babies are usually nursed in supine or lateral positions.

CPAP is no contraindication to feeding. Once the baby is hemodynamically stable, minimal enteral nutrition should be started as 10 mL per kg of expressed breast milk by orogastric (OG) tube. It can be gradually increased depending on baby's clinical status and the unit policy. Abdominal girth and pre-feed aspirate should be monitored 2 hourly. Feed intolerance can occur due to gastric dilation secondary to CPAP.

Small, preterm babies with respiratory distress syndrome rarely require any sedation. However, trichlofos can be used occasionally to calm a agitated term infant. Agitation can be further reduced by "nesting" the baby in linen made boundaries, decreasing environmental light and sound stimuli and minimal handling of baby. If these fail to decrease agitation, either the baby does not need CPAP or switch over to IMV may be required.

Adverse Effects and Complications

Though CPAP is less invasive and safer than, it is not free of side effects.

1. Pulmonary air leaks (PAL) are probably the most important clinically significant adverse effect(36,54). The incidence of

Key Messages

- CPAP in preterms with RDS is a life saving, relatively simple and noninvasive technique. It is most useful when used early in course of disease.
- CPAP helps by recruiting atelectatic alveoli and improving surfactant metabolism .
- Early use of CPAP reduces the need of subsequent ventilation and decreases risk of chronic lung disease.
- Exogenous surfactant administration in conjunction with early CPAP may become a viable option for developing countries.

pneumothorax during nasal CPAP increases with increasing gestation age(54). PAL tend to occur when oxygen requirements are decreasing and lung compliance is improving(55).

2. Use of excessive PEEP may compromise oxygenation. Excessive increase in PEEP may increase the blood flow to unventilated region, which causes ventilation and perfusion mismatch; this leads to decrease in oxygenation.
3. Abdominal distension and gastric rupture are well documented complications of CPAP. This can be minimized by routine use of orogastric tube. The use of nasogastric tubes should be avoided because most neonates are preferential nasal breathers and occlusion of one nostril decreases air entry and increases the work of breathing; moreover, with nasal CPAP, fixation and seal become a problem with nasogastric tube.
4. Cardiac output is believed to decrease due to decrease in venous return, because CPAP causes increase in intrathoracic pressures, decreased right ventricular stroke volume and altered dispensability of left ventricle(55,56). The effects are exaggerated in hypovolemic patients. These effects can be minimized by using optimal CPAP and achieving adequate intravascular volume.
5. Local complications like nasal septum deformity can occur on prolonged use of nasal prongs. Flaring of nostrils and snubbing of the nose can occur after prolonged nasal CPAP(57).

In India, there is high burden of prematurity due to high birth rate and lack of good antenatal care. Lack of awareness and suboptimal practice of administering antenatal steroids, results in frequent RDS in premature babies. Early use of CPAP will be low-cost, simple and noninvasive option for a country like India, where most places cannot provide invasive ventilation. With the cost of surfactant likely to decrease markedly, use of early CPAP in conjunction with surfactant, when indicated can prove to be a boon in future for preterms in India.

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