Workbook on

CPAP

Science, Evidence & Practice

Learner's Guide

from:

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All India Institute of Medical Sciences, New Delhi ;
Post Graduate Institute of Medical Education Research, Chandigarh ;
Fernandez Hospital , Hyderabad

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Programme CPAP Workshop

Pre Lunch - Inaugural function & Introduction 15 minutes

A. Each talk 30 minutes (includes 10 min Discussion) 9am to 12am (15 min break)

1. Science behind CPAP -
2. Evidence CPAP including INSURE, Delivery Room CPAP -
3. Art of CPAP: initiation, monitoring, weaning, -
4. Failure & Success- How to predict, complication of CPAP -
5. Monitoring and related procedures -
   (Monitoring chart, X-rays, pain relief, feeding, umbilical line, surfactant administration)

B. Mini workshops 20 minutes each (One before Lunch) (12am to 1pm)

1. Equipment of CPAP (Local/Bubble) -
2. Flow Driver and Humidification -
3. Fixation of patient interface (Hudson/Argyle) -
4. Fixation of patient interface (Fisher and Paykel/ others) -

C. Case Studies 3 cases (2 to 3.30pm) - One hour 30 min

Success, Failure, INSURE CPAP

D. Panel discussion on How to set CPAP services 40 minutes - All Faculty

Open House - 20 minutes

Valedictory Function - 10 minutes

Preface

CPAP is a non-invasive and gentler method of providing respiratory support to spontaneously breathing infants. If used in early phase of respiratory distress syndrome, with or without surfactant, CPAP convincingly improves neonatal outcome. In this modular **participatory** learning program, the participant will imbibe the science and physiological basis of CPAP. The art and practice of CPAP however , would have to be pursued on the bedside.

In this workshop, both animal as well as clinical evidence for improved outcomes with CPAP will be discussed. Although the usefulness of CPAP is proven, it is not clear what is the best way to use CPAP for babies with respiratory distress. Confusion is added by the multitude of CPAP machines and interfaces. Very few studies have compared physiological and even fewer, the clinical effects of various CPAP devices. The participant will also learn about an ideal CPAP machine and the limitations of the current indigenous systems. There is a lot of scope for innovation and research in low cost CPAP machines. This modality of respiratory support will be most successful, if it is used in newborn units with established systems for handling premature VLBW babies. One requires a team of dedicated health professionals especially nurses to manage a baby on CPAP. Babies who survive must be evaluated for short term (IVH, ROP) and long term (hearing, neuro developmental) outcomes.

It is a must that all participants attend the full course and understand the physiological basis, application and monitoring of CPAP. The teaching and learning is interactive with self reading material, FAQs, case discussions, demonstration of equipments, video clips and MCQs. It is desirable that all health care professionals who work in level-II NICUs be skilled with the art of CPAP application and monitoring. This can salvage most of the babies even in remote places and only few babies would have to be transferred to higher centers.

August 15, 2009

Editors : Deorari, Praveen, Srinivas

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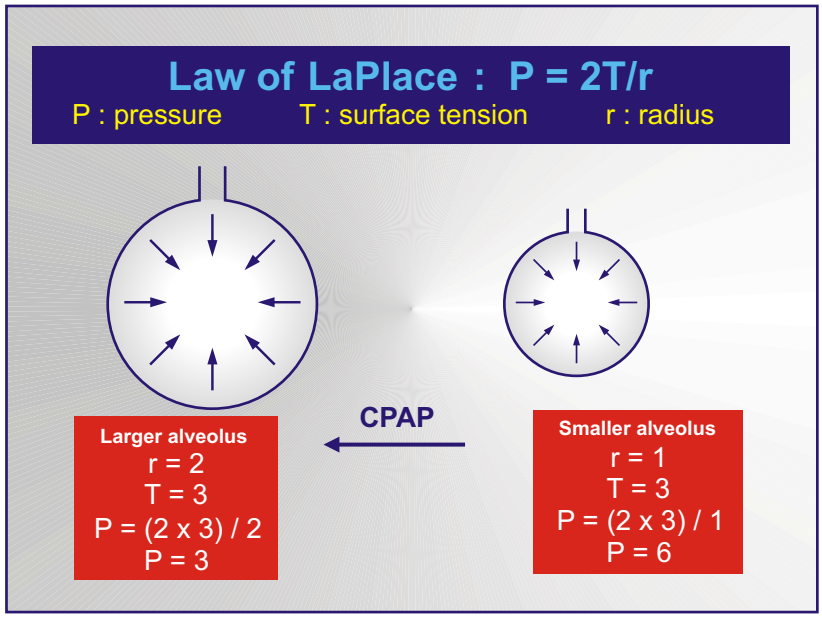
Science & Physiology of CPAP

Dr. Ashok Deorari
Division of Neonatal unit, Department of Pediatrics, AIIMS

CPAP, also called continuous distending pressure (CDP), refers to the application of continuous pressure during both inspiration and expiration in a spontaneously breathing baby. By providing constant airway pressure, the alveoli are kept open which increases the functional residual capacity (FRC) of the lungs resulting in better gas exchange.

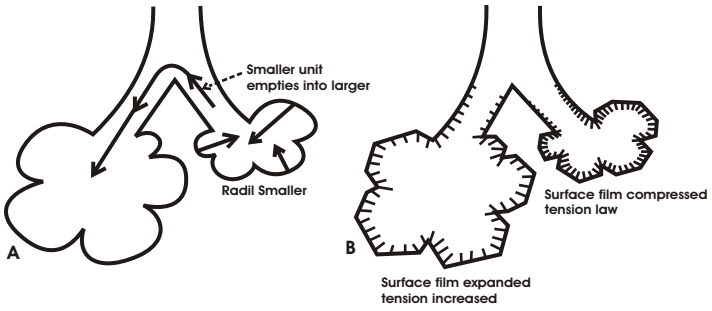
Effects of CPAP

1. In a baby with hyaline membrane disease (HMD), the FRC is usually reduced below the closing volume (volume below which the terminal airways connected to alveoli get closed). CPAP increases the FRC to a level above the closing volume so that the terminal airways remain open throughout the respiratory cycle.
2. According to Laplace's law, an alveoli lined by water molecules exerts inward pressure to collapse the alveoli. This is determined by the formula:



$P = \frac{2T}{R}$ (P is inward pressure making alveoli to collapse, T is surface tension and R is radius of the alveoli)

Thus smaller (diameter) alveoli will have a tendency to empty into larger (diameter) alveoli connected to each other. If the surface tension is reduced by giving



exogenous surfactant, the inward pressure which leads to collapse can be reduced. By giving CPAP, one neutralizes the inward collapsing pressure. The net effect of both is more than additive.

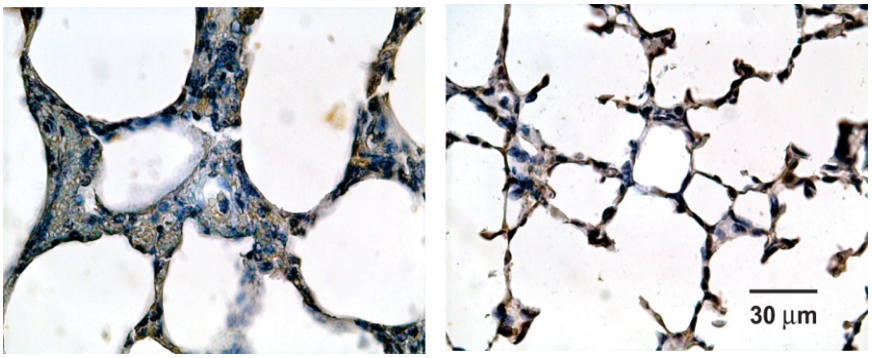
Physiological benefits

CPAP

- results in improved oxygenation, wash out of CO2, and better blood pH.
- splints the upper airways thus preventing obstructive apnea.
- stimulates 'J' receptors by stretching the lung/pleura and providing positive feedback to respiratory centre by Hering Bruer reflex.
- results in better Type II-pneumocyte function and even recycling of surfactant thus contributing to early recovery from HMD.
- results in better ventilation-perfusion match, improved minute ventilation and decreased work of breathing.

Disadvantages of conventional ventilation (CV)

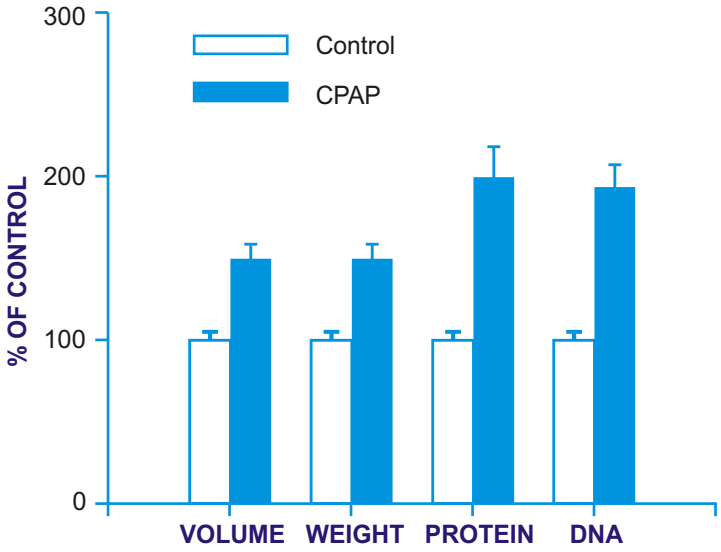
CV of premature lung results in inflation and deflation of alveoli at high pressure (Barotrauma); tidal volumes (volutrauma); few alveoli collapse & reopen from collapsed stage resulting in atelecto-trauma. In addition, endotracheal tube is a foreign material resulting in inflammation & infection (Biotrauma). Using nasal CPAP would avoid most of the ill effects of mechanical ventilation. Use of CV results in rupture of interalveolar septa thus decreasing the surface area for gas exchange despite increasing lung volume. In animal models, as little as 72 hours of CV has been shown to result in thickened alveolar septa.



Advantages of CPAP

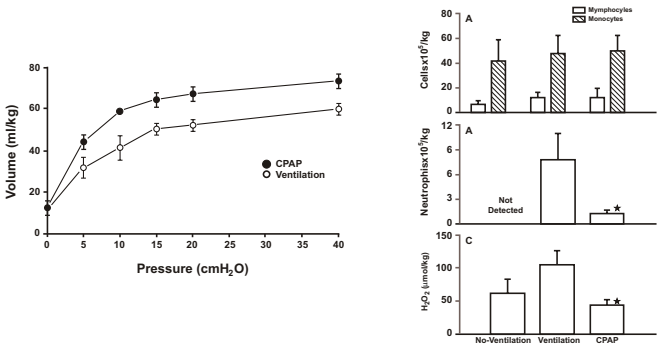
a. Effect on lung growth

CPAP promotes growth in premature lung, as evidenced by increased DNA and protein per gm of lung tissue following CPAP application, while conventional ventilation initiates inflammatory response in the lung as evidenced by increased polymorphs and free oxygen radicals in the lung lavage.



Lung volume, lung weight, protein and DNA content at the end of study were higher in CPAP-group than in control group ($P<0.01$). Strain-induced growth of the immature lung. Zhang S. et al. J. Appl Physiol 1996;81:1471-6

✓ *CPAP Decreases Acute Lung Injury in Preterm Lambs*
CMV vs. Bubble CPAP x 2 hours

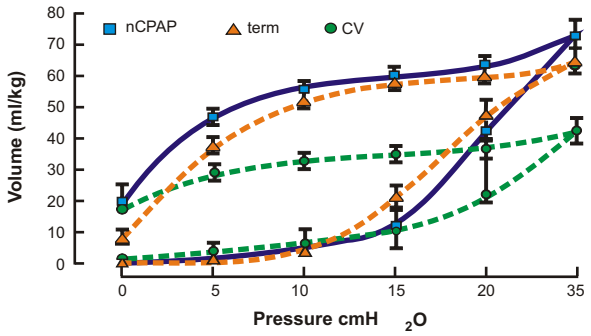


(Jobe AH: Pediatr. Res. 2002)

B. Effect on compliance

Animal experiments have demonstrated that lung compliance of premature lung following 28 days of CPAP application either matches that of a term lung or is better. In contrast lung compliance is reduced following conventional ventilation.

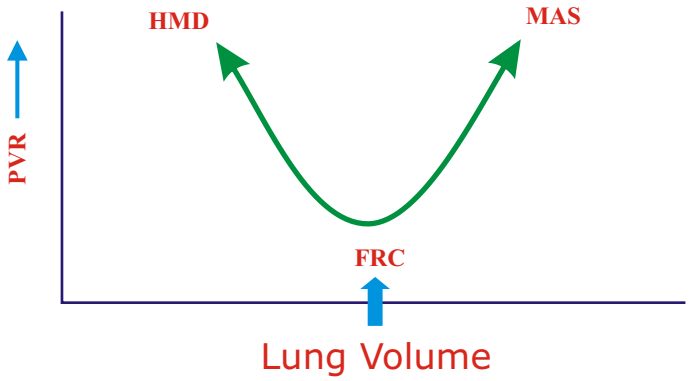
Early (24hr) CPAP in Surfactant-treated Preterm Baboons (125 days gestation)



(Thomson MA AJRCCM 169:1054, 2004

C. Effect on pulmonary vascular resistance

By providing optimal CPAP , the lung is kept open at the FRC . The architect of blood vessels in the lung is such that, PVR is least at FRC and increases when the lung volume is reduced below FRC (HMD) or increased above FRC (MAS evidence).



Based on physiological principles and studies on animal models, there is strong evidence to use early CPAP as a primary modality with or without surfactant for babies with respiratory distress syndrome.

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CPAP - Evidence for use

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Continuous positive airway pressure (CPAP) was first used as a method of supporting the breathing of preterm infants in 1971[1]. Since the introduction of surfactant into the therapeutic armamentarium, the thrust was on new and sophisticated ventilation strategies in the management of respiratory distress syndrome in newborns. Nevertheless, chronic lung disease (CLD) remained a frequent sequel of prematurity. Ventilation itself was identified as the most important cause of CLD[2]. The term "ventilator-induced lung injury" (VILI) implies that lasting damage can be avoided by preventing VLBW infants from being ventilated. "VILI" stimulated the reinvention of CPAP as a gentler and effective mode of ventilation. Renowned institutions in New York and Scandinavia have practiced primary nasal CPAP in very preterm infants for three decades, resulting in less usage of surfactant and ventilation and impressively low rates of CLD[3,4]. Today the rapidly growing number of neonatologists, eager to emulate this experience, face a difficult choice from among a variety of devices and practical approaches. This review may provide some orientation to the increasingly complex debate surrounding CPAP and its further development.

How does CPAP work?

CPAP supports the breathing of premature infants in a number of ways. The upper airway of the preterm infant is very compliant and therefore prone to collapse. CPAP splints the upper airway and therefore reduces obstruction and apnoea[5]. Preterm infants struggle to establish and maintain lung volumes due to surfactant deficiency, muscle hypotonia, slow clearance of lung fluid and a compliant chest wall. CPAP assists expansion of the lungs and prevents alveolar collapse. In doing so it reduces protein leak and conserves surfactant.

CPAP devices

CPAP has been applied to preterm infants using an array of devices. Gregory used it by enclosing the head in a plastic pressure chamber[1]. Subsequent CPAP devices included a pressurized plastic bag fitted over the infant's head[6], face chamber[7] and face masks[8]. The use of facial masks and devices requiring a neck seal declined as a consequence of serious complications or difficulty in maintaining an adequate seal. However nasal devices have remained popular, as they facilitate better access to the infant. Devices in common use for the delivery of nasal CPAP include single and double (binasal) prongs and in both short (nasal) and long (nasopharyngeal) forms.

Single long and short nasal prong CPAP, using a cut endotracheal tube passed through the nostril, continue to be used widely despite evidence of better results using short binasal devices[9]. In its long form, the tip of the endotracheal tube lies just above the epiglottis and in the short form the endotracheal tube is passed only 1-2 cm into one nostril with about 3 cm outside the nose. The long form has the disadvantage of a high resistance and a large reduction in delivered pressure from the other nostril.

There are several different designs of short bi-nasal prongs and all have two short tubes which provide low resistance. They include the Argyle prongs, Hudson prongs, infant flow driver (IFD) or Aladdin Generators, INCA prongs and Medijet prongs. The evidence, from a meta-analysis of randomized clinical trials (RCT's) of nasal CPAP devices in very preterm neonates, is that short bi-nasal devices are more effective at preventing re-intubation when compared with single nasal prong devices [RR 0.59 (0.41, 0.85), RD -0.21 (-0.35, -0.07), NNT 5 (3, 14)][9]. A randomized trial in more mature preterm infants with early respiratory distress reported better oxygenation, respiratory rate, and weaning success with a short bi-nasal device when compared with single prong nasopharyngeal CPAP[10]. Probably the main reason that these devices are more effective is that they have a lower resistance, allowing greater transmission of the applied pressure to the airway[11].

The IFD has been compared with other short bi-nasal devices but there are few studies comparing the performance of the other short bi-nasal devices. A RCT comparing the tolerance and efficacy of Hudson and Argyle prongs concluded that both these devices were equally effective for nasal CPAP delivery, but the Argyle prong is more difficult to keep in the nostrils of active patients, and nasal hyperemia occurs more frequently among infants using this prong[12]. Currently both these devices are widely used.

Another delivery device is the small nose mask manufactured to fit the IFD instead of the prongs. They are used in the belief that they reduce trauma to the nostrils but their effectiveness has not been reported. However, it is difficult to produce a good seal without undue pressure on and around the nose and it may traumatise the junction between the nasal septum and the philtrum[13]. Recently a new generation of nose masks have been developed which anecdotally have been noted to deliver CPAP effectively while causing minimal nasal trauma. These promising devices have not yet been subject to proper clinical comparison with nasal prongs.

Techniques for pressure generation

Expiratory flow valve (e.g. ventilator)

The ventilator PEEP valve controls the CPAP delivered. The flow is usually set to about 6 l/min. If the flow is too low or if there are large leaks, adequate pressure will not be delivered and the work of breathing may be increased. The work of breathing was found to be increased with conventional ventilator driven CPAP (circuit flow

limited to 6 l/min) compared with an IFD system maintaining pressure at the device level with variable flow (set inspiratory flow not specified)[14].

Underwater tube 'bubble' CPAP

Underwater bubble CPAP remains in use since first devised in the early 1970's[1]. With this technique gas flows past the nasal device and the pressure is generated in the circuit by placing the distal limb of the CPAP circuit under a known depth of water. This is a simple and effective technique which can be applied with inexpensive equipment. A unique feature is that loss of CPAP pressure is detectable by the disappearance of the bubbling. A comparison of underwater bubble endotracheal (ET) CPAP with ventilator derived ETCPAP in preterm neonates suggested that the bubbling contributed to gas exchange.

Bubble CPAP produces pressure oscillations of up to 4 cm H_2O measured in the circuit. It has been suggested that bubble CPAP is more effective than ventilator CPAP because of these oscillations[15]. However, Kahn et al. showed that bubble CPAP pressure oscillations are progressively attenuated distal to the prongs[16]. This suggests that very little effect of the oscillations will be transmitted to the periphery of the lungs. Interestingly, a preterm lamb model compared bubble CPAP with ventilator-generated CPAP and found that the bubble technique was associated with a slightly higher pH, better oxygenation and decreased alveolar-exuded protein, compared with the ventilator group[17]. However, a short-term cross-over study of human neonates comparing fast bubbling with minimum bubbling did not find any difference in blood gases[18]. Also a study comparing bubble CPAP with variable flow CPAP in VLBW neonates with minimal respiratory distress showed that the breathing may be more labored and asynchronous with bubble NCPAP and this may lead to higher failure rates[19]. In vitro study suggests that the noisy pressure waveform of bubble CPAP superimposed on pressure fluctuations as a result of spontaneous breathing may promote airway opening events as a result of stochastic resonance[20]. This observation needs further confirmation.

Variable flow nasal CPAP devices

These devices have an integrated nasal interface and pressure generator and use a higher gas flow than other devices. The most commonly used device is the IFD system. Pressure in the system is created at the level of the nasal device ('Generator') to which short binasal prongs are attached. The pressure generated in this device is controlled directly by adjusting the flow and flow in excess of 8 l/min is needed to generate pressures around 5 cm H_2O. The "expiratory" limb of the IFD is unusual among CPAP devices in that it is open to the atmosphere. Potentially, the baby can inspire with a higher flow than that delivered through the inspiratory limb. This extra gas can be drawn from the expiratory limb ("variable flow"). This reduces the possibility of the pressure falling with large inspirations and therefore may reduce the work the baby expends to take large breaths.

Inspite of widespread popularity of IFD, few clinical data are available to substantiate its clinical superiority over other devices. In a short-term cross-over

study of 20 neonates receiving 30% oxygen, Ahluwalia et al compared single-prong nCPAP with the IFD. They found no significant differences in FiO_2, respiratory rate, heart rate, blood pressure or comfort score of infants[21]. But in 2001, an RCT of 36 preterm infants comparing IFD with nasopharyngeal bubble CPAP found that the IFD group had significantly improved oxygenation and respiratory rates[22]. In the same year, Courtney et al showed that in premature infants with mild respiratory distress lung volumes measured were significantly higher with the IFD compared to the INCA prongs and nasal cannula[23]. Similarly in 2007, Boumecid et al found that the IFD increased tidal volume and improved thoraco-abdominal synchrony compared with bi-nasal CPAP and nasal cannula, in preterm infants[24]. Interesting Stefanescu et al found no important difference in rates of extubation failure in ELBW infants between IFD and INCA prongs[25]. An analysis of studies so far show that more research is required to determine whether the IFD has clinically important benefits over less expensive bi-nasal systems.

Arabella is another variable flow nasal CPAP system which is not widely used. A comparison study between IFD and Arabella in VLBW infants with mild respiratory distress showed no difference in lung volume recruitment, work of breathing, compliance, tidal volume, respiratory rate, and minute ventilation between the two devices[26].

Studies on CPAP using Infant Flow Driver

Author	Study population	Study Design	Results
Mazzella et al(2001)	N = 36 preterm neonates	Randomized controlled study	IFD had lower FiO_2 requirement($p<0.05$), Lower respiratory rate
Moa G et al(1988)	Lung model simulated breathing of new born	Experimental study	Paw variation and external workload were less with new device
Ahluwahlia et al(1998)	n= 20 preterm neonates	Crossover study	No significant difference in respiratory rate, heart rate, blood pressure, or comfort score

(IFD, infant flow driver; FiO_2,fraction of inspired oxygen)

The Benveniste valve is a technically simple device consisting of a constant gas jet directed through a ring towards the connection with the nasal interface[4]. A high gas flow of 14 L/min. is required to create a pressure of between 3 and 10.5 cm H_2O in the oro-pharynx. Despite being a relative simple and inexpensive device it has not gained popularity outside the Scandinavian countries and studies comparing it with other devices are lacking.

High flow nasal cannulae

Nasal cannulae with an outer diameter of 3 mm and flows up to 2 l/min, have been reported to deliver CPAP[27]. Studies of CPAP via nasal cannulae found it as effective as conventional CPAP prongs in the treatment of respiratory distress and apnoea of prematurity[28, 29]. The problem with this technique is that the CPAP pressure is usually not measured in clinical practice. When measured, pressures are highly variable and depend on the flow rate, the size of the leak around the nasal cannula, and the degree of mouth opening[30, 31]. Also in the post extubation setting there was a significantly higher failure rate with high flow nasal cannula when compared to the IFD[32]. Based on the available study results high flow nasal cannulae should not be be used as a routine replacement for a standard CPAP device[33].

Practical problems of nCPAP

Fixation of nasal devices

There are many different techniques for fixing the devices to the infant. The exact technique does not matter as long as the device is secure and not traumatising the nose, face, or head. More research is needed to define the least traumatic nasal device and method of fixation.

Leak at the nose and mouth

Nose and mouth leaks are inherent problems with any CPAP delivery device and the set CPAP level is rarely maintained in the pharynx[34]. The best ways to reduce nose leak are to ensure the usage of a snugly fitting prong and by usage of chin straps

Optimal pressure to be used

A pressure of 5 cm H_2O is traditionally used. Some neonatal intensive care units hardly vary this and claim good results whereas some use higher levels, often starting at 8 cm H_2O and going upto 10 cm H_2O. A study of infants with mild RDS, showed the highest end expiratory lung volume and tidal volume, and the lowest respiratory rate and thoracoabdominal asynchrony, at a pressure of 8 cm H_2O compared with 0, 2, 4, and 6 cm H_2O[35]. There are no good RCT's in this regard and the optimal CPAP pressure is still not known and may depend on the condition treated. Judging how much pressure is needed is still an art. If the infant shows evidence of worsening lung disease with increasing oxygen requirements, a more opaque chest X-ray, and is having chest retractions, an increase the pressure in increments of 1 cm H_2O, up to 8-10 cm H_2O is required whereas a hyperinflated chest X-ray might necessitate decrease in CPAP.

Clinical indications for nCPAP

Post-extubation

Atelectasis and apnoea often follow extubation to air or head box oxygen in preterm infants and nCPAP is used in an attempt to reduce the need to re-ventilate infants. A metanalysis of nine trials showed that infants extubated to nCPAP had a reduction in the need for additional respiratory support [RR 0.62 (0.51, 0.76); RD -0.17 (-0.23, -0.10); NNT 6][36]. However, there was no significant difference in rates of bronchopulmonary dysplasia (BPD) and there does not appear to be any harm (in terms of rates of eventual endotracheal re-ntubation) from delaying treatment with nCPAP until an infant displays signs of respiratory failure, a strategy that could be used in resource poor settings.

Delivery room CPAP and prophylactic CPAP for preterm infants

To date, there are no prospective, randomized, sufficiently powered clinical trials comparing CPAP with positive-pressure ventilation (via bag and mask or ETT) in spontaneously breathing neonates during active resuscitation. But three published RCT's have addressed the question of whether nCPAP commenced soon after resuscitation, irrespective of respiratory status, reduced mortality and morbidity of very preterm infants[37, 38, 39]. In all three RCT's infants were randomized to receive CPAP or no CPAP after initial resuscitation in the delivery room. After randomization, Finer et al routinely instituted CPAP after shifting the infant to the NICU but in the other two RCT's, CPAP was instituted only after specific indications. Finer et al reported no difference in the need for subsequent intubation in the two groups. A Cochrane meta-analysis is available for the two other trials and it showed no difference in the rates of death, BPD, subsequent endotracheal intubation or intra-ventricular hemorrhage (IVH)[40].

CPAP for respiratory distress syndrome

Randomized trials evaluating this therapy against head box oxygen were conducted mostly in the 1970's on more mature infants and used a variety of devices. These studies were conducted predominantly before widespread use of antenatal corticosteroids and surfactant. Pooled analysis of these trials showed that continuous distending pressure use reduced the overall rate of mortality [RR 0.52 (0.32, 0.87), RD -0.15 (-0.26, -0.04), NNT 7 (4, 25)] and the rate of the combined outcome, death or assisted ventilation [RR 0.70 (0.55, 0.88), RD -0.22 (-0.35, -0.09), NNT 5 (3, 11)]. However, the use of CPAP was associated with an increased risk of pneumothorax [RR 2.36 (1.25, 5.54), RD 0.14 (0.04, 0.23), NNH 7 (4, 24)][41]. A related trial performed in the modern era in infants >30 weeks, born in level 2 units with respiratory distress showed that nCPAP had a reduction in the need for transfer to a higher level of care but there was again a trend towards an increased rate of pneumothorax in the nCPAP group[42].

The recent multicenter COIN trial investigated the effect of using early nCPAP rather than intubation and ventilation from 5 min of life, on the incidence of death or BPD, and related morbidities in infants between 25 and 28 weeks. The nCPAP group showed a significantly lower risk of death or oxygen therapy requirement at 28 days compared with the ventilated group. However, at 36 weeks post-conceptional age, the difference was no longer significant ([OR 0.80 (95% CI 0.58 to 1.12); p = 0.19]. There was little difference in mortality. Most difference observed was in oxygen treatment. In the nCPAP group 46% of the infants were eventually intubated within the first five days of life. In this group, surfactant use was halved in comparison to the ventilated group of infants. The nCPAP group received significantly fewer days of intubation and ventilation. The incidence of pneumothorax was 9% in the nCPAP group compared with 3% in the ventilated group ($p < 0.001$) but without any increase in morbidity. There is a also a trend suggesting that 27-28 week infants might benefit the most from early nCPAP. The simple message of the COIN trial is that nCPAP is an acceptable alternative to endotracheal intubation in the delivery room[43].

Randomized controlled trials of CPAP to treat RDS

Author	Study population	Study Design	Results
Belenky et al (1976)	N = 72 neonates >1000gm with RDS	RCT	CPAP and PEEP did not significantly altere the outcome of HMD
Durbin et al(1976)	N = 24 neonates >1000gm with RDS	RCT	Overall survival rate increased by 5% if CPAP is used
Fanaroff etal(1973)	N = 29 neonates >1000gm with RDS	RCT	CPAP reduces exposure to high oxygen concentration ($p<0.05$), need for ventilator therapy
Rhodes et al(1973)	N = 24 neonates with RDS	RCT	Significant difference in survival rate. (7 out of 11 in control group died compared to none in 13 in CPAP group in > 1500gm birth weight)

(RCT, randomized controlled trial; HMD, hyaline membrane disease; CPAP, continuous positive airway pressure; PEEP, peak end expiratory pressure; RDS, respiratory distress syndrome)

Trials comparing early with late CPAP for treatment of HMD

Author	Study population	Study Design	Results
Allen et al(1977)32	N = 24 preterm neonates with RDS	RCT	Early CPAP: Increased PaO2, High concentration O2 for shorter time ($p<0.05$), ventilated at lower pressure [RR,95% CI; 0.57(0.22, 1.45)]
Gerard et al(1975)29	N = 23 preterm infants with RDS	RCT	FiO2 requirement and duration was lower in Early CPAP. no ventilation [RR,95% CI;0.12(0.001, 2.01)]
Krouskop et al (1975)34	N = 23 preterm neonates with RDS	RCT	Early CPAP needed lower FiO_2 (0.55) and less severe course
Mockrin et al (1975)36	N = 23 preterm neonates with RDS	RCT	Less time with O_2 therapy, no ventilation [RR,95% CI; 0.12(0.01, 0.87)], fewer complication
Hegyi et al(1981)33	N = 38 preterm neonates with RDS	RCT	Lesser duration of CPAP(42 versus 72 hrs) lesser number of air leaks (0 versus 3) and ventilation(0 versus 5) in Early CPAP[RR,95% CI; 0.17 (0.01, 2.84)]
Ho JJ et al80	165 neonates with RDS	Meta analysis	Early CPAP group had reduction in IMV use [RR,95% CI; 0.55(0.32-0.96)], no effect on mortality

(RCT, randomized controlled trial; CPAP, continuous positive airway pressure; PaO2 partial pressure of arterial oxygen; FiO_2, Fraction of inspired oxygen;O_2, oxygen)

Early surfactant administration followed by nCPAP

Starting nCPAP from shortly after birth might prevent the complications related to intubation but it also prevents the beneficial use of early surfactant in premature infants[44]. Neonatologists treating premature infants in the delivery room are often faced with the dilemma of whether to intubate or not and a balance needs to be struck between helping infants in the most efficient way, without applying potentially harmful and expensive treatments where they are not required. Two studies address this important question of how to combine surfactant and nCPAP.

The IFDAS trial[45] aimed to establish whether the early use of nCPAP with prophylactic surfactant was an effective and safe way to manage infants with or at risk of developing RDS. The primary hypothesis of this prospective multicenter trial was that the early use of nCPAP following the administration of prophylactic surfactant would reduce the need for subsequent mechanical ventilation. Inborn 27-29 week infants were randomised to 4 treatment groups. Group 1 = early nCPAP after prophylactic surfactant; group 2 = early nCPAP and selective rescue surfactant; group 3 = early intermittent positive pressure ventilation (IPPV) with prophylactic surfactant; group 4 = conventional management i.e. rescue IPPV and selective rescue surfactant. The requirement for mechanical ventilation within the first 5 days of life was the highest in group 3 and the lowest in group 1. There was no difference between the groups for the duration of total respiratory support (mechanical ventilation + nCPAP). No difference was found between groups for oxygen dependency at 28 days of age or 36 weeks post-conceptional age, or any neonatal morbidity. The authors concluded that the use of nCPAP following prophylactic surfactant or nCPAP alone was safe and reduced the need for mechanical ventilation when used as initial respiratory support, but did not demonstrate a reduction in BPD.

The REVE (REduction of VEntilation) trial is a recent French multicentre randomized trial aiming to demonstrate the efficacy of early nCPAP use after prophylactic surfactant administration compared to mechanical IPPV with prophylactic surfactant on the duration of mechanical ventilation[47]. Infants 25 to 27 weeks were randomized at birth when they presented with mild respiratory distress. The results are as yet unpublished but have been presented. The REVE trial suggests that intubation with early surfactant administration followed by nCPAP mostly benefits to 25-26 week infants.

Does nasal CPAP increase the risk of air leak?

Many recent RCT's and metanalysis have shown that infants receiving early nCPAP have an increased risk of pneumothoraces[41, 43], a data that was contrary to earlier observational studies. An increased rate of pneumothorax may be a concern because past evidence has suggested that such an increase was associated with increased morbidity like BPD, PVL and IVH. But reassuringly, in the COIN trial, there was no significant increase in the rate of death, grade 3 and 4 intraventricular hemorrhage, peri-ventricular leukomalacia, bronchopulmonary dysplasia, or other adverse outcomes[43]. However the increased risk of air leak remains a concern and the challenge is to identify strategies which preserve the benefits of nCPAP but reduce the rate of pneumothorax.

Gastric distension and CPAP

What is surprising is not that CPAP sometimes causes gaseous distension of the stomach but that it does so rarely. This may be because the tone in the upper and lower oesophageal sphincters is higher than the applied CPAP[47]. It seems appropriate to use a stomach tube open to atmosphere to vent any gas. If it occurs, the "CPAP belly syndrome" is likely to be benign[48].

Conclusion

Non-invasive ventilation is increasingly used both as a primary method of respiratory support for preterm infants and to facilitate early extubation if an endotracheal tube is used. CPAP is an effective alternative to endotracheal intubation when managing RDS. Some important adverse outcomes are reduced but nCPAP is associated with an increased rate of pneumothorax. Bi-nasal interfaces have the lowest resistance and are the most clinically effective.

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