

## Bubble continuous positive airway pressure as a primary modality of respiratory support in meconium aspiration syndrome

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### ABSTRACT

**Background:** Approximately 3–4% of neonates with meconium-stained amniotic fluid (MSAF) develop meconium aspiration syndrome (MAS), of which nearly 30–50% need continuous positive airway pressure (CPAP) or mechanical ventilation (MV).

**Objective:** The objective of the study was to evaluate the usefulness of bubble CPAP as a respiratory support in neonates admitted with MAS and to enumerate factors affecting the CPAP failure. **Materials and Methods:** A prospective study was conducted, involving all the neonates born with a history of MSAF with respiratory distress within 6 h of life (Downe's score 4–7), SpO<sub>2</sub> <90% with chest X-ray suggestive of MAS. Bubble CPAP was started with pressure and FiO<sub>2</sub> adjusted to maintain a SpO<sub>2</sub> between 89% and 95%, maximum pressure limit of 6 cm, and FiO<sub>2</sub> of 100%, respectively. CPAP was removed when SpO<sub>2</sub> was >90% with FiO<sub>2</sub> requirement <25% and when respiratory distress was passive (Respiratory rate <60/min, no or mild retractions and no grunt). The primary outcome was measured in terms of improvement in Downe's score and clinical condition of neonates. CPAP failure was defined as the need for MV, pulmonary leak syndrome, persistent pulmonary hypertension, and progression of Downe's score. **Results:** Downe's score at the start of CPAP was 6 which decreased to 4, 6 h post-CPAP. There was an improvement in FiO<sub>2</sub>, RR, and heart rate from 68%, 76/min, and 181/min to 84%, 48/min, and 123/min post-CPAP, respectively. The success rate of CPAP was 77% and failure rate was 23%.

**Conclusion:** Early initiation of CPAP in MAS neonates decreases the need for MV and improves outcomes.

**Key words:** Bubble continuous positive airway pressure, Mechanical ventilation, Meconium aspiration syndrome

Meconium-stained amniotic fluid (MSAF) complicates approximately 5–10% of live births [1]. Its incidence is more common in 37 weeks or older babies who are post-mature and small for gestational age, whereas in preterm, its incidence is very low. Babies born with MSAF are 100-fold more likely to develop substantial respiratory distress than those born with clear amniotic fluid [2]. Intrauterine hypoxia may cause passage of meconium in the amniotic fluid [3,4]. As meconium causes severe ventilation-perfusion mismatch requiring respiratory support, various ventilation strategies have been designed for its management.

Continuous positive airway pressure (CPAP) is a well-established mode of respiratory support in preterm newborns. In meconium aspiration syndrome (MAS), application of CPAP can be beneficial by resolving the atelectatic alveoli due to injury and secondary surfactant deficiency [5-7]. About one-third of infants with MAS require intubation and mechanical ventilation (MV) [8]. Ventilatory management of the neonate with MAS is challenging due to the complicated pulmonary pathophysiology. This results from the areas of atelectasis and hyperinflation, in association with ventilation-perfusion mismatch, airway compromise, and pulmonary leak. There is

little evidence from the clinical trials regarding the respiratory support of neonates with MAS. This study was done to evaluate the usefulness of bubble CPAP as a primary respiratory support in neonates admitted with MAS and to enumerate factors affecting CPAP failure.

### MATERIALS AND METHODS

A prospective study was conducted in the neonatal intensive care unit (NICU) of a tertiary care teaching institution over a period of 2 years. Patients were recruited after getting approval from the Institutional ethical committee and after taking written consent from the parents of legal guardians of the baby. A total of 657 neonates were admitted to NICU with diagnosis of MSAF, of which 325 neonates were enrolled in the study. The study included all the neonates born with a history of MSAF with the development of respiratory distress within 6 h of life (Downe's score 4–7), SpO<sub>2</sub> <90% with chest X-ray suggestive of MAS. Neonates with birth weight >2000 g and <4000 g and gestational age >34 weeks including post-matured neonates were included in the study. Newborn with comorbid conditions including congenital heart disease, chromosomal anomalies,

lethal congenital anomalies, and severely asphyxiated neonates requiring intubation at admission was excluded from the study.

Bubble CPAP was started if SpO<sub>2</sub> <90% with oxygen at 10 L/min and Downe's score was 4–7. CPAP pressure and FiO<sub>2</sub> were adjusted to maintain a SpO<sub>2</sub> between 89% and 95% with a maximum pressure limit of 6 cm and FiO<sub>2</sub> of 100%. CPAP was removed when the SpO<sub>2</sub> was >90% with FiO<sub>2</sub> requirement <25% and when respiratory distress was passive (RR <60/min, no or mild retractions and no grunt). Post-CPAP, oxygen was given either with hood or with binasal oxygen prongs, as appropriate. Neonates with MAS who had hypoxemia (PaO<sub>2</sub> <50 mmHg), hypercarbia (PaCO<sub>2</sub> >60 mmHg) or acidosis (pH <7.25), and saturation <89% in oxygen-enriched environment with FiO<sub>2</sub> >60% were considered as candidates for MV.

The primary outcome was an improvement in Downe's score and clinical condition of neonates. CPAP failure was defined as the need for MV, pulmonary leak syndrome, persistent pulmonary hypertension (PPHN), and progression of Downe's score. Outcome variables were compared between the infants who failed CPAP and those who were successfully managed with CPAP.

Categorical variables were compared with Chi-square test, while continuous variables were analyzed using Student's t-test for normal distribution. Significance was defined as p<0.05 for the predefined outcome variables and p<0.01 for other outcome variables explored *post hoc*. Odds for CPAP failure were analyzed using logistic regression analysis.

## RESULTS

The mean birth weight of enrolled neonates was 2706±200 g and mean age was 37±1.2 weeks. A total of 68% of enrolled neonates were male and 32% were female. A total of 16% of the enrolled neonates were preterm, 60% were term, and 24% were post-term, respectively. Out of the total admitted neonates, 33.4% were

born to mothers with pregnancy-induced hypertension, 5.8% to mothers with gestational diabetes mellitus; however, 38% were out born (n=25). Cesarean section was mode of delivery in 40% of neonates. Growth restriction at birth was present in 40 neonates most of them being born to pre-eclamptic mothers. Mean Apgar score at 1 min and 5 min was 6 (interquartile range [IQR] 4–7) and 8 (IQR 4–9), respectively (Table 1).

Meantime to start of CPAP was 0.34 h. Mean SpO<sub>2</sub> without oxygen supplementation was 74.23±9%, mean Downe's score before starting CPAP was 6 (IQR 4–7), and mean RR and heart rate were 86±8 and 72±12/min, respectively (Table 2). Mean highest peak end-expiratory pressure (PEEP) during CPAP was 6. A total of 320 chest radiographs were available for analysis. Hyperinflation on chest radiograph (>8 intercostal spaces) was seen in 254 patients (79%), moderate infiltrates in 117 (36%) infants, and bilateral severe infiltrates were seen in 136 (42%) infants. A significant decline in the need for FiO<sub>2</sub>, mean Downe's score, mean RR, and heart rate was observed from the baseline to 8 h of CPAP. Median duration of CPAP was 38.5 h (range: 12–54 h), median duration of oxygen supplementation was 74.8 h (range: 24–168 h), and median duration of hospital stay was 14 days (range: 8–22 days).

A total of 23 (35%) neonates developed culture-positive sepsis during the hospital stay. Neonatal seizures were treated in 250 (76%) infants. Neonates requiring sedation during CPAP were 46 and phenobarbitone was used for sedation. A total of 65 neonates (20%) had significant nasal trauma due to CPAP interface, and 8% (2.4) of cases developed necrotizing enterocolitis. A total of 30 (9.2%) neonates died of severe PPHN. Failure of CPAP and requirement of MV (synchronized intermittent mandatory ventilation mode) was observed in 75 neonates. Reasons were increased in Downe's score (54%), pulmonary leak syndrome (23%), pulmonary hemorrhage (19%), recurrent apnea (3%), and others (1%). On analysis,

**Table 1: CPAP success versus failure**

Predictor variables	Success (250)	Failure (75)	p-value
Birth weight in grams*	2706±200	2132±100	<0.001
Gestational age in weeks*	37±1.2	35±0.8	<0.001
Sex: Male	146 (58.4)	44 (58.7)	0.9632
IUGR	16 (40)	24(40)	0.3741
Outborn	76 (30.4)	46 (61.33)	<0.0001
Saturation at start of CPAP	78±4	68±5	<0.0001
Non-vigorous baby	50 (20)	10 (13.33)	0.1923
APGAR at 1 min 4–6	160 (64)	60 (80)	0.0095
APGAR at 5 min 4–6	42 (16.8)	14 (18.7)	0.7028
Maximum PEEP during CPAP	5±0.8	7±0.8	<0.0001
PEEP after 1 h of beginning of CPAP	5±0.4	6±0.9	<0.0001
Severe infiltrates on chest X-ray	54 (21.6)	36 (48)	<0.0001
FiO <sub>2</sub> at the beginning of CPAP*	56±4	72± 2	<0.0001
Time of start of CPAP (min)	32±5	72±7	<0.0001
PPHN	120 (48)	48 (64)	0.0152

\*Values are expressed in median±standard deviation, other values in percentage (n), CPAP: Continuous positive airway pressure, PEEP: Positive end-expiratory pressure, PPHN: Persistent pulmonary hypertension, IUGR: Intrauterine growth restriction

**Table 2: CPAP parameters before and after 6 h**

CPAP parameters	At the start of CPAP	6 h post-CPAP	p-value
Downe's score	6±0.45	4±0.50	<0.001
FiO <sub>2</sub> (%)	68±22	48±20	<0.001
RR/min	76±12	48±18	<0.001
Heart rate (beats/min)	181±11	123±18	<0.001

Values express in number/percentage (%). CPAP: Continuous positive airway pressure

factors associated with failed CPAP were outborn status, male sex, preterm, growth-restricted babies, high FiO<sub>2</sub> at 1 h, and high PEEP at 1 h of start of CPAP. CPAP failure was more commonly seen in neonates with recurrent apnea.

## DISCUSSION

Despite the improvement in obstetrical and neonatal care, MAS continues to be a neonatal disorder with high morbidity and mortality. Management of MAS complicated with PPHN requires multimodal approach which includes MV, high-frequency ventilation, inhaled nitric oxide, and extracorporeal membrane oxygenation which are not usually available in most of the NICUs including government sectors. CPAP being an emerging modality in the management of moderate-to-severe MAS is as effective as MV with lesser risk of pulmonary leak syndromes, pneumonia, and hypotension. In meconium-stained babies, MAS is more likely in the presence of respiratory distress starting immediately after birth. The current study showed that the early initiation of low-level bubble CPAP in neonates with MAS reduces the subsequent need for MV. For every five newborns with MAS started on bubble CPAP, four newborns were protected from MV. The need for MV in the first 7 days of life was significantly lower.

Many studies have been done to identify risk factors for developing severe MAS in live-born babies [5-9], but no study has been done to identify risk factors for success or failure of CPAP in MAS. Being outborn was an important predictor of CPAP failure in our study. Increased risk of unreported asphyxia, lack of antenatal and perinatal monitoring, poor availability of skilled personnel for resuscitation at birth, and delay in initiation of respiratory support in outborn infants may be the reasons for increased severity of MAS and CPAP failure in these infants. On subgroup analysis, outborn infants were more immature and a higher proportion depressed at birth compared with inborn infants.

Fox *et al.*, in their retrospective analysis of records of 14 patients with MAS, evaluated the role of CPAP for MAS. The study revealed that PEEP can be effective without simultaneous MV [10]. Malik and Gupta conducted a prospective study on the role of CPAP in 116 consecutive neonates suffering from respiratory distress including 18 babies with MAS [11]. Babies with respiratory distress were first treated with humidified oxygen by hood at a rate of 4–6 L/min. Indications for shifting to CPAP ventilation were failure to maintain SaO<sub>2</sub> >85%, persistent or increased Downe's score of 6 or more, and recurrent apneic spells. All MAS infants required CPAP with

one failed CPAP and required MV, 12 of the 18 infants (66%) survived. Reasons for CPAP failure and mortality were not reported in the study [11].

Bhagwat *et al.* [12], in their prospective study, showed that out of enrolled 66 infants, 50 (76%) with moderate-to-severe MAS were managed with CPAP alone and concluded that the use of early CPAP resulted in a lesser need for ventilation. The duration of oxygen requirement, hospitalization, and ventilation is very similar to the results of our study. Pandita *et al.* [13], in their randomized clinical trial involving 135 infants with moderate or severe MAS, showed that 2 infants (3%) supported with nasal CPAP required subsequent MV in the first 7 days of life versus 17 infants (25%) who were supported with hood oxygen, which was a significant difference. They concluded that there is reduction in subsequent need for MV in infants in whom nasal CPAP was used as initial respiratory support which is also consistent with the present study.

Manandhar [14], in his study involving 63 babies with respiratory distress, showed that 39 (61%) showed improvement of respiratory distress with bubble CPAP with confidence interval of 38–62%, whereas 24 (39%) babies required MV and other modalities. This is in consistent with our study. This is one of the first studies evaluating the role of CPAP in neonates with moderate-to-severe MAS. Well-defined inclusion criteria and uniform implementation of the study protocol are some of the merits of this study. The limitations of our study are lack of randomization, with no perinatal data in all outborn infants, and inability to generalize the data to all infants with MAS.

## CONCLUSION

CPAP is an emerging modality in the management of moderate-to-severe MAS and is as effective as MV with lesser risk of pulmonary leak syndromes, pneumonia, and hypotension. Early initiation of CPAP in MAS neonates decreases the need for MV with improved outcome.

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