

Original Research Article

A Retrospective Cohort Study to Compare the Efficacy of Continuous Positive Airway Pressure and Non-Synchronised Nasal Intermittent Positive Pressure Ventilation as Primary Post Extubation Respiratory Support in Preterm Neonates Admitted for Severe Respiratory Distress Syndrome in a Tertiary Care NICU

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ABSTRACT

Background - Evidence clearly shows that reducing the duration of invasive mechanical ventilation and early extubation helps to improve the long-term outcomes of preterm neonates. However, what is not clear is the initial mode of non-invasive support post extubation that may be provided to these preterm neonates. Resource limited public sector NICUs in developing countries like India often face a challenge of ensuring adequate number of machines to deliver NIPPV for all these preterm babies in post extubation period.

Methods – This is a retrospective cohort study which included 60 neonates who were directly extubated to CPAP and were compared with 60 neonates extubated to non synchronised NIPPV, who were selected after propensity score matching with CPAP group. The primary outcome of interest was rate of extubation failure within 72 hours and need for escalation of respiratory support. Other outcomes that were looked at included the duration respiratory support; duration of hospital stay and rates of other complications between the two groups.

Results – 13 babies in CPAP group experienced extubation failure while 11 in NIPPV group experienced it (p value = 0.84, cOR = 1.07); with results being not statistically significant. There was a significant reduction in duration of hospital stay (median = 5 days, p= 0.035, r= 0.11), however this did not translate to overall significant reduction in duration of hospital stay (p=0.48, r = 0.06) and other adverse outcomes. Kaplan Meier analysis revealed that probability of baby remaining extubated was also comparable in both groups.

Conclusion- Standalone Bubble CPAP is equally efficacious as non synchronised NIPPV delivered by ventilator device in terms of preventing extubation failure and does not increase the overall duration of hospital stay and other adverse outcomes in preterm neonates. However more adequately powered randomised trials are needed to confirm these results.

Keywords – Preterm baby, respiratory distress syndrome, extubation failure.

INTRODUCTION

Advances in perinatal and neonatal intensive care have significantly improved survival rates of preterm neonates; however, respiratory complications continue to account for a large share of adverse outcomes in this vulnerable population. Among these, respiratory distress syndrome (RDS) remains one of the most common and serious conditions affecting preterm neonates, especially those born before 34 weeks of gestation.^{1,2}

While mechanical ventilation is often lifesaving, its use is associated with several well recognised complications, including ventilator-induced lung injury, air leak syndromes, volutrauma, barotrauma, and an increased risk of developing bronchopulmonary dysplasia (BPD).³

Consequently, contemporary neonatal care emphasizes strategies that minimize the duration of invasive ventilation and promote early extubation whenever clinically feasible. However, successful extubation and maintenance of adequate spontaneous respiration in preterm neonates with severe RDS remain challenging, with reported extubation failure rates ranging from 20% to 50%.^{4,5}

Extubation failure and need for reintubation are associated with increased exposure to oxygen and positive pressure ventilation, heightened risk of infection, prolonged NICU stay, and higher incidence of chronic lung disease and mortality. Therefore, the choice of effective non-invasive respiratory support following extubation is critical in improving respiratory outcomes and reducing complications in this population.^{4,5}

Recent evidence suggests superiority of Non-invasive Positive Pressure Ventilation (NIPPV) over Conventional Positive Airway Pressure (CPAP) delivered by standalone bubble CPAP machine, as primary post extubation support in preterm neonates, with reduced chances of extubation failure.^{6,7} However, most of this evidence is from high income countries, where synchronised NIPPV is used. When contemplating this evidence to developing countries like India, there are two important issues- one, most of the public sector units in India use Non synchronised

NIPPV, superiority of which over NIPPV needs to be established and second, most of the public sector units in India are resource limited, thereby challenging the availability of NIPPV as primary post extubation respiratory support for all preterm babies. So, this single centre retrospective review was conducted to compare Non synchronised NIPPV delivered by ventilator and CPAP delivered by standalone bubble CPAP machine, as a primary post extubation respiratory support in preterm neonates.

The primary objective was to compare the rates of extubation failure in two groups, defined as need for invasive mechanical ventilation within 72 hours of extubation. Other outcomes like duration of respiratory support, incidence of BPD and other complications and overall length of hospital stay were also compared between the two groups.

MATERIAL AND METHODS

This retrospective cohort study was conducted in NICU of tertiary care teaching hospital in western Gujarat. The unit has close to 2000 admissions annually which includes both intramural and extramural babies.

Case selection was done from medical records of patients admitted to NICU between January 2024 and January 2026. Analysis of results was done between February to April 2026. We included babies born between 28 to 34 weeks of gestation after parental consent. Babies with less than 28 weeks of gestation were excluded since these babies were always extubated to NIPPV primarily as per unit protocol. Beyond 34 weeks of gestation, incidence of RDS is minimal and most babies were managed with CPAP only. Babies with severe perinatal asphyxia and those with congenital anomalies were excluded from study. Institutional Ethics Committee of the institute approved this study.

Sample Size

In a recent Cochrane meta-analysis by Lemyre et al, published in 2023, the rates of CPAP failure and NIPPV failure in post extubation setting were 36.4%

and 27.3% respectively. Now considering the level of significance at 95% and power of study at 80%, ideal sample size for this study would be 407 subjects per group.

However, since this was a single centre study and the unit started using NIPPV as a treatment modality for last 3 years only, and also with improved steroid coverage the incidence of RDS needing intubation being reduced, we only included 60 subjects per group.

We first selected 60 babies with RDS needing intubation for stabilization and who were extubated directly to standalone bubble CPAP for some or other reason.

To increase the study credibility and to reduce confounders, we then did propensity score matching for common confounders and included 60 neonates with RDS needing intubation and extubated to NIPPV, such that both groups were comparable.

Categorical variables (such as mortality, BPD, and sepsis rates) were analyzed using Fisher's exact test or Pearson's chi-square test where appropriate, and the magnitude of association was expressed using conditional odds ratios (OR) with 95% confidence intervals. Continuous variables were found to be non-normally distributed and are presented as medians with interquartile ranges (IQR).

Differences between the NIPPV and CPAP groups for continuous variables were evaluated using the Mann-Whitney U test (Wilcoxon rank-sum test). The strength of association for non-parametric continuous variables was quantified using the Wilcoxon effect size (r). For all analyses, a p-value of less than 0.05 was considered statistically significant. All statistical computations were performed using Microsoft Excel. We further did a subgroup analysis, where the enrolled babies were subdivided in two groups: 28-32 weeks and 32.1-34 weeks, and Kaplan Meier analysis was done to identify the probability of remaining extubated at end of 72 hours in both groups.

For the purpose of this study, we considered the following definitions,

Respiratory Distress Syndrome-

Preterm neonates who were vigorous at birth and having a normal umbilical cord pH with a documented Silverman Anderson (SA) score of 5 or more in the

initial case records and needing intubation for respiratory distress primarily, were included.

CPAP Failure –

Babies who were extubated to bubble CPAP initially and later required escalation of support to NIPPV or Mechanical Ventilation for respiratory distress primarily, within first 72 hrs of extubation.

NIPPV Failure –

Babies who were extubated to non synchronised NIPPV support initially and later required intubation and mechanical ventilation primarily due to respiratory distress within first 72 hrs of extubation.

Criteria for considering failure of primary non-invasive support post extubation-

- 1) FiO₂ requirement of more than 60% while on noninvasive support.
- 2) Respiratory acidosis with pH < 7.20
- 3) Increased Work of breathing with SA score more than or equal to 5 despite PEEP of 6 cm H₂O.
- 4) Desaturation/ Bradycardia episodes (at least one episode requiring Bag and Mask ventilation or > 4 episodes requiring moderate stimulation).

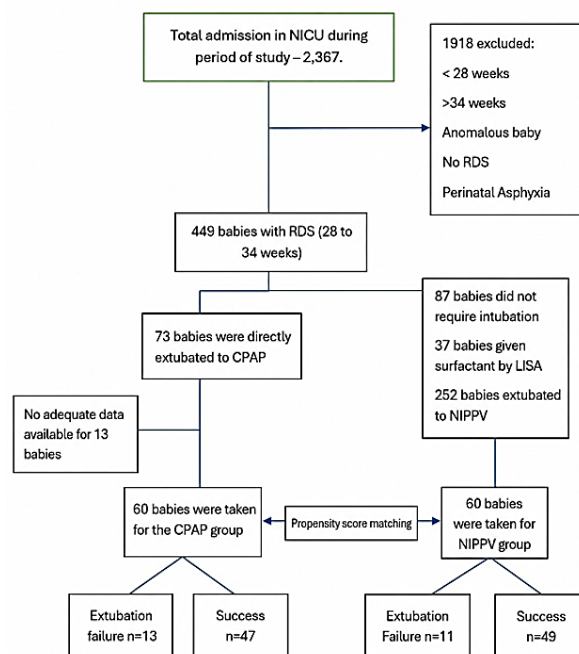


Figure-1: Study Flow Diagram

RESULTS

A total of 120 neonates were included in the study, with 60 belonging to each of the two main groups.

Table-1: Demographic Characteristics of neonates enrolled in study

Characteristic	CPAP (n = 60)	NIPPV (n = 60)	p value
Maternal age, median (IQR), years	29 (18–37)	31 (17–41)	0.67
Mode of delivery, n (%)			
Normal vaginal delivery	25 (41.6)	28 (46.6)	0.5
LSCS	28 (46.7)	30 (50.0)	0.7
Instrumental delivery	7 (11.6)	2 (3.3)	0.08
Antenatal steroid (ANS) coverage, n (%)			
None	7 (11.6)	3 (5.0)	0.2
Partial	48 (80.0)	50 (83.3)	0.67
Complete	5 (8.4)	7 (11.7)	0.5
Gender, n (%)			
Male	35 (58.3)	32 (53.3)	0.58
Female	25 (41.7)	28 (46.7)	0.58
Gestational age, mean $\pm$ SD (weeks)	31.2 $\pm$ 1.5	31.0 $\pm$ 1.6	0.49
Birth weight, median (IQR), kg	1.9 (0.76–2.20)	1.7 (0.69–2.12)	0.63

Table 1 shows the demographic details of the neonates included in the study. Both groups were comparable with regards to maternal age, mode of delivery, antenatal steroid coverage, gestational age at birth, gender and birth weight.

Table – 2: Comparison of outcomes between two groups

Outcome	CPAP (n = 60)	NIPPV (n = 60)	p value	Effect size*
Extubation failure, n (%)	13 (21.7)	11 (18.3)	0.84	cOR 1.07 (0.77–1.21)
Death, n (%)	3 (5.0)	4 (6.7)	0.70	cOR 0.94 (0.44–1.10)
IVH grade $\geq$ 2, n (%)	2 (3.3)	3 (5.0)	0.65	cOR 0.83 (0.51–1.27)
Bronchopulmonary dysplasia, n (%)	8 (13.3)	5 (8.3)	0.56	cOR 1.04 (0.81–1.23)
Nasal trauma, n (%)	10 (16.7)	8 (13.3)	0.79	cOR 1.01 (0.68–1.31)
Feeding intolerance, n (%)	11 (18.3)	15 (25.0)	0.51	cOR 1.09 (0.77–1.21)
Pneumothorax, n (%)	0	5 (8.3)	0.057	cOR 0.76 (0.44–1.13)
Sepsis, n (%)	10 (16.7)	12 (20.0)	0.81	cOR 1.02 (0.78–1.26)

Duration of respiratory support, median (IQR), days	18 (11–38)	12 (5–29)	0.035	$r = 0.11$ (0.01–0.21)
Duration of hospital stay, median (IQR), days	29 (11–43)	26 (9–39)	0.48	$r = 0.06$ (–0.05–0.13)

Rates of extubation failures between the two groups were not different significantly (21.7% vs 18.3%, p value = 0.84). When comparing the duration of respiratory support, there was a statistically significant reduction in the duration of respiratory support in babies extubated to NIPPV, with median difference being 6 days. Median duration of hospital was also higher in CPAP group as compared to NIPPV group; however, this difference was not statistically significant.

When a comparison of adverse outcomes was made between the two groups, there was a higher incidence of feed intolerance and chances of Pneumothorax in NIPPV group as compared to CPAP group, however these differences were not statistically significant. We did a Kaplan Meier analysis to find out the probability of a baby remaining extubated at 72 hours post extubation in both CPAP and NIPPV groups. For this purpose, we stratified the data in 2 groups based on gestational age at time of birth – 28-32 weeks and 32.1-34 weeks.

This analysis demonstrated that the probability of remaining extubated at 72 hours was higher in the NIPPV group of 28–32 weeks subgroup compared to CPAP group of 28- 32 weeks subgroup (figure -2). In contrast, in the 32.1–34 weeks group, these probabilities were almost equal for CPAP and NIPPV, indicating either of these modes can be used as primary post extubation respiratory support (figure-3).

Within the 28–32 weeks group, NIPPV demonstrated better extubation stability compared to CPAP, whereas in the 32.1–34 weeks group, CPAP and NIPPV shows almost equal effect. A possible reason for this difference might be improved respiratory

stability and less severity of RDS with advancing gestational age.

1. Gestational Age: 28 - 32 Weeks

Graph shows continuous lines up to 72 hours and dotted lines for the extension to 84 hours. Y-axis lower limit is 0.5.

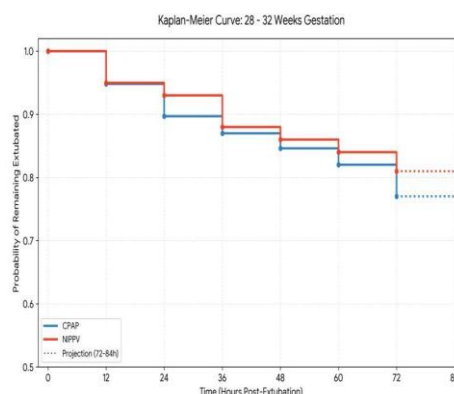


Figure -2 : Kaplan Meier Analysis showing probability of remaining extubated for 28-32 weeks

2. Gestational Age: 32.1 - 34 Weeks

Graph shows continuous lines up to 72 hours and dotted lines for the extension to 84 hours. Y-axis lower limit is 0.5.

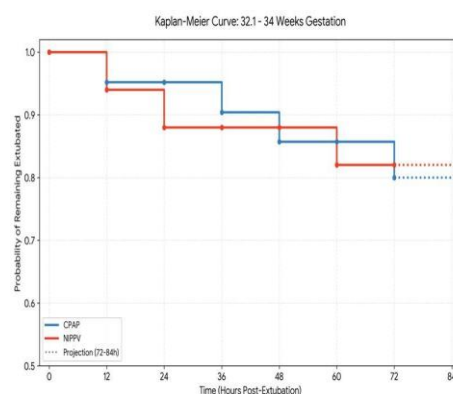


Figure -3 : Kaplan Meier Analysis showing probability of remaining extubated for 32.1-34 weeks

DISCUSSION

Unlike most other studies that are done on this topic previously, this was a retrospective cohort study. While there is a lot of data to support the superiority of synchronised NIPPV over bubble CPAP^{7,8}, the same cannot be claimed for non synchronised NIPPV, which is very commonly used in developing countries like India. So, this retrospective study was undertaken to compare the efficacy of non-synchronised NIPPV and CPAP as primary post-extubation respiratory support in preterm neonates admitted with severe RDS in a tertiary care NICU. By focusing on real-world clinical practice rather than controlled trial conditions, this study provides valuable insight into the performance of these modalities in routine neonatal care.

With regard to the mode of delivery, our study found no significant difference between CPAP and NIPPV groups, with LSCS being a predominant mode in both arms. This finding is consistent with Mukerji et al., who reported similar cesarean section rates between CPAP and NIPPV groups (71.2% vs 69.1%), suggesting that delivery mode does not differentially influence post-extubation respiratory outcomes.⁹

In terms of other risk factors associated with RDS severity, our study found no difference in two groups with respect to gender, gestational age at birth, birth weight and coverage of antenatal steroids. Mukerji et al. and Kriplani et al. similarly reported balanced antenatal and perinatal variables, particularly antenatal steroid exposure, across their study groups, emphasizing the importance of baseline equivalence in pragmatic datasets.^{7,9}

Our study showed a slight male predominance in both CPAP and NIPPV groups, with no statistically significant difference. The rates of extubation failure, as defined by need for escalation of support to a superior modality, were comparable in both groups and there was no statistically significant difference between CPAP and NIPPV group. These findings are different from a similar study by Zhu et al.¹⁰ in 2022, where NIPPV was superior to CPAP in reducing rates of reintubation. However, our findings are correlating well with Mukerji et al.,⁹ who concluded that both CPAP and NIPPV are equally effective in preventing

need for reintubation. A prospective study by Pooja Yadav et al from India, also found similar results as ours.¹¹ Meta analysis by Lemeyre et al, published in 2023 also concluded superiority of NIPPV over CPAP, but there the focus was on synchronised NIPPV.⁸

In our study, NIPPV group had significantly lower duration of respiratory support than CPAP group (6 days difference in median duration of respiratory support), which is similar to findings of study by Zhu et al.¹⁰ who reported a reduction in duration by 5 days with NIPPV. However, this reduction in duration of respiratory support did not translate to a significant reduction in duration of hospital stay, which is similar to findings by Pooja Yadav et al.¹¹ There was no statistically significant difference in rates of BPD, IVH, feed intolerance and sepsis in both groups. This is similar to findings of Kriplani et al, Pooja Yadav et al and Mukerji et al.^{7,9,11}

Ahmad HA et al.¹² also conducted a retrospective study comparing CPAP and NIPPV, which showed that odds of extubation failure were similar in both CPAP and NIPPV groups, however they have used high CPAP pressures of 9 cm of H₂O in post extubation support. We do not use higher pressures in our unit since there is lack of sufficient evidence to support the safety of such high pressures in preterm neonates.

The Kaplan Meier Analysis showed that the probability of baby remaining extubated at 72 hours was comparable in both CPAP and NIPPV groups. This further confirms the findings of our study and other similar studies that CPAP is non inferior to NIPPV as primary post extubation respiratory support in preterm babies with RDS. There are not many previously reported studies that have compared the probability of baby remaining extubated after 72 hrs in both CPAP and NIPPV groups.

Some of the limitations of this study include retrospective study design limiting control over confounding variables and the possibility of selection and documentation bias; single-center setting restricting the generalizability of findings to other NICUs with different protocols, patient populations, and staffing expertise; insufficient sample size to

detect differences in rare but clinically significant outcomes such as severe BPD or pneumothorax; focus only on short-term NICU outcomes rather than long-term respiratory and neurodevelopmental outcomes; not accounting for ventilator settings variability, interface types, or caregiver experience, which may influence outcomes and not including other newer modes of non-invasive ventilation like nasal high frequency ventilation.

CONCLUSIONS

This study demonstrates that non-synchronised NIPPV and CPAP are both effective and safe modalities for post-extubation respiratory support in preterm neonates with severe respiratory distress syndrome. The two groups were well matched with respect to maternal, obstetric, and neonatal baseline characteristics, strengthening the validity of outcome comparisons.

Non-synchronised NIPPV showed a significant advantage in reducing the duration of respiratory support, suggesting improved respiratory mechanics and earlier stabilization following extubation. However, this benefit did not translate into a significant reduction in reintubation rates or NICU stay duration. Importantly, the incidence of severe complications remained low and comparable in both groups with a trend towards higher rates of Pneumothorax. It can be safely implied that in resource limited settings, preterm babies with RDS can be safely extubated to bubble CPAP, and that rates of extubation failure do not differ significantly between non synchronised NIPPV and standalone bubble CPAP.

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Source of support: Nil

Conflict of interest: None declared

How to cite: Pathak M, Dattani Y, Tilwani S, Kesharani T, Thaddane R. A Retrospective Cohort Study to Compare the Efficacy of Continuous Positive Airway Pressure and Non-Synchronised Nasal Intermittent Positive Pressure Ventilation as Primary Post Extubation Respiratory Support in Preterm Neonates Admitted for Severe Respiratory Distress Syndrome in a Tertiary Care NICU: An Original Research Article. GAIMS J Med Sci 2026;6(2): 111-118

<https://doi.org/10.5281/zenodo.21526118>