Early Management of Newborn with Meconium Aspiration Syndrome Using Continuous Positive Airway Pressure as a Special Modality

Saber A.M. El-Sayed[1], Mohamed M. Shehab[2*], Mostafa M. Ahmady[1], Ahmed Baraka[3]

[1]Department of Pediatrics, National Research Centre, Cairo, Egypt
[2]Department of Pediatrics, Faculty of Medicine, Zagazig University, Egypt
[3]Department of Clinical and Chemical Pathology, Faculty of Medicine, Zagazig University, Egypt

ABSTRACT

Background: There is still a lot of doubt for use of CPAP in treatment of meconium aspiration syndrome (MAS). We applied the use of CPAP as a first treatment modality in patients suffering of MAS and tried to know the factors affecting CPAP failure. Objectives: The aim of the study was to know the failure rates among cases of MAS used CPAP (either on bubble or ventilator nasal CPAP) as a modality of treatment. Design: Many centers sharing in the analytical study for comparison CPAP failures with CPAP success for perinatal and neonatal periods. Methods: From Marsh 2014 to August 2015, 84 babies were admitted and diagnosed as MAS. 60 babies (71, 4%) started Bubble or ventilator nasal CPAP when the oxygen saturation (SpO 2) in room air was less than 90%. The need for mechanical ventilation (MV) was defined as CPAP failure. The outcome variables were compared between the MAS infants with failed CPAP management and those who were successfully managed with CPAP. Results: 14 babies (23%) out of 60 failed to CPAP. Reasons for failure were: 9 babies needed increased oxygen requirement (6 had persistent pulmonary hypertension and 3 had sepsis with multi organ failure), 2 babies (3.3%) ventilated for poor efforts (due to frequent seizures), 3 babies (5%) for worsening pneumothorax and 1 baby (1.6%) for severe metabolic acidosis. Baseline comparison was done between the babies who failed CPAP and the others who were successfully managed with CPAP alone. On statistical analysis, factors significantly associated with CPAP failure were out-born status, abnormal cardiograph, high FiO 2 at 1 h and high positive end-expiratory pressure at 1 h ($P < 0.05$) of starting CPAP. On logistic regression analysis, only out-born status was independently associated with CPAP failure (OR = 25, 97% CI: 1.6-120, $P < 0.01$) and there was CPAP failure in newborn babies with respiratory depression at birth (OR = 10, 97% CI: 1-120). Conclusion: Babies with severe MAS managed early with CPAP reduce the need for MV.

Key Words: Failure of Continuous positive airway pressure, meconium aspiration syndrome, Continuous positive airway pressure failure predictors.

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INTRODUCTION

Newborn babies develop grades of respiratory distress when are born with meconium-stained amniotic fluid (MSAF) more than newborn babies come with clear amniotic fluid. [1] Meconium aspiration syndrome (MAS) occurs in about 4-10% of babies born through meconium stained amniotic fluid MSAF [2,3]. The decreased mortality rates of newborn babies with MAS from 40% to 25% in recent studies; [4,5] is directly related to change in obstetric qualifications and use of respiratory supports as exogenous surfactant, nitric oxide and high frequency ventilation. Babies with MAS have bad outcome in developing countries due to some factors as ignorant monitoring during pregnancy and labor, low Apgar scores which need mechanical ventilation and

Corresponding author: Mohamed M Shehab
Address: Department of Pediatrics, Faculty of Medicine, Zagazig University, Egypt.
E-mail: ✉ Mohmmdshehab@yahoo.com
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unavailable essential respiratory therapies that help decreasing mortality. [6,7] Babies with MAS having difficult access to a tertiary level neonatal intensive care unit (NICU) for MV are common cases in developing countries. Respiratory distress in newborn babies is managed in many centers with oxygen alone and develops high morbidity and mortality. Approximately, 40% of newborn with MAS will have severe form of respiratory distress that need mechanical ventilation. [8,9] Both invasive and noninvasive ventilation (NIV) play an equal role in the management of MAS which is a lifesaving measure, need a prolonged stay in the hospital with increased costs [10,11]. As a first line of treatment of MAS, continuous positive airway pressure (CPAP) may be appropriate in resource-limited country like us. The aim of this work was to study the role of CPAP in MAS, its failure and success rates and the factors leading to CPAP failures [12].

METHODS AND DESIGN

Two centers were sharing this prospective observational analytical study. The study was conducted in the Pediatrics department [Neonatal Intensive Care Unit] of Zagazig General Hospital as well as in Health Insurance Hospital in Sharkiaa Egypt; during the period from Marsh 2014 to August 2015.
Informed consent was obtained from the children's parents or caregivers. The study was approved by the ethical committee of the Faculty of Medicine; Zagazig University and the hospital's directors.

Requirements

Eighty-four newborn babies were admitted to NICU during the study from the period of Marsh 2014 to August 2015 (18 months), with a diagnosis of MAS. MAS were defined as the presence of MSAF at birth, clinically presence of respiratory distress within 6 h of life and CXR suggestive of aspiration pneumonia. Mainly term/late preterm babies admitted to NICU within the first 24 h of life and with a diagnosis of MAS, saturation <90% on room air, and Downe score >5 was included in the study. Downe score is an objective method to assess the severity of respiratory distress in newborns. It includes respiratory rate, recessions, grunting, air entry and fractional oxygen requirement. Each one is scoring on a scale of 0, 1 and 2 according to increasing of severity. The total score ranges from 0 to 10. A gestation age from 34 1/7 days to 36 6/7 days defined as late preterm gestation. Gestational age assessment was calculated from the mothers LMP and later confirmed by New Techniques Examination Admission to NICU of intubated newborn babies, having severe and lethal congenital malformations, pneumothorax babies we excluded them from our study.

Monitoring and Summative

CPAP started with the available ventilators, bobble CPAP generator for the newborn babies sharing the study after consent from the parents. Using nasal prongs (Hudson prongs or Rams cannula). Hudson prongs were fixed as per standard guidelines. CPAP started at a pressure of CPAP was 5 cm; FiO 2 was 50% and flow of 5 L/min. CPAP pressure and FiO 2 adjusted to maintain a SpO 2 between 89% and 95% with a maximum pressure limit of 6 cm and FiO 2 of 100%. Then CPAP removed when the SpO 2 became more than 90% with FiO 2 requirement less than 25% and when passive respiratory distress obtained (RR less than 60/min, no or mild retractions and no grunt). Hood or bi nasal oxygen prongs used for given postextubating oxygen. Port holes of the hood w closed or opened to maintain SpO 2 between more than 90%. Weaned off from the oxygen started gradually when SPO2 more than 95%. Management of other co-morbid conditions such as pulmonary hypertension or shock in newborn babies sharing in the study was done using the Downe's score. A chest radiograph was done before sharing in the study. Seizures, renal dysfunction, therapeutic hypo-thermic, fluid, electrolyte, acid and base imbalances were at the discretion of the attending physician. Regular monitored for clinical signs of respiratory distress for all an arterial blood gas analysis was done at the start of sharing and at 6 h after intervention. Neonates failing CPAP were started on synchronous intermittent mandatory ventilation (SIMV) mode of ventilation. Criteria for MV was defined as SpO 2 less than 90% or PaO 2 less than 50 mm Hg on FiO 2 100% or PaCO 2 more than 60 mm Hg with a pH less than 7.25 or poor respiratory efforts or new onset pneumothorax with unstable vitals. Higher modes of ventilation such as high frequency oscillatory (HFO), and iNO were used as existing protocol. Surfactant was given by Insure technique if the FiO 2 was consistently (more than 2 h) above 50%. A predesigned case reporting all perinatal and neonatal data were collected either discharged or death.

Evaluation and factors of continuous positive airway pressure failure:

CPAP failure was considered when MV was needed in primary outcome variables. Secondary outcome variables were rate of survival, duration of oxygen in hours, duration of ventilation in hours, duration of stay in hospital and change in Downe score, heart rate, RR and FiO 2 from staring to 6 h of intervention. Factors of CPAP failure studied include birth weight, gestation, sex, abnormal cardiograph, Apgar score at 1 and 5 min, echo diagnosis of persistent pulmonary hypertension (PPHN), chest X-ray (CXR) categorization (low volume/hyperinflation/mild or moderate or severe infiltrates), maximum FiO 2 requirements in the first hour of CPAP, maximum pressure requirement at the end of first hour of CPAP. Infiltrates were classified as mild if they were present in one or two zones, moderate if they were present in 3-5 zones and severe if all zones of the lung were showing infiltrates.

Statistical analysis

Variable outcomes were compared between the babies with failed CPAP and babies with successful CPAP management. Categorical variables were compared with Chi-square test, while continuous variables were analyzed using Student's t-test for normal distributions. 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

During the study period, a total of 84 newborn babies admitted to NICU with a diagnosis of MAS; 60 newborn babies were sharing in the study [Figure 1]. The mean birth weight of the sixty babies was 3155 ± 366 g and mean gestational age was 38 ± 3 weeks. Sixty-six percent of them were males (n = 40). Growth restriction at birth was present in 4 babies. Thirty-five percent of babies were out-born (n = 21). Caesarean section was the mode of delivery in 62 % of infants. Out of them, 45 % were emergency Caesarean sections.

Twenty-two (36.6%) newborn babies with respiratory depression at birth required intubation and endotracheal suction.

Median Apgar score at 1 min was 5 (IQR 1-7) and median Apgar score at 5 min was 6 (IQR 3-9). Mean time for the start of CPAP was 5.55 ± 0.64 h. Mean SpO 2 off oxygen supplementation 71,02 ± 18%, mean Downe score before starting CPAP was 5 (IQR 5-7), mean RR was 74 ±10 in 14 (23%) babies, and heart rate were 77 ± 12 and 160 ± 15/min respectively. Twelve babies with chest radiographs were used for analysis. Hyperinflation on chest X-Ray was found in 3 patients (5 %). Moderate infiltrates on chest X-Ray bilaterally 22 (36.6 %) babies. Radiographic cardiothoracic ratio was more than 0.6 found in 9 (15%) babies.

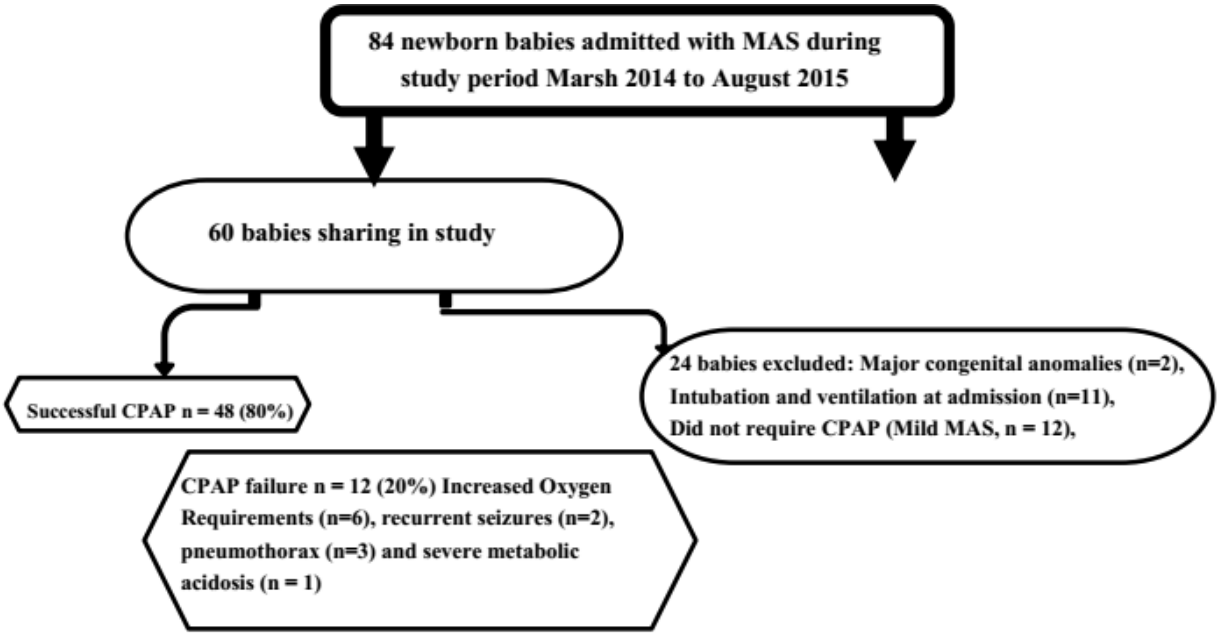

Table (1) shows a significant decrease in the need for FiO_2, mean Downe score and mean H.R., and respiratory rate was observed from the baseline to 6 h of CPAP. Median duration of CPAP was 24 h (IQR 12-50), median duration of oxygen supplementation was 44.5 h (IQR 10-94) and median duration of hospital stay was 7 days (IQR 5 – 12).

Twenty (33, 3%) babies had given vasoactive agents as they had shock. Three babies had pneumothorax (5 %); one had pneumothorax before starting of CPAP and in two after initiation of CPAP. Of the two infants with pneumothorax post CPAP, one baby was continued on CPAP and did not require insertion of chest drain. Thirty-two (53.3 %) babies had ECHO proven PPHN and of those, 11 (34 %) had moderate to severe PPHN. Twenty babies (30 %) by culture found positive sepsis during the hospital stay. 2 babies treated for neonatal seizures (3.3 %). None of sharing babies had required sedation during CPAP and none had any nasal trauma due to CPAP administration, and no babies developed NEC. Only one from sharing babies died of severe PPHN.

Twelve babies (20 %) of the 60 babies had failed CPAP and required MV (SIMV and or HFO). Three of the 12 babies also required high frequency ventilation (1 for failed SIMV and 2 for pneumothorax). Reasons for failure were: 6 babies for increased oxygen requirement (2 had PPHN and 3 had sepsis with multisystem failures), one baby for poor respiratory efforts (recurrent seizures), in three infants for worsening pneumothorax and in one infant for severe metabolic acidosis. Median time for initiation of ventilation was 12 h (IQR 5-20 h) and the median duration of ventilation 140 h (IQR 40-165 h). One baby managed with NIV. 15 newborn babies were

given surfactant for high oxygen requirement and radiograph suggesting secondary RDS.

Table 1. CPAP status (before and after 6 h)

CPAP parameters	Before	After 6 h	p
Downe score	5 ± 1	1.52 ±1.5	< 0.05
Respiratory rate (per/min)	74 ± 10	64 ± 14	< 0.05
Heart rate (per/min)	77 ± 12	152.5 ± 13.45	< 0.05
FiO2 (%)	62±20	42 ± 26	< 0.05
Downe score. Continuous Positive Airway Pressure CPAP			

Table 2. CPAP success and CPAP failure SD-standard deviation

variability Factors	Success (n=48)	Failure (n=12)	*p*
Gestational age (weeks)*	38.6±1	38±0.8	0.14
Birth weight (g)*	3124±475	38±224	0.84
Less active baby	25 (48)	10 (50)	0.60
Out born infant	12 (26)	4 (39)	0.012
Little amniotic fluids	3 (3)	4 (22)	0.10
Apgar 1 min <5	12(30)	7 (33)	0.33
Apgar 5 min <5	3 (6)	3 (13)	0.25
CTG abnormalities	12 (20)	8 (40)	0.04
Saturation before CPAP*(SaO2)	70±55	65±25	0.10
PEEP at 1 h*	4±1	5±1.7	<0.001
FiO2 at 1 h*	50±11	70±1	0.001
Sever infiltrates on X-ray	12 (30)	7 (44)	0.24
Moderate and sever PPHN	6 (15)	7 (34)	0.07
Surfactant	6 (15)	7 (34)	0.07
Time of starting CPAP*	5±10 h	2±5 h	0.22
IUGR	4 (7)	1 (5)	0.97

CPAP- continuous Positive airway pressure; IUGR: intrauterine growth restriction; PEEP-Positive end-expiratory Pressure; PPHN-Persistent pulmonary hypertension.

CPAP failures in babies who had moderate to severe PPHN and antenatal amniotic fluids less than expected were noticed. On statistical analysis, only out born babies were associated with CPAP failure (OR = 25, 97 % CI: 1.6-120, P < 0.01) and there was a trend towards CPAP failure in babies depressed at birth (OR = 10, 97% CI: 1.2 -120). On subgroup analysis, out born babies with more immature (36.6 ± 0.5 vs. 38.9 ± 1.1 weeks) and a higher proportion of babies were less active at birth (68% vs. 41%, P = 0.03).

DISCUSSION

Our study showed about 70% of newborn babies suffering from moderate to severe meconium aspiration syndrome were managed with only CPAP. Pneumothorax incidence was 5% (n = 3). Early CPAP applied in the study resulted in a lesser need for mechanical ventilation and the same rate of pneumothorax was detected in a recently published study on MAS by Hofmeyr GJ, et al. [13]. In a study by Klarc RH, et al.[14], 99 newborn babies diagnosed MAS, ventilation was applied in 42 % of them (42 babies) and (6%) of them (6 babies) were diagnosed as pneumothorax. The duration of (oxygen therapy, hospitalization and ventilation) days is the same or slightly less than in our study as in Lyen HS, et al. [15]. In this study application of Downe score and partial oxygen pressure from sharing until 6 h post CPAP showed improved respiratory and heart rate. The pressure of CPAP was kept at a level that maintained the airways and the alveoli opened during expiration to prevent and decrease air trapping. Moderate CPAP pressure application resolved atelectasis by sufficiently expanding the partially obstructed small air ways. Parth WH, et al., Phaskiar CH, et.al. [16, 17] recorded 12 newborn babies with meconium aspiration syndrome in relation to CPAP pressure. End expiratory pressure in a range of 1 to 14 cm H_2O were recorded with either CPAP or mechanical ventilation. The mean change of PO 2 response to EEP at low (1-3 cm H 2 O), middle (4-7 cm H 2 O), and high (8-14 cm H 2 O) pressures revealed that the maximum Po 2 response was observed in the middle range of EEP with a decreased response in the higher range. 10 of the 12 babies survived. Their study cleared that EEP can be effective without simultaneous MV by Phatyia PD, et. al.[18]. Rybakowski C, et al. [19] reported a study of 116 newborn babies suffering from respiratory distress managed by CPAP. Eighteen babies of them were suffering meconium aspiration syndrome. Respiratory distressed babies were treated firstly by humidified oxygen 5 L/min. using hood box. If there was failure to maintain oxygen saturation more than 85%, recurrent apneic spells, increasing Downes score of 6 or more as reported by Sbong CY, et al.[20] CPAP was introduced. Risk factors of severe MAS in live born babies were mentioned in many studies (Sharmaa VK, et. al. [21], Sivanandam HS, et.al [22], Smithgold GP. [23], Sywain B, et.al.[24], Terasaka D, et.al.[25], however; no study was done to know the risk factors of CPAP success or failure during management. Insufficient monitoring of antenatal and perinatal period, increased unreported asphyxia, insufficient well-trained personals for resuscitation of distressed babies for any reasons increasing MAS and failure CPAP which was more common in extremely premature newborn babies as reported by Turner PS, et. al. [26], Vain NE, et.al. [27], Yasta UM, et.al. [28].

CONCLUSION

Continuous positive airway pressure applied early in the management of MAS is safe and may decrease the need for MV.

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