

Outcomes of Continuous and Non-Invasive Positive Pressure Ventilation in Neonates

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ABSTRACT

Objective: To compare the clinical outcomes of non-invasive nasal intermittent positive pressure ventilation (NIPPV) with nasal continuous positive airway pressure (NCPAP) in preterm neonates following extubation.

Study Design: Descriptive, analytical study.

Place and Duration of the Study: Department of Paediatrics and Child Health, the Aga Khan University Hospital, Karachi, Pakistan, from October 2023 to March 2024.

Methodology: Preterm neonates born between 27 and 36+6 weeks of gestation who required mechanical ventilation at birth and were subsequently extubated to either NCPAP or NIPPV were enrolled in the study. A total of 95 neonates were included: 49 received NCPAP, and 46 received NIPPV. Outcomes were measured over the first week post-extubation.

Results: The median gestational age was comparable between the groups [NCPAP: 32 weeks (IQR 30–35), NIPPV: 32.2 weeks (IQR 30–35)]. Extubation failure occurred significantly more frequently in the NCPAP group (55.1%) compared with the NIPPV group (8.7%, $p < 0.001$). Neonates in the NCPAP group required longer durations of mechanical ventilation, non-invasive support, and hospital stay. In multivariate analysis, NCPAP was independently associated with higher odds of extubation failure (OR 6.61, 95% CI: 1.53–28.62; $p = 0.01$). Mortality rate was low and similar across both groups.

Conclusion: NIPPV was associated with a substantially lower risk of extubation failure and shorter recovery time compared with NCPAP. These findings suggest that NIPPV may be considered a preferred mode of post-extubation support in preterm neonates.

Key Words: Preterm neonates, Non-invasive positive pressure ventilation, Continuous positive airway pressure, Extubation failure.

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INTRODUCTION

With 39 deaths per 1,000 live births, Pakistan has one of the highest rates of neonatal mortality worldwide.¹ In many low- and middle-income countries (LMICs), preterm delivery is a primary cause of these high mortality rates, especially among late preterm infants who would typically survive in high-resource settings.² Among premature neonates, most deaths are due to pre-term complications, with the prevalence of neonatal respiratory distress syndrome (NRDS) among low-birth-weight neonates ranging from 12% to 15%.³

Non-invasive ventilation (NIV) is increasingly recognised as an effective respiratory support strategy for preterm newborns. The recent evidence shows that NIV modalities such as nasal intermittent positive pressure ventilation (NIPPV) and non-invasive high-frequency oscillatory ventilation (NHFOV) significantly reduce the need for invasive mechanical ventilation and lower the risk of ventilator-associated complications, including bronchopulmonary dysplasia (BPD).^{4,5}

Two commonly utilised non-invasive measures included nasal continuous positive airway pressure (NCPAP) and NIPPV. By providing a steady gas flow through an interface sealed against the upper airways, NCPAP maintains consistent positive pressure throughout the baby's breathing cycle. As a result of the produced pressure, the nasopharyngeal cross-sectional area expands, airway resistance decreases, lung compliance improves, endogenous surfactant release increases, diaphragmatic activity enhances, apnoea frequency decreases, and ventilation-perfusion matching improves.^{6,7}

In contrast, NIPPV increases the amount of positive pressure breaths that are intermittent over a baseline of positive end expiratory pressure (PEEP), while maintaining a predetermined peak inspiratory pressure (PIP), inspiratory time, and respiratory rate. The sporadic positive breaths enhance alveolar recruitment, boost tidal volume supplied, enhance naso-pharyngeal inflation, and raise pressure delivered to lower airways.⁸

However, despite the use of non-invasive techniques, in some cases they fail to maintain adequate functional residual capacity post-extubation, and reintubation becomes necessary. Therefore, it is crucial to predict extubation failure and use the ideal ventilation technique. Compared to head-box oxygen, NCPAP significantly reduced the frequency of extubation failure, according to a major meta-analysis conducted by Ferguson et al.⁹

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In comparison to infants extubated to NCPAP, preterm infants <30 weeks who were extubated to NIPPV within 60 minutes of surfactant therapy required fewer reintubations, spent less time on mechanical ventilation, and had lower rates of BPD, according to Ramanathan *et al.*¹⁰ However, these comparisons are based on using data and resources from high-income countries, offering limited insight on their effectiveness in resource-limited settings.

While research from high-income countries has shown that both NIPPV and NCPAP can help prevent extubation failure in preterm newborns, there is little evidence from countries such as Pakistan, where healthcare systems operate under different constraints. Even in well-equipped tertiary care centres, factors such as staffing ratios, access to advanced monitoring, and local protocols can influence the performance of these non-invasive ventilation. The current study was designed to address this gap by comparing NIPPV with NCPAP in a real-world neonatal intensive care unit setting in Pakistan, a lower-middle-income country, to determine which approach may offer better outcomes for vulnerable preterm infants.

METHODOLOGY

This descriptive, analytical study was conducted prospectively at the Department of Paediatrics and Child Health, the Aga Khan University Hospital, Karachi, Pakistan, from October 2023 to March 2024. Ethical approval was obtained from the Ethical Review Board of the Aga Khan University, Karachi, Pakistan (Approval ID: 2023-9104-26717). A total of 95 preterm neonates were included in the study, with gestational ages ranging from 27 to 36 weeks and 6 days. All neonates required invasive mechanical ventilation at birth (for >6 hours) and were subsequently extubated to either NIPPV or NCPAP by the attending neonatologist.

Neonates with major congenital anomalies, congenital heart disease, pneumothorax, or structural anatomical defects such as craniofacial or skeletal malformations were excluded. Caffeine was administered to newborns as per institutional protocols. After extubation, infants receiving NIPPV were assigned to Group A, while those on NCPAP were assigned to Group B. Both modes of non-invasive support were delivered using SLE 5000 and SLE 6000 ventilators (SLE Ltd., UK), which are routinely used in the NICU of the study hospital. NCPAP was delivered via a RAM cannula at a pressure of 8 cm H₂O, while NIPPV was administered using the same interface with initial settings of 20/10 cm H₂O (PIP/PEEP). All neonates were monitored for one week post-extubation. The main outcome of the study was extubation failure, which was defined as the need for reintubation within 72 hours to 7 days. This failure was determined by the presence of respiratory acidosis (with a pH <7.25 and PCO₂ >60 mmHg), the increased oxygen requirement (with a FiO₂ between 30% and 40%), and the occurrence of frequent or severe apnoeic episodes. Additionally, post-extubation mortality was also considered as part of the primary outcome. Secondary outcomes included achieving full oral feeding (150 ml/kg/day), length of hospital stay, and discharge weight. The

primary NICU team monitored the neonates, and a trained research assistant recorded clinical events using a standardised data collection proforma.

Statistical analysis was conducted using STATA version 18. Continuous variables with normal distribution were expressed as mean and standard deviation, while variables without a normal distribution were reported as median with interquartile range (IQR). Categorical data were presented as frequencies and percentages. Continuous variables were compared using the independent sample t-test or the Mann-Whitney U tests, while categorical variables were analysed using the Chi-square or Fisher's exact test. Logistic regression was performed to identify predictors of reintubation, and a p-value less than 0.05 was considered statistically significant.

The sample size was calculated using OpenEpi (version 3.01), based on an anticipated post-extubation reintubation rate of 20% derived from previously published literature.¹¹ Assuming a 5% level of significance and aiming for adequate statistical power to detect group differences, the minimum required sample size was 47 neonates per group, yielding a total of 95 participants.

RESULTS

Baseline characteristics of the study participants are summarised in Table I. A total of 95 neonates were included, with 49 (52%) receiving NCPAP and 46 (48%) receiving NIPPV post-extubation. The median birth weight was 1.72 (1.21–2.30) kg in the NCPAP group and 1.92 (1.20–2.35) kg in the NIPPV group. The NCPAP group had a higher proportion of neonates born to mothers with premature rupture of membranes, while the NIPPV group had a higher proportion of maternal hypertension and multiple births. Other variables such as gestational age, birth weight, gender distribution, and antenatal steroid exposure were broadly comparable between the two groups. Antenatal steroids were administered to 62.5% of neonates in the NCPAP group and 55.56% in the NIPPV group. Lower segment caesarean section (LSCS) was the most common mode of delivery across both the groups. Most mothers had no comorbidities. Among those who had, 33.6% had gestational diabetes mellitus (GDM), 22.1% had hypertension, and 18.95% had premature rupture of membranes (PROM).

Positive pressure ventilation was required by 23 participants in the NCPAP group and 18 in the NIPPV group (Table I), both with a 5-minute APGAR score of 8 (7–9). Surfactant was administered to 78.9% of the neonates.

A significant association ($p < 0.001$) was observed between the NCPAP and NIPPV groups for extubation failure, with 55.1% of the NCPAP group having failure compared to only 8.7% of the NIPPV group. Among neonates who experienced extubation failure, the median time to reintubation was 3 days in the NCPAP group and 2.5 days in the NIPPV group. Neonates in the NCPAP group required a significantly longer duration of both mechanical ventilation and non-invasive respiratory support compared to those in the NIPPV group.

Table I: Descriptive analysis by post-extubation group.

Descriptive analysis by post-extubation group	Total n = 95	NCPAP n = 49	NIPPV n = 46	p-values
Gestational age (weeks): Median (Q1-Q3)	32.00 (30.00-35.00)	32.00 (30.00-34.86)	32.21 (30.00-35.00)	0.69
Birth weight (kg): Median (Q1-Q3)	1.80 (1.20-2.30)	1.72 (1.21-2.30)	1.92 (1.20-2.35)	0.60
Gender				0.38
M	56 (58.95%)	31 (63.27%)	25 (54.35%)	
F	39 (41.05%)	18 (36.73%)	21 (45.65%)	
Multiple birth				0.20
Y	14 (14.74%)	5 (10.20%)	9 (19.57%)	
N	81 (85.26%)	44 (89.80%)	37 (80.43%)	
Ante-natal steroid				0.50
Y	55 (59.14%)	30 (62.50%)	25 (55.56%)	
N	38 (40.86%)	18 (37.50%)	20 (44.44%)	
Course of ante-natal steroid dosages: Median (Q1-Q3)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	
Mode of delivery				0.19
LSCS	90 (94.74%)	45 (91.84%)	45 (97.83%)	
SVD	5 (5.26%)	4 (8.16%)	1 (2.17%)	
Diabetic/GDM				0.51
Y	32 (33.68%)	15 (30.61%)	17 (36.96%)	
N	63 (66.32%)	34 (69.39%)	29 (63.04%)	
Hypertensive				0.017
Y	21 (22.11%)	6 (12.24%)	15 (32.61%)	
N	74 (77.89%)	43 (87.76%)	31 (67.39%)	
Premature rupture of membranes				0.15
Y	18 (18.95%)	12 (24.49%)	6 (13.04%)	
N	77 (81.05%)	37 (75.51%)	40 (86.96%)	
Need of PPV during resuscitation				0.44
Y	41 (43.16%)	23 (46.94%)	18 (39.13%)	
N	54 (56.84%)	26 (53.06%)	28 (60.87%)	
APGAR score at 5 minute: Median (Q1-Q3)	8.00 (7.00-9.00)	8.00 (7.00-9.00)	8.00 (7.00-9.00)	0.31
Surfactant administration				0.87
Y	75 (78.95%)	39 (79.59%)	36 (78.26%)	
N	20 (21.05%)	10 (20.41%)	10 (21.74%)	
Extubation failure				<0.001
Y	31 (32.63%)	27 (55.10%)	4 (8.70%)	
N	64 (67.37%)	22 (44.90%)	42 (91.30%)	
Extubation failure within: Median (Q1-Q3)	3.00 (2.00-4.00)	3.00 (2.00-4.00)	2.50 (1.50-4.50)	0.98
Mode of mechanical ventilation before extubation				0.91
PTV/TTV ¹	88 (93.62%)	46 (93.88%)	42 (93.33%)	
SIMV ²	6 (6.38%)	3 (6.12%)	3 (6.67%)	
Duration of mechanical ventilation: Median (Q1-Q3)	5.00 (2.00-7.00)	6.00 (4.00-8.00)	3.00 (2.00-5.00)	<0.001
Duration of non-invasive respiratory support: Median (Q1-Q3)	8.00 (4.00-13.00)	12.00 (7.00-14.00)	5.50 (3.00-12.00)	0.001
Caffeine treatment given				0.52
Y	67 (70.53%)	36 (73.47%)	31 (67.39%)	
N	28 (29.47%)	13 (26.53%)	15 (32.61%)	
Occurrence of pneumothorax				
Y	0 (0.00%)	0 (0.00%)	0 (0.00%)	
N	95 (100.00%)	49 (100.00%)	46 (100.00%)	
Occurrence of IVH				0.44
Y	6 (6.32%)	4 (8.16%)	2 (4.35%)	
N	89 (93.68%)	45 (91.84%)	44 (95.65%)	
Occurrence Of PDA				0.92
Y	19 (20.00%)	10 (20.41%)	9 (19.57%)	
N	76 (80.00%)	39 (79.59%)	37 (80.43%)	
sepsis Status				0.88
Y	31 (33.33%)	16 (34.04%)	15 (32.61%)	
N	62 (66.67%)	31 (65.96%)	31 (67.39%)	
Mortality				0.96
Y	2 (2.11%)	1 (2.04%)	1 (2.17%)	
N	93 (97.89%)	48 (97.96%)	45 (97.83%)	
Achievement of full oral feeding: Median (Q1-Q3)	7.00 (6.00-10.00)	8.00 (6.00-10.00)	6.50 (5.00-10.00)	0.11
Length of hospital stay: Median (Q1-Q3)	16.00 (10.00-24.00)	22.00 (14.00-26.00)	11.00 (8.00-20.00)	<0.001
Discharge weight (kg): Median (Q1-Q3)	1.90 (1.50-2.50)	1.90 (1.60-2.50)	1.90 (1.50-2.40)	0.91

¹PTV: Patient triggered ventilation; GDM: Gestational diabetes mellitus; TTV: Targeted tidal volume; PDA: Patent ductus arteriosus.

²SIMV: Synchronised intermittent mandatory ventilation; PPV: Positive pressure ventilation.

LSCS: Lower segment caesarean section; IVH: Intraventricular haemorrhage; SVD: Spontaneous vaginal delivery; NCPAP: Nasal continuous positive airway pressure; NIPPV: Non-invasive positive pressure ventilation.

The median duration of non-invasive support was 12 days in the NCPAP group compared to 5.5 days in the NIPPV group ($p < 0.001$). It suggested that NIPPV may be associated with faster respiratory recovery and earlier weaning from ventilatory support. No significant associations were found in caffeine treatment of the two groups; however, 70.5% were managed with caffeine.

A significant difference was observed in the length of hospital stay between the two groups, with the NCPAP group having a longer median stay of 22 days compared to 11 days in the NIPPV group ($p < 0.001$), suggesting a more prolonged recovery period associated with NCPAP.

Table II: Regression analysis.

Extubation failures	Bivariate			Multivariate		
	OR	[95% CI]	p > z	OR	[95% CI]	p > z
Post extubation group						
NIPPV	References			References		
NCPAP	12.89	4.00-41.52	<0.001	6.61	1.53-28.62	0.01
Gestational age (weeks)	0.88	0.74-1.05	0.17	--	--	--
Birth weight (kg)	0.50	0.24-1.05	0.07	--	--	--
Gender						
Male	References			--		
Female	0.71	0.29-1.72	0.44	--	--	--
Antenatal steroid						
N	References			--		
Y	1.99	0.79-5.02	0.15	--	--	--
Premature rupture of membranes						
N	References			--		
Y	1.88	0.66-5.37	0.24	--	--	--
Surfactant administration						
N	References			--		
Y	1.17	0.40-3.40	0.78	--	--	--
Caffeine treatment given						
N	References			--		
Y	1.67	0.62-4.51	0.31	--	--	--
Occurrence Of PDA						
N	References			--		
Y	2.21	0.79-6.18	0.131	--	--	--
Occurrence Of BPD						
N	References			--		
Y	4.38	1.17-16.32	0.03	--	--	--
Sepsis status						
N	References			--		
Y	4.02	1.58-10.22	0.003	--	--	--
Achievement of full oral feeding	1.15	1.04-1.27	0.011	0.58	0.39-0.87	0.008
Length of hospital stay	1.16	1.08-1.24	<0.001	1.40	1.18-1.67	<0.001
Discharge weight (kg)	0.84	0.36-1.97	0.689	--	--	--

NCPAP: Nasal continuous positive airway pressure; NIPPV: Non-invasive positive pressure ventilation; PDA: Patent ductus arteriosus; BPD: Bronchopulmonary dysplasia.

Clinical outcomes after extubation are shown in Table II. Extubation failure occurred significantly more often in the NCPAP group (12.89 times higher odds of experiencing extubation failure). These neonates also required longer durations of mechanical ventilation and non-invasive respiratory support. The NCPAP group had a notably longer median hospital stay and took more time to achieve full oral feeding compared to the NIPPV group. Mortality was low overall, with one death reported in each group (2.04% in NCPAP vs. 2.17% in NIPPV), and there was no significant difference between them. No cases of pneumothorax were reported in either group. Although not as a primary outcome of interest, sepsis also showed a statistically significant association, with 4 times higher odds of extubation failure, highlighting it as a potential contributing factor in this clinical context.

DISCUSSION

In recent years, there has been a global shift in neonatal respiratory care, with increasing emphasis on non-invasive respiratory support strategies immediately after birth to improve outcomes.¹² Prompt weaning and early extubation to non-invasive support have been the emphasis and ultimate objective over the past decade, as prolonged mechanical ventilation is linked to severe morbidity in premature infants.¹³ However, even within non-invasive ventilation, optimisation is still required, thereby necessitating the evaluation completed by this study.

NCPAP was associated with an increase in extubation failure, considering confounding factors such as age, comorbidities, and complications. These findings are consistent with the Cochrane systematic review, including the 2023 update, which demonstrated that NIPPV is more effective than NCPAP in reducing the incidence of extubation failure and the need for reintubation in preterm neonates.¹⁴ Other studies have reported similar findings, with NCPAP shown to be inferior to NIPPV. A previous meta-analysis revealed that both synchronised and non-synchronised NIPPV significantly reduced extubation failure compared to NCPAP.⁹ A study involving 22 Canadian NICUs reported that although NCPAP was inferior to NIPPV in preventing extubation failure within 72 hours, it was non-inferior for reintubation.¹⁵ When NIPPV was used instead of NCPAP, a systematic review revealed a reduction in both extubation failure and the requirement for reintubation within 48 hours to 7 days.¹⁶

A study including very preterm neonates found that BiPAP to safely reduce early extubation failure compared to NCPAP.¹⁷ Similarly, Kirpalani *et al.* examined the use of NCPAP in combination with either BiPAP or NIPPV in 1,009 preterm infants born at <30 weeks of gestation and weighing <1,000 grams who were receiving non-invasive support for the first time. The study reported a borderline reduction in extubation failure with the use of NIPPV compared to NCPAP.¹⁸

In another prospective observational study involving 51 neonates, which aimed to identify predictors of extubation

failure, no significant difference was observed between those who successfully extubated (80%) and those who needed reintubation (20%) in terms of clinical characteristics, maximum ventilator requirements, or laboratory parameters $\frac{3}{4}$ except for minute ventilation, which was found to be significantly higher among those who failed extubation.¹⁹

In bivariate analysis, sepsis was associated with a 3.37 times increased risk of extubation failure, consistent with definite predictors reported in a 2023 meta-analysis.²⁰ Initially in sepsis, an inflammatory storm is triggered by inflammatory substances that target immature lung tissue. This leads to alveolar cells and interstitial damage, disrupting ventilation function and pulmonary vascular haemodynamics, which may be irreversible. Other specific factors, including gestational age, were not significant in this analysis. Additionally, pre-extubation variables such as pH, FiO₂, and PCO₂ were not collected. Therefore, future research should incorporate these respiratory values to help identify the causes of extubation failure.

NCPAP was also associated with a greater length of hospital stay. Prolonged neonatal length of hospital stay is associated with an increased risk of hospital-acquired infections and increased emotional and financial stress on families.²¹ Extended hospitalisation may also influence parent-infant bonding and family integration, highlighting the importance of incorporating family-centred care approaches in the NICU setting.²² Therefore, the consideration of these elements, along with treatment failure, is crucial in selecting the ideal respiratory support.

Although the results indicate that the NIPPV is a better option than the NCPAP regarding extubation failure, the outcomes are not solely determined by one factor. The success of extubation depends on the strength of the respiratory muscles, the amount of strain they endure, and the adequacy of the respiratory drive. Therefore, reliance on composite measures is more likely to result in failure. Future studies should explore additional pre-intubation factors, especially respiratory parameters. Nonetheless, due to the lack of uniform standards and consensus on the ideal non-invasive respiratory support modality, further studies are needed. Alternative modalities such as nasal high-frequency oscillatory ventilation may offer benefits over NCPAP.²⁰

CONCLUSION

NIPPV has been found to be a more effective post-extubation strategy for preterm neonates compared to NCPAP. The use of NIPPV resulted in significantly lower rates of extubation failure, shorter durations of respiratory support, and reduced length of hospital stays. These findings emphasise the need to reconsider current respiratory practices, as NIPPV may improve both respiratory function and overall outcomes in neonatal care.

ETHICAL APPROVAL:

Ethical approval was obtained from the Ethical Review Board of the Aga Khan University Hospital, Karachi, Pakistan (Approval ID: 2023-9104-26717).

PATIENTS' CONSENT:

The study did not involve any intervention beyond routine clinical care, investigations or management already indicated for the neonates. Data were collected prospectively as part of routine observation, with no additional risk to the participants.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

RM, MSS: Conceptualised the study, designed the methodology, and analysed the collected data.

RM, NC, AAB: Contributed to the writing of the manuscript and interpretation of the results.

RM, HMA: Contributed significantly to the collection of the data required.

All authors approved the final version of the manuscript to be published.

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