

Nasal intermittent positive pressure ventilation in neonates with meconium aspiration syndrome

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Background: Nasal intermittent positive pressure ventilation (NIPPV) as primary respiratory support in neonates with meconium aspiration syndrome (MAS) has not been studied. The present study applied the use of NIPPV as a treatment modality in MAS and tried to identify factors predicting NIPPV failure. **Objective:** The aim was to identify failure rates of MAS on NIPPV and potential predictors of NIPPV failure. Design: Observational analytical study. **Methods:** 86 neonates were admitted during the study period of 2 years of which 60 were included and NIPPV was applied as the primary modality of respiratory support with available ventilators. Outcome variables were compared between the MAS infants who failed NIPPV and those who were successfully managed with NIPPV. **Results:** 7 neonates (11.7%) out of 60 enrolled neonates failed on NIPPV. There was a significant decrease in Downe score, respiratory rate, heart rate, fio2 requirement after 6 hours compared to a baseline measurement ($p < 0.01$). On univariate analysis factors associated with NIPPV failure were high Fio2, high PEEP, at one hour of starting NIPPV ($p < 0.05$). However, on logistic regression none of the factors were predicting failure independently. **Conclusion:** NIPPV applied early may reduce the need for mechanical ventilation in neonates with moderate to severe MAS.

Keywords: Nasal intermittent positive pressure ventilation, Meconium aspiration syndrome, Predictors of NIPPV failure

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Introduction

Meconium aspiration syndrome (MAS) is a complex respiratory disease contributing to significant morbidity and mortality in neonates [1]. MAS includes a unique combination of airflow obstruction, atelectasis, and lung inflammation with a high risk of coexistent pulmonary hypertension in the relatively mature lung, hence management of MAS in particular ventilator management has been a difficult challenge. (2).

Among the neonates requiring respiratory support, 10-20% are treated with CPAP alone and about one-third require intubation and mechanical ventilation [3,4]. While a large number of neonates with MAS will need respiratory support, the ideal ventilatory strategy remains unknown [5]. Since lung mechanics are altered with significant atelectasis and obstruction in MAS, respiratory management has historically included hood oxygen without positive pressure to limit the risk of worsened air trapping and resultant air leak [5].

However prolonged high oxygen exposure is not benign and has been shown to worsen pulmonary arterial constriction in lambs as well as increased the risk of free radical injury [6,7]. As an alternative nasal continuous positive airway pressure (NCPAP) has been proposed for the prevention of mechanical ventilation as it provides positive pressure with reduced oxygen administration [8]. Application of nasal intermittent positive pressure (NIPPV) combines NCPAP with additional intermittent breaths above the baseline [9,10].

Nasal intermittent positive pressure ventilation is a mode of non-invasive ventilation which may be used as a substitute for mechanical ventilation as invasive ventilation is associated with costs of prolonged hospital stay, need for continued critical care, and other morbidities. The evidence is in favor of NIPPV in reducing the need for invasive ventilation in the first few days of life [11,12,13,14]. However, there are no studies of this mode of ventilation in MAS, hence the current study was conducted to see if these benefits could be extrapolated in the setting of MAS.

Aims and Objective

01. To assess the efficacy of NIPPV in providing respiratory support in term neonates with MAS
02. To assesses the safety and predictors of failure of NIPPV in MAS.

Materials and Methods

Setting: The study was conducted in a tertiary care neonatal unit in Bangalore

Duration and type of study: Two years. Observational analytical study

86 babies were admitted with a diagnosis of MAS during the study period of 2 years of which 60 neonates fulfilling inclusion criteria were included. NIPPV was administered after having obtained consent with available ventilators and the interface used was Ram's canula. Neonates were started on NIPPV with PEEP 5, Fio₂ adjusted to maintain saturation, and PIP maximum of 15.

Inclusion Criteria

01. Neonates are born through meconium-stained amniotic fluid.
02. Gestation \geq 36weeks with a birth weight of >1800 grams.
03. Admitted to NICU in first 24 hours of birth.
04. Respiratory distress is defined as Downe score >4 and spo₂ $<90\%$ on room air.

Exclusion Criteria

01. Intubation at admission for severe respiratory distress.
02. Severe asphyxia 5 min APGAR score <3 .
03. Pneumothorax/air leak at admission.
04. Major congenital malformation.

NIPPV failure was defined by

01. po₂ $<90\%$ with PEEP6, Fio₂ 260% .
02. worsening respiratory distress.
03. BG pH <7.2 with severe metabolic acidosis.

Outcomes

The primary outcome variable was the need for mechanical ventilation. The secondary outcome variable was changed in Downe score, heart rate, respiratory rate, Fio₂ from enrollment to 6 hours post-intervention, and complication in terms of nasal injuries, pneumothorax.

Statistical Analysis

Outcome variables were compared between neonates with MAS who failed NIPPV and those who were successfully managed with NIPPV. Data were entered into Microsoft Excel datasheet and were analyzed using SPSS 22 version software.

Categorical data was represented in the form of frequencies and proportion. The chi-square test was used as a test of significance for qualitative data. Continuous data were expressed as mean and standard deviation. The Independent t-test was used as a test of significance to identify the mean difference between two quantitative variables. a p-value of <0.05 was considered as statistically significant.

Results

In the study out of 60 enrolled neonates 11.7% (7 neonates) had failure and 53 (88.3%) had been successfully treated with NIPPV. Mean birth weight, gestational age between success, and failure groups were similar. Mean Downe score before initiation of NIPPV was 5.02+ 0.948 and after 6 hours was 1.88+1.896. Mean Fio2, RR, Heart rate before NIPPV was 57, 72.72, 158.3 respectively and after 6 hours of NIPPV was 38.17, 59.17, 136.88.

There was a significant decrease in Downe score, Fio2 RR, and heart rate after 6 hours compared to baseline measurements (P<0.01)(Table1,2). On univariate analysis factors significantly associated with NIPPV failure were high Fio2 and high PEEP at 1 hour (P<0.05) of starting NIPPV.

However, on multiple logistic regression none of the factors were predicting failure independently. (Table3,4). None of the infants had pneumothorax or nasal injury two neonates in the success group were given surfactant by INSURE method and five neonates required surfactant in the failure group.

Out of 7 subjects who failed on NIPPV 4.3% had severe distress, 42.9% had PPHN and another 14.3% had sepsis. No mortality was noted.

Table-1: DOWNE Score before and after 6 hours.

| | | N | Mean | SD | P-value |
|-------------|--------------|----|------|-------|---------|
| DOWNE Score | Before | 60 | 5.02 | 0.948 | <0.001* |
| | After 6 hour | 60 | 1.88 | 1.896 | |

In the study, Downe Score before was 5.02±0.948 and after 6 hours was 1.88±1.896. There was a significant decrease in Downe score after 6 hours.

Table-2: Parameters on NIPPV (before and after 6 hrs).

| | | N | Mean | SD | P-value |
|------|---------------|----|--------|--------|---------|
| FIO2 | Before | 60 | 57.00 | 6.901 | <0.001* |
| | After 6 hours | 60 | 38.17 | 15.254 | |
| RR | Before | 60 | 72.72 | 6.613 | <0.001* |
| | After 6 hours | 60 | 59.17 | 10.038 | |
| HR | Before | 60 | 158.30 | 13.417 | <0.001* |
| | After 6 hours | 60 | 136.88 | 18.660 | |

In the study, there was a significant decrease in FIO2, RR, and HR after 6 hours compared to baseline values.

Table-3: NIPPV success versus NIPPV failure.

| | Success | | | | P-value |
|----------------------------------|---------|------|---------|-------|---------|
| | Success | | Failure | | |
| | Mean | SD | Mean | SD | |
| Saturation before starting NIVPP | 81.40 | 5.79 | 73.86 | 7.45 | 0.003* |
| Gestational Age | 38.92 | 1.84 | 38.86 | 2.19 | 0.929 |
| Birth Weight | 2.83 | 0.45 | 2.91 | 0.46 | 0.666 |
| PEEP at 1 hour | 5.15 | 0.36 | 6.14 | 0.38 | <0.001* |
| FIO2 at 1 hour | 39.55 | 7.50 | 69.29 | 11.70 | <0.001* |

In the study there was a significant difference in Saturation before starting NIPPV, PEEP at 1 hour, and FIO2 at 1 hour between the Success and failure group.

Table-4: Predictor variables with NIPPV success versus failure.

| | | Success | | | | P-value |
|--------------------|----------------|---------|-------|---------|--------|---------|
| | | Success | | Failure | | |
| | | Count | % | Count | % | |
| Inborn or Out born | Inborn | 27 | 50.9% | 6 | 85.7% | 0.082 |
| | Out born | 26 | 49.1% | 1 | 14.3% | |
| Gestational Age | <37 Weeks | 6 | 11.3% | 1 | 14.3% | 0.785 |
| | 37 to 40 weeks | 37 | 69.8% | 4 | 57.1% | |
| | >40 weeks | 10 | 18.9% | 2 | 28.6% | |
| Gender | Female | 24 | 45.3% | 4 | 57.1% | 0.554 |
| | Male | 29 | 54.7% | 3 | 42.9% | |
| SGA/AGA/LGA | AGA | 43 | 81.1% | 7 | 100.0% | 0.453 |
| | LGA | 1 | 1.9% | 0 | 0.0% | |
| | SGA | 9 | 17.0% | 0 | 0.0% | |

| | | | | | | |
|-----------------------------|---------|----|-------|---|-------|---------|
| Sever Infiltration on X-Ray | No | 31 | 58.5% | 2 | 28.6% | 0.135 |
| | Yes | 22 | 41.5% | 5 | 71.4% | |
| CTG Abnormal | Absent | 38 | 71.7% | 5 | 71.4% | 0.988 |
| | Present | 15 | 28.3% | 2 | 28.6% | |
| Surfactant | No | 51 | 96.2% | 2 | 28.6% | <0.001* |
| | Yes | 2 | 3.8% | 5 | 71.4% | |

In the study, there was a significant difference in Surfactant b/w Success and failure.

Discussion

Ventilator management of the neonates with MAS is challenging because of the complicated pulmonary pathophysiology resulting from atelectasis and areas of hyperinflation in association with ventilation-perfusion mismatch and airway compromise. There is very little evidence from clinical trials regarding the ventilator treatment of neonates with MAS. NIPPV as a mode of noninvasive ventilation, when applied for neonates with MAS, may resolve atelectasis and stabilizes the collapsing terminal airways to enhance gas exchange [5]. Data from surfactant deficient piglets indicate that NIPPV results in less lung inflammation [15].

In our observational study, 88.3% were successfully managed with NIPPV which is evident by lesser need for mechanical ventilation and the results were similar to other modes of noninvasive ventilation like CPAP reported by Srinivas Murki et al in their multicentre open-label randomized control trial who concluded that starting early low-level CPAP in comparison with hood oxygen in neonates with MAS reduces the subsequent need for mechanical ventilation. For every 5 newborns with MAS started on NCPAP one newborn is protected from mechanical ventilation [16].

The most recent Cochrane meta-analysis concluded that NIPPV decreased the risk of meeting respiratory failure in post-extubation setting (relative risk (RR),0.71:95%CI 0.61-0.82) and need for re-intubation (RR,0.76:95% CI0.65-0.88) [17], similar benefits of NIPPV was seen in the setting of MAS as demonstrated in the present study. Saber A.M et al in an observational study reported that 70% of neonates with MAS were managed with CPAP alone. [18] which supports that noninvasive mode NIPPV similar to CPAP can be used as a primary modality in MAS. As there are no published studies of the use of NIPPV in MAS, the present study is one of the first one to evaluate the role of NIPPV in MAS.

The exclusion of infants with severe perinatal asphyxia may be the reason for lesser mortality in the present study cohort compared to studies using CPAP in MAS. Lack of randomization, small sample size, use of short term hospital-based outcomes, and inability to generalize to all infants with MAS are some of the limitations of this study.

Conclusion

Despite the improvement in obstetric and neonatal care meconium aspiration syndrome continues to be a disorder with high morbidity and mortality. Non-invasive ventilation in the form of NIPPV when applied early may reduce the need for invasive mechanical ventilation in newborns with MAS. However larger studies comparing other modes of non-invasive ventilation are required.

What does the study add to existing knowledge?

As there are no published studies of the use of NIPPV in MAS, the present study is one of the first one to evaluate the role of NIPPV in MAS which suggests that NIPPV could be used as the primary mode of respiratory support in neonates with MAS which may reduce the need for invasive mechanical ventilation.

Author's contribution

Dr. Jagadish AS: Study concept and design, acquisition, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

Dr. Vikranth: Data collection, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

Dr. Ravichander B.: Analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content and final approval, agrees to be accountable for all aspects of the study.

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