Continuous Positive Airway Pressure (CPAP) in Neonates

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mahi Publication

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ISBN: 978-93-89339-89-5

First Edition: 2020

PRICE ₹ 199 /-

PUBLISHER
MAHI PUBLICATION

Office No.1, Krishnasagar Society, Nr. Shivsagar sharda Mandir Road, Ahmedabad-380007

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+(91) 798 422 6340

www.mahipublication.com

LIST OF ABBREVATIONS USED

BPD	:	Bronchopulmonary dysplasia
CDP	:	Continuous distending pressure
CLD	:	Chronic lung disease
CNP	:	Continuous negative pressure
CPAP	:	Continuous positive airway pressure
DS	:	Down's score
ELBW	:	Extremely low birth weight
ET	:	Endotracheal tube
FRC	:	Functional residual capacity
HMD	:	Hyaline membrane disease
IFD	:	Infant flow driver
IPPV	:	Intermittent positive pressure ventilation
MV	:	Mechanical ventilation
NNPD	:	National Neonatal Perinatal Database
PDA	:	Patient ductus arteriosus
PEEP	:	Positive end expiratory pressure
RDS	:	Respiratory distress syndrome
ROP	:	Retinopathy of prematurity
VLBW	:	Very low birth weight

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INTRODUCTION

Intermittent positive pressure ventilation (IPPV) with surfactant is the standard treatment for RDS. Initial attempts at artificial ventilation were done with negative pressure ventilators and subsequently with intermittent positive pressure ventilators. In 1960s, mechanical intermittent positive pressure ventilation became widely accepted as the standard treatment of RDS in newborn[1]. Although varying degrees of success was reported with assisted ventilation as therapy for RDS, in all series mortality was high when infants were less than 1500 grams or required ventilation before 24 hours of age.[2,3]

Therefore another method for improving oxygenation in infants with RDS was sought and in 1971 Gregory et al[4] used continuous positive airway pressure (CPAP) in the treatment of idiopathic respiratory distress syndrome. It was though that application of CPAP might overcome atelectasis and improve arterial oxygenation. The effect of grunting respiration on arterial oxygenation also suggested that CPAP might be useful. Infants who grunt exhale against a partially closed glottis which increases transpulmonary pressure and probably decreases or prevents atelectasis. If grunting is prevented by insertion of endotracheal tube, arterial oxygen tension (PaO_2) decreases; however when tube is removed and grunting is resumed PCO_2 rises. This was welcomed as a missing link between the oxygen and ventilatory therapy with great enthusiasm.

The major difficulty with IPPV is that it is invasive and contributes to airway and lung injury including the development of chronic lung disease. The advent of less invasive CPAP has permitted early treatment of RDS in neonateswith aims to intervene as early as possible and to avoid intubation and reduced mucociliary flow and risk of mucosal injury or secondary infection and to minimize volutrauma to the airways and lung parenchyma. In 1976 Wung et al[5] stated that "introduction of continuous distending pressure (CDP) was a major breakthrough and remained an important modality of treatment in RDS". This view was supported by

number of studies which indicate that early intervention with CDP might modify the course of illness and lower the need for more aggressive therapy.

Continuous distending pressure (CDP) has been used for the prevention and treatment of RDS as well as the prevention of apnea, and in weaning from IPPV. CPAP results in progressive recruitment of alveoli, inflates collapsed alveoli and reduces intrapulmonary shunt.[6,7] It increases the FRC and inturn gaseous exchange. It reduces inspiratory resistance by dilating the airways. This permits a larger tidal volume for a given pressure, so reducing the work of breathing.[8] It reduces the compliance of very compliant lungs and in these lungs, reduces the tidal volume and minute volume. It regularizes and slows the respiratory rate. It increases the mean airway pressure and improves ventilation perfusion mismatch. It conserves surfactant on the alveolar surface.[9,10,11]

In extremely low birth weight babies (ELBW), the chest wall is very complaint 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. Thus, permitting a larger tidal volume for a givenpressure, 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. Furthermore, it has been shown that both inspiratory and expiratory times increases with CPAP.[10,11]

CDP has been applied as a continuous positive airway pressure (CPAP) or as a continuous negative pressure (CNP). CNP is applied externally to the thorax using a negative pressure chamber with the seal around the neck; it produces lung distension as a result of negative intrathoracic pressure. CPAP is applied via a face mask, nasopharyngeal tube, or nasal prongs, using a conventional ventilator, bubble circuit or CPAP driver. Application of positive compared with negative pressure might have different results in terms of effectiveness and complications.

Bubble CPAP is a newer CPAP delivering system. It 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.[12] Bubble CPAP has also been shown to reduce need for intubation and mechanical ventilation[13], postnatal steroids and trend towards decreased incidence of chronic lung disease.[14] With an underwater blow off system, sufficient flow creates continuous bubbling from the end of the underwater tube, placed at a specified depth underwater, to ensure that circuit pressure is maintained. A comparison of underwater bubble endotracheal (ET) CPAP with conventional ventilator derived (ET) CPAP in preterm neonates suggests that such oscillation contributes to gas exchange[12]. It is relatively a simple and inexpensive way of generating CPAP. It also has theadvantage that if there is inadequate pressure owning to a large leak the bubbling can be seen to stop.

REVIEW OF LITERATURE

EARLY NASAL CPAP

HISTORICAL BACKGROUND

Poultan and Oxan[15] used positive pressure therapy in 1936 for acute ventilatory insufficiency. They used facemask for positive pressure therapy. Later it was abandoned when mechanical ventilation became feasible.

In 1960s mechanical intermittent positive pressure ventilation became widely accepted as standard treatment of respiratory distress syndrome (RDS). When it became evident that low volume was a consequence of the disease, continuous distending pressure (CDP) was developed as a means of increasing lung volume and improving oxygenation.[4] They applied CPAP to 20 infants (birth weight 930-3800 grams) with idiopathic respiratory distress syndrome through endotracheal tube (in 18 infants) and plastic pressure chamber (in 2 babies). They found no difference in the effects of CPAP applied through an ET tube or by a plastic chamber. 17 of the 20 infants treated with CPAP recovered from RDS. Arterial oxygenation increased in all infants after the application of CPAP permitting to lower inspired oxygen concentration to an average of 37.5% within 12 hours.

However, several workers utilized cautious approach to deliver CPAP due to inherent risks of endotracheal tube.

In 1973 Agostino et al[16] reported the first small series of infants with RDS treated with nasal canula CPAP. This was based on the fact that most infants were nasal breathers and would spontaneously form a seal between thepalate and tongue. In case of too high pressure the mouth could act as a natural popoff valve. Over subsequent years variety of non-nasal CPAP devices were developed including pressurized plastic bag fitted over infant's head[17], face chamber[18] and face masks.[19]

The role of CPAP in preterm infants with RDS has long been debated in neonatal literature with early interest focused on a multicenter study by Avery et al[50]. Avery et al published a paper in 1987 that compared the respiratory outcome in 1625 infants born with a birth weight between 700 and 1500 g from eight NICUs across North America. The incidence of CLD, defined as need for oxygen at 28 days, was relatively consistent between seven units but the rate was much lower in the eighth. This centre, Columbia University Medical Center in New York City, appeared to have similar patient demographics and the survival rate was comparable but they quite clearly had better respiratory outcomes. Each of the eight centers was then asked to describe their practices regarding respiratory management. Again, Columbia stood out as being different from the rest. It was therefore reasonable to hypothesize that their low incidence of CLD resulted from their unique approach to respiratory support of very low birth weight neonates.

These distinctive elements of their approach included:

- The provision of nasal CPAP shortly after birth to any infant showing signs of respiratory distress.
- Tolerance of a $PaCO_2$ as high as 60 mm Hg before intubating.
- For those babies requiring intubation and ventilation: the avoidance of hyperventilation, prohibition of muscle relaxants and the supervision of ventilatory management by one clinician.

Although it is not easy to tease out which aspects of the 'Columbia approach' contributed most to the reduction in CLD, the avoidance of endotracheal intubation and mechanical ventilation is likely to be one of the most important elements, the early and liberal use of nasal CPAP being used to achieve this.

Whereas CPAP was first introduced in the 1970s as a treatment for preterm babies with established RDS or to facilitate extubation, the group at Columbia and their disciples advocate the elective application of nasal CPAP soon after birth. The rationale for this is that the CPAP will help to establish the functional residual capacity and promote the release of surfactant, thereby creating and maintaining an adequate air-liquid interface in the lung. They allow the $PaCO_2$ and FiO_2 to rise, tolerate apnoeic spells and reserve intubation for only those infants who demonstrate, without a doubt, that they require ventilation to survive.

The first few minutes after birth represent the most profound period of physiological adaptation that humans must undergo. The transition from intrauterine life requires major changes to the respiratory and circulatory systems to allow a neonate to maintain adequate respiratory gas exchange without the benefits of the placental circulation. Inflation of the lungs with air, the release of surfactant, the establishment of functional residual capacity, the reabsorption of lung liquid, increases in pulmonary blood flow and theestablishment of a regular respiratory pattern are necessary for successful postnatal adaptation. Although any infant can have difficulty with these complex processes, those born preterm are particularly vulnerable to respiratory problems during this critical period. Within neonatal intensive care units, these babies are often provided with various types of support to compensate for inadequate respiratory drive, abnormalities in their surfactant system and/ or difficulties with the reabsorption of lung liquid. Assisted ventilation, continuous positive airway pressure (CPAP) and surfactant- replacement therapy are often used to support lung expansion and adequate gas exchange.

CPAP Delivering Devices :
The goal of any CPAP delivering device is to prevent atelectasis and airway closure. An ideal CPAP delivery system should include a patient system interface that is easy and rapid to apply, remove and remain connected to the airway, is non-traumatic to the neonate, efficiently maintains pressure at the desired levels, allows easy humidification of gases and oxygen control, has low resistance to breathing, minimal dead space, is easily sterilized and is safe and cost effective.

Fundamentally the delivery of continuous positive airway pressure requires three components:

1. Flow generation
2. An airway interface
3. A positive pressure system.

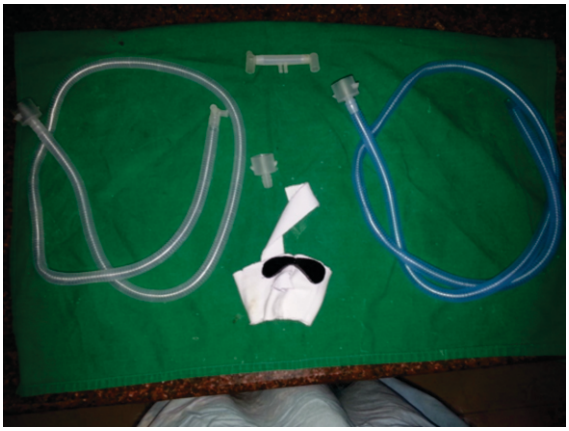

Fig. 1 : CPAP device

Flow Generation:

Two major varieties exist; constant flow and variable flow (demand). The flow generator usually also warms and humidifies the inhaled gases. Constant flow is usually provided by an infant ventilator, which because it can be used in two ways, may limit expenditure on hardware. Most often, the amount of flow is set by the clinical team. Alternatively, variable flow devices use a dedicated flow generator. Here the 'expiratory' limb of the circuit is open to the atmosphere and the infant can draw extra gas from this limb to support inspiratory efforts. This device has gained widespread acceptance in Europe and North America. Despite the theoretical advantages of the variable flow device, there are no consistent data showing clinical long-term meaningful benefit over constant flow devices.[21]

Airway Interface :

Different types of interfaces between the circuits and the infant's airway are in use: single prongs, binasal prongs (short and long), nasopharyngeal prongs, endotracheal tubes, head boxes, pressurized plastic bag, nasal cannulae and face masks. The most commonly used route today -nasal CPAP, was introduced in the early 1970s. Nasal prongs are very easy to apply and comparatively non-invasive to the airways. The infant can still be nursed and handled with unintemipted CPAP.

NON-NASAL DEVICES :

Endotracheal Tube:

Gregory et al[4] applied CPAP in 18 out of 20 patients through endotracheal tube. An endotracheal tube bypasses the larynx so PEEP should be applied to reduce loss of lung volume. Endotacheal CPAP may be used just before extubation, to ensure the baby does not become apnoeic without intermittent inflation.

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[22] review 2003 was performed to study the results of extubation from low-rate intermittent positive airway pressure versus extubation after a trial of endotracheal continuous positive airway pressure in intubated preterm infants. Results of the review shows direct extubation from low rate ventilation is associated with a trend towards increased chance ofsuccessfulextubationwhencomparedtoextubationafteraperiod of endotracheal CPAP; RR 0.45 (0.19, 1.07), RD - 0.103 (-0.200, -0.006), NNT 10(5,167).

Facemask :

Rhodes and Hall[19] studied the use of CPAP delivered by facemask in infants with idiopathic RDS. A significant difference in survival ($p<0.05$) was noted in treated compared with control patients. Complications were confined to difficulties with mask fit and local skin care.

Facemask provides a positive pressure but it is difficult to get a good seal on the baby's face. Pressure is lost when the mask is removed. It is difficult to use a nasogastric or orogastric tube.

Head Box with a Seal :

Used first by Gregory et al[4] (1971) to deliver CPAP in 2 out of 20 patients treated with CPAP. There was no difference between endotracheal tube or pressure chamber. This is a head box which seals round the baby's neck and has a valve to control the pressure. It is difficult to get a good seal, and there is poor access to the baby's face. Attention to the face causes loss of pressure, and the high gas flow cools the baby; it is also noisy.

Negative Pressure Box :

This is a negative pressure cuirass around the baby's chest and abdomen. It is difficult to get a good seal, and there is poor access to the baby. Handling the baby causes loss of pressure, and the high gas flow cools the baby.The use of tight-fitting facial masks and devices requiring a neck seal declined as a consequence of serious complications associated with their application, including an increased incidence of cerebellar hemorrhage[23] and post-hemorrhagic hydrocephalus.[24] Nasal devices remained popular as they facilitated better access to the infants.[6]

Nasal CPAP Devices :

Nasal CPAP is widely used for a range of neonatal respiratory conditions. In Australia and New Zealand a massive upsurge in the popularity of nasal CPAP has seen its use, increase four-fold over the past decade. It is established as an effective method of preventing extubation failure, is used in the management of apnea of prematurity, and is increasingly seen as an alternative to intubation and ventilation for the treatment of respiratory distress syndrome (RDS).

Devices in common use for the delivery of nasal CPAP include single and double (binasal) prongs, nasal canula and long (nasopharyngeal) forms.

Nasal Prongs :

This is the most effective and least unsatisfactory method of delivering CPAP. As neonates are nose breathers, nasal CPAP is easily facilitated. One or two prongs are inserted into the nostrils and attached to a ventilator or a device for delivering CPAP.

Single versus Double Prong Devices :

Single prong CPAP, using a cut down endotracheal tube, continues to be used widely despite evidence of better results using short binasal devices. Arandomized trial in more mature preterm infants with early respiratory distress reported better oxygenation, respiratory rate, and weaning success with a short binasal device when compared with single prong nasopharyngeal CPAP.[25]

There are several short binasal prongs available to the clinician including the Argyle prong[26], Hudson prong[27,28], infant flow driver[25] and 1NCA prongs.

In vitro resistance of different devices used for the delivery of nasal continuous positive airway pressure (NCPAP) were compared in neonates Flows of 4-8 liters/ min were passed through a selection of neonatal NCPAP devices (single prong, Duotube, Argyle prong, Hudson prong, Infant Flow Driver), and the resultant fall in pressure measured using a calibrated pressure transducer. Study showed large variation in the potential fall in pressure using different devices. Devices with short double prongs had the lowest resistance to flow.[29]

Kamper J et al[26] studied early treatment of idiopathic respiratory distress syndrome using binasal continuous positive airway pressure at department of pediatrics, Odense University Hospital, Denmark. During a 3-year period (1979-81) 85 premature infants with idiopathic respiratory distress (IRDS) were treated early with an easily applicable light weight CPAP-system with a binasal tube and a gas jet. They used conservative criteria for ventilator treatment. CPAP treatment was initiated as soon as a concentration of oxygen in the inspired air of atleast 40% was needed to prevent PO_2 values below 60 mm Hg and/or general cyanosis. The treatment proved sufficient in 18 out of 25 infants with a birth weight less than or equal to 1500 g and in 53 out of 60infants with a birth weight greater than 1500 g. Seven infants developed pneumothorax during CPAP treatment. Seventy-four infants survived all without bronchopulmonary dysplasia. With the criteria used, early CPAP proved effective in the majority of infants with idiopathic RDS.

Kamper J et al[30] performed another study of early treatment with nasal continuous positive airway pressure in very low-birth-weight infants at Department of Pediatrics, Diagnostic Radiology, Odense University Hospital, Denmark. During 1988 and 1989, a regional cohort of 81 infants with birth weight less than 1501 g were treated with oxygen only (n=ll), early continuous positive airway pressure (CPAP) (n=68) or mechanical ventilation from birth (n=2). They used an easily applicable light weight CPAP system with nasal prongs and a gas jet supplemented with ventilator treatment if necessary, but with conservative criteria for ventilator treatment with tolerance of high PC02. A total of 65 infants (80%) survived to discharge, 61 of whom were supported solely with CPAP or oxygen. No survivors had bronchopulmonary dysplasia.

The results suggested that treatment by early CPAP with nasal prongs with tolerance of high PCO_2 may be effective and lenient in most infants more than 25 weeks' gestation.

In a prospective study from South Africa, Pieper et al[31] conducted a quasi-randomized control trial of CPAP for infants weighing between 775- 1160g who were denied access to NICU compared to the standard therapy of head box oxygen. Although the CPAP was initially placed by respiratory therapists, the ongoing care was continued by nursing staff with no intensive care or CPAP experience. The infants who received CPAP in thesecircumstances had a significantly improved short-term survival (at 24 hours), with trends towards improved long-term survival.

Nasal Cannulae :
Nasal cannulae are used to deliver oxygen into the nose at low flow, usually with no intention of generating positive pressures in the airway. However, nasal cannulae with an outer diameter of 3 mm and flows up to 2 liter/min, have been reported to deliver CPAP.[32] A study of CPAP via nasal cannulae found it as effective in the treatment of apnoea of prematurity as conventional CPAP prongs.[33] No studies have examined its role in the treatment of RDS or in the post-extubation settings. It has been shown that CPAP pressures are unlikely to be delivered effectively to the airway, because flows used are low and leaks around the cannulae are large. Monitoring of the pressure generated by a given flow and achieving adequate humidity are problematic.

Nasal Masks :
Nasal masks were an early means of applying CPAP to neonates.[34] They lost favour because of the difficulty in maintaining an adequate seal and a tendency to obstruct the nasal airway.[35] Recently a new generation of nasal 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 comparisons with nasal prongs.

Nasopharyngeal Prongs :
Prongs inserted up to nasopharyngeal level has been shown to deliver effective CPAP.[36] They received early criticism because they were perceived to be poorly tolerated and difficult to insert.[16] However, nasopharyngeal prongs were continued to be used and featured in trial, which examined binasal[37] and single forms.[38]

Advantages and Disadvantages of various CPAP Delivering Devices

Method	**Advantages**	**Disadvantages**
Endotracheal tube	Patent airway, easy attachment to respirator; easily stabilized and controlled	Complications associated with intubation, high airway resistance.
Head box	Easy to apply; eliminates intubation	Leaks, compression of neck vessels, tissue necrosis and infant accessibility is difficult
Mask	Easy to apply and eliminates intubation	Leaks, dangers of aspiration, CO2 retention if flow is inadequate
Nasopharyngeal tube	Easily inserted and eliminates intubation	Loss of PEEP; high airway resistance, abdominal distention from swallowed air
Nasa prongs	Easy to apply; flexible and infants position can be changed. Eliminates intubation, low airway resistance.	Nasal septum erosion and necrosis; abdominal distension from swallowed air

Circuit for Flow of Inspiratory Gases :

Oxygen and compressed air sources provide the required inspired gases and oxygen blender enables to deliver appropriate FiO_2. The rate of flow of inspired gases is controlled by a flow meter. The amount of gas flow through the CPAP circuit is important. Insufficient set flow limits the flow available for inspiration, increasing airway pressure fluctuation, and raisin* the work of breathing. The flow required is affected by the degree of 'leak' of gas from the infants's nose and mouth. If the mouth is open the pressure in the pharynx will fall and the flow will need to be increased to maintain it If the mouth is tightly closed and the nasal prongs are a good fit (that is, minimal 'leak') the flow required will be less. The flow required and its dynamics are also affected by the system used to generate the CPAP.

The bubble CPAP pressure generating system used in our study has the advantage that the adequacy of flow can be seen and heard. If the leak is high the flow causing the bubbling is too low and the bubbling stops. If the flow is too high the bubbling becomes very vigorous.

The minimum flow rate should be two and half times the infants minute ventilation and should also compensate for the inherent leaks around the apparatus. Usually flow rates of 5 to 10 liters per minute is sufficient. The gases should be humidified prior to delivery to the infant.

POSITIVE PRESSURE SYSTEM :

Infant Flow Driver System :

Infant flow driver system 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.[39] Altering the flow into the CPAP device directly changes the delivered pressure with the IFD. It needs flows in excess of 8 liters/ min to generate pressures around 5 cm H_2O. The actual flow delivered to the airway and the effect of leaks, using 'variable flow' devices such as the IFD, has not been studied.

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.

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 and fewer extubation failures. However, others have not observed this superiority of IFD over NCPAP.[40]

Benveniste Device :

The Benveniste device[41] requires high gas flows with up to 14 liter/ minute to generate pharyngeal pressures of between 3 arid 10.5 cm H_2O. Comparisons with other flow sources for CPAP generation are lacking. As

with the IFD, altering the flow to the Benveniste device directly alters the pressure at the level of the attached nasal prongs. Benveniste device in conjunction with a binasal tube has been shown a simple and effective nasal CPAP system for the treatment of RDS.

Bubble CPAP :

As evident from the above description there exists a multiplicity of CPAP delivery systems. Not all are similar and success with nasal CPAP depends on specific device used to deliver CPAP. Bubble CPAP is an inexpensive and a simple mode for delivering CPAP. Bubble CPAP delivers mechanical oscillatory vibrations which are transmitted into the chest secondary to the non-uniform flow of gas bubbles across a downstream underwater seal. Its proponents point to generated waveforms, in the airway similar to those produced by high-frequency ventilation.[12]

Lee et al[12] performed a randomized cross over study in 10 premature infants ready for extubation to test whether bubble CPAP contributes to gas exchange compared to conventional ventilator-derived CPAP. Measurements of tidal volume and minute volume were made using the Bear-Cub neonatal volume monitor, and gas exchange was measured using an oxygen saturation monitor and a transcutaneous carbon dioxide (tcp CO_2) monitor. Authors found 39% reduction in minute volume ($p<0.001$) and 7% reduction inrespiratory rate ($p=0.004$) with no change in tcp CO_2 or O_2 saturation for infants supported with bubble versus ventilator-derived CPAP. They concluded bubble CPAP might offer an effective and inexpensive option for providing respiratory support to premature infants.

There are not many studies that have examined the effectiveness of bubble CPAP via the nasal route. Narendran V. et al[14] studied outcomes in extremely low birth weight babies with early application of bubble CPAP. Study was performed at Division of Neonatology, Cincinnati Children's Hospital Medical Center, Cincinnati. Outcomes of all infants weighing 401 to 1000 g born in a level 3 neonatal intensive care units between July 2000 and October 2001 (period 2) were compared using historical controls (period 1). It was shown that delivery room intubations, days on mechanical ventilation and use of postnatal steroids decreased ($p<0.001$) in period 2, while mean days on CPAP, number of babies on CPAP at 24 hours ($p<0.001$) and mean weight at 36 weeks corrected gestation also increased ($p<0.05$) after introduction of early bubble CPAP.

They concluded that early bubble CPAP reduced delivery room intubations, days on mechanical ventilation, postnatal steroid use and was associated with increased postnatal weight gain with no increased complications.

De Klerk and De Klerk[13] studied effects of Bubble CPAP on respiratory and non-respiratory outcomes in preterm infants at Department of Pediatrics, Middlemore Hospital, South Auckland, New Zealand.Outcomes in two groups of preterm infants with a birth weight of 1000- 1499 g were compared retrospectively over a 5-year period before (period I; n=57) and after (period II; n=59) the introduction of a primarily nasal CPAP- based approach to respiratory support. From period I to period II, there was a decline in the number of infants ventilated (65 vs 14%, respectively) and receiving surfactant (40 vs 12%, respectively) and in the median days of ventilation (6 vs 2, respectively) and oxygen (4 vs 2, respectively).

Recent study by Jobe et al[42] has sown bubble CPAP in preterm lambs results in lower indicators of acute lung injury (neutrophils and hydrogen peroxide) than mechanical ventilation in the first two hours of life.

With this background we intended to study early nasal CPAP in the treatment of babies with respiratory distress (HMD).

Equipments used to Set-up Bubble CPAP :

1. Fisher and paykel nasal prongs
2. Container with lid, filled with sterile water to a depth of 10 cm H_2O.
3. Column to fit through the lid of this container with graduated scale from 0-10 cm H_2O.
4. Oxygen blender with flow meter attached.
5. Oxygen tubings
6. Humidifier
7. Inspiratory and expiratory circuits.
8. Cap or stockinette

Bubble CPAP is delivered through Fisher and Paykel nasal prongs. They are soft, pliable and gentle on the baby's nares and are automatically curved fora comfortable fit. They are available in 9 sizes based on prong diameter and width of septum. Fisher and Paykel nasal prongs have the largest bore possible to reduce resistance to flow and work of breathing (WOB).

Oxygen tubing is connected to the flow meter and attached to the inlet port of the humidifier. Flow rates of oxygen is between 5-7 liters/min. The flow rate will provide adequate pressure to wash out carbon dioxide in the system, compensate for the normal air leakage from the tubings and generate adequate CPAP pressure. Connect one light weight non-kinking corrugated tube to the humidifier. Choose appropriate size nasal prongs as mentioned above and attach one side to the corrugated tubing coming from the humidifier. Prongs should fit the nares snugly without pinching the nasal sepium. If the prongs are too small there will be increase in the airway resistance and increases air leak from the system. Fill the container with sterile water to 10 cm H_2O and place the container below the level of the infant. The column should be fitted into the container through the lid and placed under the fluid level to desired pressure i.e., initially 6-7 cm H_2O; the expiratory circuit from the infant is connected to the column. The expiratory circuit will need a port and pressure tubing leading to a calibrated manometer.

Technique of Application :

- Position the baby with head end elevated to 30 degrees. Place a small roll under the baby's neck.
- Place the stokinette over the head to hold CPAP in place. The needed length and width varies with size of the baby.
- Gently suction the mouth and nose of the baby to remove any secretions.
- Place the nasal prongs curve side down into the baby's nose. It is important to have the prongs and tubing to be positioned properly to reduce nasal irritation. When they are properly positioned tubings will not be touching the baby's skin, there will be no lateral pressure on baby's nasal septum and prongs should not rest on the philtrum.
- Once everything is in place double check the system to ensure smooth working of the system.

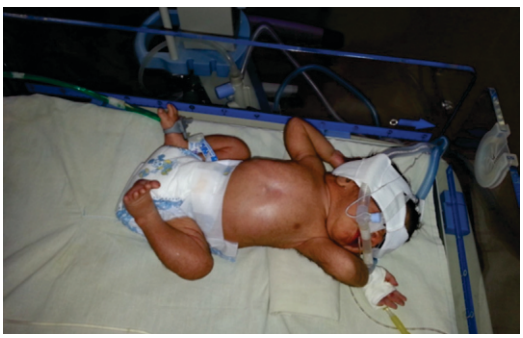

Fig.2 : Baby with HMD put on bubble CPAP in our NICU

Maintaining Bubble CPAP :

- Baby is evaluated with Downes scoring, SpO_2 and regular arterial blood gas (ABG) analysis.
- Oxygen blender is set at appropriate amount of oxygen. Fi02 will vary according to SpO_2 and ABG analysis.
- Underwater bubbling is constantly checked. It indicates that there is enough flow in the system.
- Carefully inspected the nasal septum for signs of irritation since nasal erosion is a potential complication of CPAP.
- 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 cm of H_2O. If still the oxygenation is compromised, $F1O_2$ is then increased to 0.6.

Monitoring of a Baby on CPAP :
Continuous monitoring of respiratory rate, respiratory distress by Downes score, 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.

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 0.25. Then pressures should be decreased in steps of 1-2 cm H_2O until a pressure of 3-4 cm H_2O is reached. The infantshould then be transferred to oxygen hood or incubator oxygen. The patients' condition will guide the speed of weaning.

Clinical Application of CPAP :
CPAP has been used in infants with respiratory distress resulting from HMD, transient tachypnea of newborn, PDA, chronic pulmonary insufficiency of prematurity. It is also used in apnea of prematurity and weaning infants from mechanical ventilation.

The effects of CPAP in managing RDS have been evaluated in several trials and fall into following groups:

Prophylactic CPAP in HMD :
Cochrane review[43] 2005 updates on role of prophylactic nasal CPAP commenced soon after birth regardless of respiratory status in the very preterm or very low birth weight infant in reducing the IPPV and the incidence of chronic lung disease (CLD). All trials using random or quasi-random patients allocation of very preterm infants 32 weeks gestation and/ or <1500 gms at birth were studied. Comparison was made between prophylactic nasal CPAP commencing soon after birth regardless of the respiratory status of the infant versus 'standard' methods of treatment where CPAP or IPPV is used for a defined respiratory condition. They found no statistically significant differences in any of the outcomes reported. There was a trend towards increase in the incidence of BPD at 28 days [RR 2.27 (0.7, 6.65)], death [RR 3.63 (0.42, 31.08)] and any IVH [RR 2.18 (0.84, 5.62)] in the CPAP group. There is currently insufficient information on prophylactic CPAP to make recommendations for clinical practice.Early

Treatment of HMD :
Initial experience with CPAP was obtained by observing clinical condition and arterial blood gases of infants with RDS before and after applying CPAP. Three RCTs[44,45] evaluated effect of CPAP vs no CPAP in treatment of RDS. These trials included total 136 babies with moderately severe distress based on clinical and radiological criteria and provided CPAP by facemask or ET tube. They showed that CPAP improves oxygenation, reduced need for subsequent ventilation and reduced death rate. However, applicability of these results in current practice is difficult to assess given the outdated methods of CPAP delivering devices.

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 sown the fact that early use of CPAP reduces the need for subsequent intubation and mechanical ventilation in RDS.

Gittermann MK et al[46] tested the hypothesis that the use of early nasal CPAP (applied as soon as signs of respiratory distress occurred, usually within 15 min after birth) reduces the need for intubation, the duration of

intermittent mandatory ventilation and the incidence of bronchopulmonary dysplasia. The study was performed at Division of Neonatology, University Women's Hospital, Bern, Switzerland. All live born VLBW infants (birth weight <1500 g) admitted to neonatal intensive care unit in 1990 (historical controls) and in 1993 (early nasal CPAP group) were the subjects of the study.The intubation rate was significantly lower after introduction of nasal CPAP (30% vs 53%, p=0.016). Median duration of intubation was 4.5 days (interquartile range 3-7 days) before versus 6 days (2.8-9 days) after nasal CPAP was introduced (p=0.73). The incidence of bronchopulmonary dysplasia was not reduced significantly (32% vs 30%, p=0.94).

They concluded that early nasal CPAP is an effective treatment of respiratory distress in VLBW infants, significantly reducing the need for intubation and intermittent mandatory ventilation without worsening other standard measures of neonatal outcome.

Cochrane review[47] (2002) was performed to determine if continuous distending pressure (CDP) reduces the need for IPPV and associated morbidity without adverse effects. The standard search strategy of the Neonatal Review Group was used. This included searches of the Oxford Database of Perinatal Trials, Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 3, 2004), MEDLINE (1966 August, 2004), and EMBASE (1980 August, 2004), previous reviews including cross references, abstracts, conference and symposia proceedings and expert informants.

All trials using random or quasi-random allocation of preterm infants with RDS were eligible. Interventions were continuous distending pressure including continuous positive airway pressure (CPAP) by mask, nasal prong, nasopharyngeal tube, or endotracheal tube, or continuous negative pressure (CNP) via a chamber enclosing the thorax and lower body, compared with standard care. It is seen that CDP is associated with a lower rate of failed treatment (death or use of assisted ventilation) [summary RR 0.70 (0.55, 0.88),RD - 0.22 (-0.35, -0.09), NNT 5 (3, II)] overall mortality [summary RR 0.52 (0.32, 0.87), RD - 0.15 (-0.26, -0.04), NNT 7 (4, 25)], and mortality in infants with birth weights above 1500 g [summary RR 0.24 (0.07, 0.84), RD - 0.281 (- 0.483,-0.078), NNT 4 (2,13)].

It was concluded that in preterm infants with RDS the application of CDP either as CPAP or CNP is associated with benefits in terms of reduced

respiratory failure and reduced mortality. Where resources are limited, such as in developing countries, for RDS may have a clinical role.

Early versus Late Initiation of CPAP :
Cochrane review[48] 2002 determines if early compared with delayed initiation of CDP result in lower mortality and reduced need for intermittent positive pressure ventilation. It was a trial among pre-term infants with respiratory distress syndrome spontaneously breathing at trial entry, which used random or quasi-random allocation to either early or delayed CDP. They found 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 not 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%.

Recent study by Sandri F et al[49] published in arch dis child 2004 evaluates the benefits and risks of prophylactic nCPAP in infants of 28-31 weeks gestation. It was a multicenter randomized controlled clinical trial conducted at seventeen Italian Neonatal Intensive Care Units. A total of 230 newborns of 28-31 weeks gestation, not intubated in the delivery room andwithout major malformations, weie randomly assigned to prophylactic or rescue nCPAP. Prophylactic nCPAP was started within 30 minutes of birth, irrespective of oxygen requirement and clinical status. Rescue nCPAP was started when FiC»2 requirement was >0.4, for more than 30 minutes, to maintain transcutaneous oxygen saturation between 93% and 96%. Exogenous surfactant was given when Fi02 requirement was >0.4 in nCPAP in the presence of radiological signs of respiratory distress syndrome.Results were surfactant was needed by 22.6% in the prophylaxis group and 21.7% in the rescue group. Mechanical ventilation was required by 12.2% in both the prophylaxis and rescue groups. The incidence of air leaks was 2.6% in both groups. They concluded that in newborns of 28-31 weeks gestation, there is no greater benefit in giving prophylactic nCPAP than in starting nCPAP when the oxygen requirement increases to a FiO_2>0.4.

CONCLUSION

Nasal CPAP is effective in babies with low birth weight with preterm with respiratory distress (HMD).Nasal CPAP is safe, inexpensive and effective means of respiratory support in HMD.Early nasal CPAP is useful in mild and moderate grade HMD. It may not be a replacement for assisted respiratory support (ventilation) in severe HMD.

In developing countries like ours, there is high burden of prematurity and low birth weight use of early nasal CPAP which is simple, non-invasive, has low capital outlay and does not require expertise, is the option for us where most places cannot provide invasive ventilation.

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