Failure and success of CPAP

Dr Praveen Kumar, Additional Professor
Neonatal unit, Department of Pediatrics, PGIMER, Chandigarh

The factors determining the success of CPAP are: choosing the right infant (weight and underlying disease process), applying it early rather than late, knowing the machine well, diligent nursing care and the conviction of the team. In addition, the threshold criteria used to define failure, will determine the CPAP failure rates. With increasing experience the success rates are likely to improve.

Infant characteristics

- Very small babies (< 750 grams) may not have good respiratory efforts while term babies may not tolerate the nasal prongs. CPAP is likely to have least failures in babies between 750-1750 grams, but it can be successful in smallest and bigger babies.
- CPAP is most successful in babies with mild to moderate respiratory disease especially hyaline membrane disease and apnea of prematurity. It is less likely to be successful in babies with CNS pathology e.g. severe asphyxia or systemic sepsis.
- Babies exposed to antenatal steroids are likely to have milder disease and more likely to succeed with CPAP.

Concomitant treatments resulting in higher success rates

- Early use of surfactant---prophylactic or early rescue---along with CPAP.
- Diligent nursing care and good supportive care would.

Maximum CPAP support criteria

Some units would use up to 8-9 cm H_2O of CPAP and 70-80% of oxygen, while others may not go beyond 6-7 cm H_2O and 60-70% oxygen due to fear of side effects or a belief that it wouild not be helpful beyond such levels. This choice of upper limit may change the success rates in different units.

Criteria for failure of CPAP

Some units are willing to tolerate $PaCO_2$ up to 65-70 mmHg and a pH up to 7.15 whereas majority will switch to IMV if paCO2 goes more than 50-55 and pH falls below 7.25. Depending upon the tolerance of paCO2 and pH, the success rates for similar disease severity would vary between units.

The machine

Although certain types of machines have been claimed to be better, what is most important is to have a complete understanding of the working of the machine being used.

Interface

- Binasal prongs have been shown to be better than single long and short nasal prong.
- 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 was more difficult to keep in the nostrils of active patients, and nasal hyperemia occurred more frequently among infants using this prong[1]. However, we have seen nasal septum injuries with Hudson prongs as well, as they could put more pressure on the nose if their position is not carefully monitored.
- Recently a new generation of cushioned 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.

CPAP generator

A variety of CPAP generators have been used : It is believed that the currently variable flow (infant flow drivers) devices best maintain uniform pressures. However, they are expensive and their clinical superiority is yet to be proven. There has been a resurgence of interest in bubble CPAP because of purported theoretical benefits and lesser cost. Overall, it seems infant drivers and bubble CPAP may be better than ventilator CPAP but one can successfully use the conventional ventilator CPAP as well.

Bubble CPAP : It has been suggested that bubble CPAP is more effective than ventilator CPAP because of the oscillations[2]. However, Kahn et al. showed that bubble CPAP pressure oscillations are progressively attenuated distal to the prongs[3]. 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[4]. However, a short-term cross-over study of human neonates comparing fast bubbling with minimum bubbling did not find any difference in blood gases[5]. 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 long tem failure rates[6]. It has also been suggested through an in vitro study 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[7].

Infant Flow Drivers : The work of breathing was found to be increased with conventional ventilator driven CPAP (circuit flow limited to 6 L/min) compared with an Infant Flow Driver (IFD) maintaining pressure at the device level with variable flow[8].

Although physiological studies have shown that the pressures are maintained more uniformly by the IFD machines, few clinical data are available to substantiate their 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 FiO2, respiratory rate, heart rate, blood pressure or comfort score of infants[9]. 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[10]. 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[11]. 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[12]. Stefanescu et al found no important difference in rates of extubation failure in ELBW infants between IFD and INCA prongs[13].

A comparison study between IFD and Arabella (another infant flow driver) in VLBW infants with mild respiratory distress showed no difference in lung volume recruitment, work of breathing and compliance.

Nasal cannulae : Studies of CPAP via nasal cannulae found it as effective as conventional CPAP prongs in the treatment of respiratory distress and apnoea of prematurity[14, 15]. In the post extubation setting there was a significantly higher failure rate with high flow nasal cannula when compared to the IFD[16]. Based on the available study results high flow nasal cannulae should not be be used as a routine replacement for a standard CPAP device[17].

Clinical situations

Post-extubation

Although, CPAP used after extubation has been shown to decrease the "failure of extubation", 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 reintubation) 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

Finer et al reported no difference in the need for subsequent intubation in the two groups. A Cochrane meta-analysis is available for two other trials and it showed no difference in the rates of death, BPD, subsequent endotracheal intubation or intraventricular haemorrhage (IVH)[18].

CPAP for respiratory distress in delivery room

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[19]. 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 ($p < 0.001$). There was a trend suggesting that 27-28 week infants might benefit the most from early nCPAP.

Recent studies on failure of CPAP

Author	Study population	Study design	Results
Ammari A et al(2005)	N=261, Birth weight <1250g	Case control study	5% failure rate; Factors predictive of CPAP failure: a. Need for positive pressure ventilation at delivery (OR, 2.37) b. A-aDO2 >180 mmHg in 1st ABG (OR, 2.91) c. Severe RDS in initial Chest X-ray (OR, 6.42)
Boo NY et al(2000)	N=97m Gestational age <37 weeks	Case control study	37% failure rate: Factors predictive of CPAP failure: a. Moderate or severe RDS (OR, 5.9) b. Septicemia (OR, 8.8) c. Pneumothorax(OR, 6.9)
Maiya PP et al (2009)	N = 50	Prospective observational study	20% failure rate; Factors predictive of CPAP failure: Severe RDS, gestational age, birth weight, antenatal steroids
Murki S et al (2009)	N = 60	Prospective observational study	25% failure rate; Factors predictive of CPAP failure: Downes score =7, FiO2 requirement =50%, even after 2 hours of CPAP

(CPAP, continuous positive airway pressure;; RDS, respiratory distress syndrome; FiO2 fraction of inspired oxygen; A-aDO2 - difference between arterial and alveolar partial pressure of oxygen)

Early surfactant administration followed by nCPAP(INSURE)

In the IFDAS trial 20 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

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. 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 25-27 week infants.

Few relevant abstracts are given below.

Bubble CPAP for Respiratory distress syndrome in Moderately Preterm Infants: The predictors of CPAP failure. Murki S et al,2009---Indian Pediatrics

Subjects: Inborn preterm infants with gestation < 35 weeks admitted to the NICU with respiratory distress and chest x- ray suggestive of RDS.

Intervention: Bubble CPAP with bi-nasal prongs.

Primary outcome: CPAP failures-Infants requiring ventilation in the first one week.

Results: 60 neonates were enrolled in the study. 15 (25%) babies failed CPAP. The variables associated with failure were: no or only partial exposure to antenatal steroids, white out on the chest x-ray , Downe's score = 7 at starting of CPAP and after 2 hours of CPAP , and FiO2 = 50% after 2 hours of CPAP .

Variables associated with the early failure of nasal CPAP in very low birth weight infants.

Ammari A, Suri M, Milisavljevic V, Sahni R, Bateman D, Sanocka U, Ruzal-Shapiro C, Wung JT, Polin RA. J Pediatr. 2005 Sep; 147(3):341-7.

OBJECTIVE: To identify risk factors and neonatal outcomes associated with the early failure of "bubble" nasal continuous positive airway pressure (CPAP) in very low birth weight (VLBW) infants with respiratory distress syndrome (RDS). STUDY DESIGN: Following resuscitation and stabilization at delivery, a cohort of 261 consecutively inborn infants (birth weight < or = 1250 g) was divided into three groups based on the initial respiratory support modality and outcome at 72 hours of age: "ventilator-started" group, "CPAP-failure" group, and "CPAP-success" group. RESULTS: CPAP was successful in 76% of infants < or = 1250 g birth weight and 50% of infants < or = 750 g birth weight. On analysis after adjusting for post menstrual age and gestational age. CPAP failure was associated with need for positive pressure ventilation (PPV) at delivery, alveolar-arterial oxygen tension gradient (A-a DO2) >180 mmHg on the first arterial blood gas (ABG), and severe RDS on the initial chest x-ray (adjusted odds ratio [95% CI] = 2.37 [1.02, 5.52], 2.91 [1.30, 6.55] and 6.42 [2.75, 15.0], respectively). The positive predictive value of these variables ranged from 43% to 55%. In analyses adjusted for PMA and severe RDS, rates of mortality and common premature morbidities were higher in the CPAP-failure group than in the CPAP-success group.
CONCLUSION: Although several variables available near birth were strongly associated with early CPAP failure, they proved weak predictors of failure. A prospective controlled trial is needed to determine if extremely premature spontaneously breathing infants are better served by initial management with CPAP or mechanical ventilation.

Is it safer to intubate premature infants in the delivery room?

Aly H, Massaro AN, Patel K, El-Mohandes AA. Pediatrics. 2005 Jun; 115(6):1660-5.

OBJECTIVES: Early nasal continuous positive airway pressure (ENCPAP) has recently emerged in neonatal units as an acceptable alternative to routine intubation and mandatory ventilation. The risks and benefits of ENCPAP have yet to be established. In this study, we aimed to examine variables that influenced the decision to initiate ENCPAP in the delivery room (DR). We also explored potential harmful effects of early intubation and examined whether unsuccessful ENCPAP attempts might subject infants to any unforeseen morbidity.

METHODS: All inborn very low birth weight (VLBW) infants admitted to the NICU, since the implementation of the ENCPAP policy were included in this retrospective study. Infants were stratified initially into 2 cohorts according to whether they were intubated in the DR or began ENCPAP. Infants were then stratified into 4 groups according to the respiratory management during their first week of life. Infants in group 1 were supported with ENCPAP in the DR and continued to receive continuous positive airway pressure (CPAP) at least for the entire first week. Infants in group 2 began ENCPAP treatment in the DR but required intubation during the first week of life. Infants in group 3 were intubated in the DR but transitioned successfully to CPAP within the first 48 hours and were treated with CPAP for the first week of life or longer. Infants in group 4 were intubated in the DR and treated with intermittent mandatory ventilation for >48 hours. Univariate analyses compared different groups with the Wilcoxon nonparametric test, Kruskal-Wallis test, and analysis of variance. A multivariate regression model adjusted for differences in birth weights (BWs), gestational ages (GAs), race, and Apgar scores between the groups. RESULTS: A total of 234 VLBW infants (weight of <1500 g) were admitted to the NICU during the period from August 1997 to December 2003. The mean BW was 977.1 +/- 305.8 g, and the mean GA was 27.7 +/- 2.7 weeks. The overall mortality rate was 11.1%, and the incidence of bronchopulmonary dysplasia among survivors was 17.4%. ENCPAP was implemented successfully in the DR for 151 (64.5%) infants, whereas 83 (35.5%) infants required intubation. Infants who required intubation had significantly lower GAs, BWs, and 1-minute Apgar scores. The use of ENCPAP in the DR increased significantly over time. The chance of successful maintenance with ENCPAP for >48 hours was not demonstrable at <24 weeks of gestation (10% success). Use of ENCPAP improved significantly by 25 weeks of gestation (45% success). Infants in group 1 required a shorter duration of oxygen use than did infants in group 3 (7.9 +/- 18.3 vs 39 +/- 32.7 days; regression coefficient [b] = 19 +/- 5.3). None of the infants in group 1 developed intraventricular hemorrhage of grade III or IV or retinopathy of prematurity of stage 3 or 4. Infants in group 3 did not show improved outcomes, compared with group 1. Compared with group 4, infants in group 2 had a higher incidence of necrotizing enterocolitis (15.6% vs 7.3%; b = 2.5 +/- 1.2).

CONCLUSIONS: The success of ENCPAP improved with increased GA and with staff experience overtime. Infants treated successfully with ENCPAP were unlikely to develop intraventricular hemorrhage of grade III or IV. Infants who experienced

ENCPAP failure were at increased risk for the development of necrotizing enterocolitis. Infants who were intubated briefly in the DR were at increased risk for prolonged oxygen requirement. An individualized approach should be considered for respiratory support of VLBW infants.

Does the experience with the use of nasal continuous positive airway pressure improve over time in extremely low birth weight infants?

Aly H, Milner JD, Patel K, El-Mohandes AA. Pediatrics. 2004 Sep; 114(3):697-702.

OBJECTIVE: Early use of nasal continuous positive airway pressure (ENCPAP) in extremely low birth weight (ELBW) infants continues to be a source of debate. Centers are applying this management strategy with varying success. Our center has implemented this strategy of care over the past 4 years, and the objective of this study was to evaluate the impact of experience over time with the use of ENCPAP on outcomes of ELBW infants.

METHODS: All ELBW infants who were born at our hospital since the institution of the ENCPAP practice (n = 101) were analyzed retrospectively. Patients were divided into 3 terciles according to their birth date. A baseline group of ELBW infants who were born in the 2 years preceding the institution of the ENCPAP practice (group 0; n = 45) were used for comparison. Trends in practices and outcomes over time were analyzed using the 2-sided Cochran-Armitage linear trend test. Statistical significance for these trends were then analyzed again using a multivariate regression model controlling for significant variables. Bivariate analyses comparing individual groups were also conducted.

RESULTS: There were no significant trends in mortality rate among the baseline group and the 3 terciles since the institution of the ENCPAP practice (26.7% vs 26.5% vs 11.8% vs 18.2%). ENCPAP management increased in the surviving infants over time (14% vs 19.2% vs 65.52% vs 70.4%), whereas the use of surfactant decreased (51.5% vs 48% vs 13.3% vs 33.3%) and the incidence of bronchopulmonary dysplasia (BPD) decreased (33.3% vs 46.2% vs 25.9% vs 11.1%). The average ventilator days per infant decreased, the rate of sepsis decreased, and the average daily weight gain increased. There were no significant trends in the incidence of intraventricular hemorrhage or necrotizing enterocolitis (NEC). When comparing the cohorts of survivors in the 3 terciles since the institution of ENCPAP system, ELBW infants who were started on ENCPAP but intubated within 1 week (CPAP failure) decreased over time (38.5% vs 13.8% vs 7.4%). There were other trends that did not reach significance, such as increased incidence of necrotizing enterocolitis (NEC). In a multivariate analysis controlling for gestational age, birth weight, and sepsis, the incidence of BPD was significantly lower over time (regression coefficient = -1.002 +/- 0.375).

CONCLUSIONS: The frequency of use of ENCPAP in ELBW infants and its success improved in our unit over time.

The major positive association in this population was a reduction in BPD rates and an increase in average weight gain. Relation of ENCPAP and NEC should be evaluated further.

References

1. Rego MA, Martinez FE.Comparison of two nasal prongs for application of continuous positive airway pressure in neonates Pediatr Crit Care Med. 2002 Jul;3(3):239-243.
2. K.S. Lee, M.S. Dunn, M. Fenwick and A.T. Shennan, A comparison of underwater bubble continuous positive airway pressure with ventilator-derived continuous positive airway pressure in premature neonates ready for extubation, Biol Neonate 1998;73;69-75.
3. D.J. Kahn, S.E. Courtney, A.M. Steele and R.H. Habib, Unpredictability of delivered bubble nasal continuous positive airway pressure: role of bias flow magnitude and nares-prong air leaks, Pediatr Res 2007;62:343-347.
4. Pillow, N. Hillman and T.J. Moss et al., Bubble continuous positive airway pressure enhances lung volume and gas exchange in preterm lambs, Am J Respir Crit Care Med 2007;176:63-69.
5. J. Morley, R. Lau, A. De Paoli and P.G. Davis, Nasal continuous positive airway pressure: does bubbling improve gas exchange? Arch Dis Child Fetal Neonatal Ed 2005;90:F343-F344.
6. Liptsen E, Aghai ZH, Pyon KH, Saslow JG, Nakhla T, Long J, Steele AM, Habib RH, Courtney SE. Work of breathing during nasal continuous positive airway pressure in preterm infants: a comparison of bubble vs variable-flow devices. J Perinatol. 2005;25(7):453-8
7. Pillow JJ, Travadi JN.Bubble CPAP: is the noise important? An in vitro study Pediatr Res. 2005;57(6):826-30.
8. Pandit PB, Courtney SE, Pyon KH, et al. Work of breathing during constant- and variable-flow nasal continuous positive airway pressure in preterm neonates. Pediatrics 2001;108:682-5
9. Ahluwalia JS, White DK, Morley CJ. Infant flow driver or single prong nasal continuous positive airway pressure: short-term physiological effects. Acta Paediatr 1998; 87:325-7.
10. M. Mazzella, C. Bellini and M.G. Calevo et al., A randomised control study comparing the infant flow driver with nasal continuous positive airway pressure in preterm infants, Arch Dis Child Fetal Neonatal Ed 2001;85:F86-F90.
11. S.E. Courtney, K.H. Pyon, J.G. Saslow, G.K. Arnold, P.B. Pandit and R.H. Habib, Lung recruitment and breathing pattern during variable versus continuous flow nasal continuous positive airway pressure in premature infants: an evaluation of three devices, Pediatrics 2001; 107:304-308.
12. H. Boumecid, T. Rakza, A. Abazine, S. Klosowski, R. Matran and L. Storme, Influence of three nasal continuous positive airway pressure devices on breathing pattern in preterm infants, Arch Dis Child Fetal Neonatal Ed 2007;92:F298-F300.

13. B.M. Stefanescu, W.P. Murphy, B.J. Hansell, M. Fuloria, T.M. Morgan and J.L. Aschner, A randomized, controlled trial comparing two different continuous positive airway pressure systems for the successful extubation of extremely low birth weight infants, Pediatrics 2003;112;1031-1038.

14. Saslow JG, Aghai ZH, Nakhla TA, Hart JJ, Lawrysh R, Stahl GE, Pyon KH. Work of breathing using high-flow nasal cannula in preterm infants. J Perinatol. 2006;26(8):476-80.

15. 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;107:1081-3

16. D.M. Campbell, P.S. Shah, V. Shah and E.N. Kelly, Nasal continuous positive airway pressure from high flow cannula versus infant flow for preterm infants, J Perinatol 2006;26;546-549.

17. N.N. Finer, Nasal cannula use in the preterm infant: oxygen or pressure?, Pediatrics 2005;116;1216-1217.

18. P. Subramaniam, D.J. Henderson-Smart and P.G. Davis, Prophylactic nasal continuous positive airways pressure for preventing morbidity and mortality in very preterm infants, Cochrane Database Syst Rev 2005; CD001243.

19. C.J. Morley, P.G. Davis, L.W. Doyle, L.P. Brion, J.M. Hascoet and J.B. Carlin, Coin Trial Investigators: Nasal CPAP or intubation at birth for very preterm infants, N Engl J Med 2008; 358:700-708.

20. Thomson MA. Early nasal CPAP + prophylactic surfactant for neonates at risk of RDS. The IFDAS trial. Pediatr Res 2001; 50:304A.

21. Omari TI, Benninga MA, Barnett CP, et al. Characterization of esophageal body and lower esophageal sphincter motor function in the very premature neonate. J Pediatr 1999;135:517-21