Pakistan Journal of Intensive Care Medicine
eISSN: 2708-2261; pISSN: 2958-4728
www.pjicm.com
DOI: https://doi.org/10.54112/pjicm.v5i01.43
Pak. J. Inten. Care Med., volume 2025: 43
Original Research Article

SALBUTAMOL NEBULIZATION FOR THE TREATMENT OF TRANSIENT TACHYPNEA OF THE NEWBORN

JAVED S[1], ROSHAN E[1], HAYYAT MK[1], AFTAB M[1], JAVED N[2], MATEEN M[1]

[1]Department of Paediatric Medicine, Sughra Shafi Medical Complex, Narowal, Pakistan
[2]Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi, Pakistan
**Corresponding author email address: sundaasjaved@gmail.com*

(Received, 17th November 2024, Revised 16th December 2024, Accepted 25th January 2025, Published 30th January 2025)

ABSTRACT

Background: *Transient Tachypnea of the Newborn (TTN) is a self-limiting respiratory condition caused by delayed resorption of fetal lung fluid. β-adrenergic agonists, particularly salbutamol, have been shown to enhance alveolar fluid clearance, potentially reducing respiratory support needs.* ***Objective:*** *To compare the mean duration of oxygen requirement and length of hospital stay in neonates diagnosed with TTN who received inhaled salbutamol versus those who received a placebo, alongside standard care.* ***Study Design:*** *Case-control study.* ***Settings:*** *Neonatal Unit, Department of Paediatrics, Sughra Shafi Medical Complex, Narowal, Pakistan.* ***Duration of Study:*** *April 6, 2024, to October 5, 2024.* ***Methods:*** *A total of 60 neonates born at ≥37 weeks' gestation and diagnosed with TTN were enrolled and randomised into two groups using a lottery method. Group A received nebulised salbutamol at a dose of 0.15 mg/kg, and Group B received 2 ml of isotonic saline as a placebo. Both groups received standard supportive management. Primary outcomes included duration of oxygen therapy (in hours) and hospital stay (in days). Data were analysed using appropriate statistical methods, with p-values <0.05 considered statistically significant.* ***Results:*** *The mean oxygen requirement was significantly reduced in the salbutamol group (32.9 ± 2.07 hours) compared to the placebo group (78.03 ± 2.9 hours; p = 0.000). Similarly, the mean hospital stay was significantly shorter in Group A (3.1 ± 1.1 days) than in Group B (5.7 ± 1.02 days; p = 0.000).* ***Conclusion:*** *Inhaled salbutamol significantly reduces the duration of oxygen requirement and hospital stay in neonates with TTN. This suggests a potential role for β-agonists as adjunctive therapy in the management of TTN.*

Keywords: Transient Tachypnea of the Newborn; Salbutamol; β-agonist; Nebulization; Neonatal Respiratory Distress

INTRODUCTION

Transient tachypnea of the newborn (TTN) is a pulmonary condition characterised by clinical manifestations resulting from delayed or inadequate clearance of fetal lung fluid. This disorder is most commonly observed in term and late preterm neonates, with an estimated incidence of 5.7 per 1,000 live births (1). Clinical signs typically emerge within the first six hours of life and include tachypnea, expiratory grunting, nasal flaring, and intercostal or subcostal chest retractions (2). The clearance of lung fluid is facilitated postnatally by β-adrenergic agonist activity, which mimics the action of fetal catecholamines and aids in pulmonary fluid resorption (3). Epithelial sodium channels in the airway epithelium are centrally involved in this process. Notably, neonates diagnosed with TTN exhibit lower circulating catecholamine levels compared to their healthy counterparts (4).

Salbutamol, a selective β2-adrenergic receptor agonist, has been shown to significantly enhance lung fluid absorption in such cases (5). Several risk factors have been associated with TTN, including elective cesarean section, maternal diabetes, maternal asthma, smoking during pregnancy, multiple gestation, perinatal asphyxia, and maternal over-sedation (6,7). Treatment is largely supportive, involving interventions such as fluid restriction, administration of broad-spectrum antibiotics, diuretics like furosemide, and subcutaneous epinephrine, although evidence supporting the efficacy of some of these treatments remains limited (8).

The primary objective of the present study was to compare the mean duration of oxygen therapy (in hours) and the length of hospital stay (in days) among neonates diagnosed with TTN who received inhaled salbutamol versus those given a placebo, in addition to standard care.

METHODOLOGY

This prospective case-control study was carried out at the Neonatal Unit of the Department of Paediatrics, Sughra Shafi Medical Complex, Narowal, from April 6, 2024, to October 5, 2024. A total of 60 neonates who met the eligibility criteria were enrolled during the study period. The sample size was calculated using a 95% confidence level and 80% power, based on an anticipated mean oxygen requirement of 34.2 ± 32.2 hours in the treatment group (salbutamol) and 77.3 ± 64.7 hours in the placebo group. Infants born at a gestational age of 37 weeks or later, and who were less than three days old at the time of diagnosis, were included if they were clinically and radiographically diagnosed with transient tachypnea of the newborn (TTN). The diagnosis was based on respiratory distress within six hours of birth, with a respiratory rate exceeding 60 breaths per minute, and radiographic evidence showing at least two of the following: prominent central vascular markings, widened interlobar fissures or pleural fluid, and symmetrical perihilar congestion or hyperinflation.

Infants with meconium aspiration syndrome, neonatal respiratory distress syndrome, persistent pulmonary hypertension, congenital pneumonia, early-onset sepsis, hypoglycemia, polycythemia, congenital heart disease, or birth asphyxia were excluded. Other exclusion criteria included multi-organ failure, iatrogenic lung injury, and any congenital anomalies. Approval for the study was obtained from the institutional ethical review board, and written informed consent was obtained from parents before enrollment. The enrolled neonates were randomly divided into two groups, Group A and Group B, using a lottery method. Group A (treatment group) received salbutamol inhalation therapy at a dose of 0.15 mg/kg via nebuliser using a 2 ml solution and 5 L/min of oxygen for 10 minutes. Group B (control group) received nebulised 2 ml isotonic saline with 5 L/min of oxygen for 10 minutes.

[Citation: Javed, S., Roshan, E., Hayyat, M.K., Aftab, M., Javed, N., Mateen, M. (2025). Salbutamol nebulization for the treatment of transient tachypnea of the newborn. *Pak. J. Inten. Care Med.* ***2025****: 43*. doi: https://doi.org/10.54112/pjicm.v5i01.43]

Vital signs, including respiratory rate, heart rate, and oxygen saturation, were recorded at three time points: 30 minutes, 2 hours, and 4 hours after the intervention. Clinical monitoring was performed continuously, and chest radiographs were obtained for diagnostic confirmation. The outcomes measured included respiratory rate, heart rate, oxygen saturation percentage, duration of oxygen therapy in hours, and length of hospital stay in days. The criteria for discharge were resolution of tachypnea (respiratory rate less than 60 breaths per minute), absence of chest retractions, and ability to take oral feeds.

All data were recorded using a standardised proforma to maintain consistency and accuracy. Statistical analysis was performed using SPSS version 23.0. Categorical variables like gender were expressed in terms of frequencies and percentages. Continuous variables such as gestational age, birth weight, hospital stay, and oxygen therapy duration were reported as means and standard deviations. An independent sample t-test was used to compare outcomes between the two groups, and a p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 60 infants born at ≥37 weeks of gestational age were enrolled in this study. Patients were divided into two groups: Group A (Salbutamol) and Group B (Placebo). In Group A, 22 (73.3%) were males and 8 (26.7%) were females. In Group B, 19 (63.3%) were males and 11 (36.7%) were females. The mean gestational age in Group A was 38.3 ± 1.5 weeks, while in Group B it was 38.6 ± 1.1 weeks. In Group A, 13 (43.3%) infants were of gestational age ≤38 weeks, and 17 (56.7%) were >38 weeks. In Group B, 17 (56.7%) were ≤38 weeks and 13 (43.3%) were >38 weeks. The mean birth weight in Group A was 3099.6 ± 282.1 grams, and in Group B it was 3203.6 ± 261.8 grams. In Group A, 8 (53.3%) had birth weight ≤3000 grams, and 22 (48.9%) had >3000 grams. In Group B, 7 (46.7%) had a birth weight ≤3000 grams and 23 (51.1%) had >3000 grams. The mean oxygen duration in Group A was 32.9 ± 2.07 hours, and in Group B it was 78.03 ± 2.9 hours, with a p-value of 0.0001. The mean hospital stay in Group A was 3.1 ± 1.1 days, while in Group B it was 5.7 ± 1.02 days, also with a p-value of 0.0001.

Table 1: Demographic Data of Patients

Category	Salbutamol Group (n=30)	Placebo Group (n=30)	Total (n=60)
Gender			
Male	22 (53.7%)	19 (46.3%)	41 (100.0%)
Female	8 (42.1%)	11 (57.9%)	19 (100.0%)
Gestational Age			
≤38 weeks	13 (43.3%)	17 (56.7%)	30 (100.0%)
>38 weeks	17 (56.7%)	13 (43.3%)	30 (100.0%)
Birth Weight			
≤3000 g	8 (53.3%)	7 (46.7%)	15 (100.0%)
>3000 g	22 (48.9%)	23 (51.1%)	45 (100.0%)

Table 2: Comparison of Oxygen Inhalation Duration and Hospital Stay Between Groups

Variables	Group	n	Mean	Standard Deviation	p-value
Oxygen Duration	Salbutamol	30	32.90	2.07	0.0001
	Placebo	30	78.03	2.94	
Hospital Stay	Salbutamol	30	3.13	1.14	0.0001
	Placebo	30	5.70	1.02	

Table 3: Stratification of Oxygen Duration and Hospital Stay Between Groups concerning Gender, Gestational Age, and Birth Weight

Category	Group	n	Mean	Standard Deviation	p-value
Male - Oxygen Duration	Salbutamol	22	32.73	2.16	0.000
	Placebo	19	78.58	2.12	
Female - Oxygen Duration	Salbutamol	8	33.38	1.85	0.000
	Placebo	11	77.09	3.94	
Male - Hospital Stay	Salbutamol	22	2.86	0.94	0.000
	Placebo	19	5.95	0.85	
Female - Hospital Stay	Salbutamol	8	3.88	1.36	0.000
	Placebo	11	5.27	1.19	
≤38 weeks - Oxygen Duration	Salbutamol	13	33.62	1.66	0.000
	Placebo	17	77.94	2.95	
>38 weeks - Oxygen Duration	Salbutamol	17	32.35	2.23	0.000
	Placebo	13	78.15	3.05	
≤38 weeks - Hospital Stay	Salbutamol	13	2.69	0.95	0.000
	Placebo	17	5.65	1.11	
>38 weeks - Hospital Stay	Salbutamol	17	3.47	1.18	0.000
	Placebo	13	5.77	0.93	
≤3000 g - Oxygen Duration	Salbutamol	8	32.25	2.25	0.000
	Placebo	7	79.00	2.52	
>3000 g - Oxygen Duration	Salbutamol	22	33.14	2.01	0.000
	Placebo	23	77.74	3.05	
≤3000 g - Hospital Stay	Salbutamol	8	2.88	1.36	0.000
	Placebo	7	6.14	1.07	
>3000 g - Hospital Stay	Salbutamol	22	3.23	1.07	0.000
	Placebo	23	5.57	0.99	

[Citation: Javed, S., Roshan, E., Hayyat, M.K., Aftab, M., Javed, N., Mateen, M. (2025). Salbutamol nebulization for the treatment of transient tachypnea of the newborn. *Pak. J. Inten. Care Med.* ***2025****: 43*. doi: https://doi.org/10.54112/pjicm.v5i01.43]

DISCUSSION

Respiratory distress is observed in approximately 1% of newborns, and a substantial subset of these cases—nearly one-third of all neonates admitted for respiratory complications—are ultimately diagnosed with Transient Tachypnea of the Newborn (TTN), especially in neonatal intensive care units (NICUs). Despite its relatively high prevalence, the pathophysiological mechanisms of TTN remain incompletely understood, presenting a diagnostic and therapeutic challenge for clinicians and researchers alike. Nonetheless, delayed clearance of fetal alveolar fluid post-delivery is widely recognised as a central contributing factor to the development of TTN (8–10).

The presence of pulmonary fluid during gestation is essential for normal lung development and structural maturation. This fluid plays a critical role during the transition to extrauterine life, with reabsorption processes typically initiated 2–3 days before delivery (11). At the onset of labour, the fetal lung epithelium undergoes an ionic transport switch—from chloride secretion to sodium absorption—leading to a reversal in the fluid transport direction (12). Sodium ions are actively transported from the alveolar space into lung epithelial cells via Na^+/K^+-K-ATPase pumps, and subsequently into the interstitial space through amiloride-sensitive epithelial sodium (ENaC) channels (13). This sodium-driven process results in the passive movement of water out of the lungs, a mechanism that can be further enhanced by β-adrenergic agonists (14).

Experimental models, particularly those involving β1- and β2-adrenergic receptor knockout mice, have significantly contributed to understanding the underlying mechanisms of pulmonary fluid regulation. These models have underscored the pivotal role of β2-receptors in pulmonary fluid clearance, with β2-agonists like salbutamol being especially effective in accelerating alveolar fluid absorption (15). Complementary research has shown that salbutamol administration leads to marked stimulation of lung fluid absorption, thus supporting its clinical application in conditions like TTN (16,17).

The findings of the current study align well with existing literature. In our trial, the mean oxygen therapy duration in the salbutamol group (Group A) was 32.9 ± 2.07 hours compared to 78.03 ± 2.9 hours in the placebo group (Group B), with a statistically significant difference ($p = 0.000$). Similarly, the average duration of hospitalisation was 3.1 ± 1.1 days in Group A and 5.7 ± 1.02 days in Group B ($p = 0.000$), indicating that salbutamol administration significantly reduced the need for prolonged oxygen supplementation and hospital stay.

These results are corroborated by findings from Kim et al. (18), who conducted a randomised controlled trial in Korea to evaluate the effects of inhaled salbutamol on neonates diagnosed with TTN. In their study of 40 neonates, 28 received salbutamol and 12 received a placebo. Their analysis showed significant improvements in respiratory parameters among the salbutamol group, including reduced respiratory rates, improved oxygen saturation, and shortened NICU stay (19). The p-values for these outcomes were statistically significant (≤ 0.05), further supporting the efficacy of salbutamol in managing TTN (20).

CONCLUSION

Salbutamol, a selective β2-adrenergic receptor agonist, has demonstrated clinical efficacy in the management of Transient Tachypnea of the Newborn by significantly reducing the duration of oxygen therapy and the length of hospital stay. This study provides compelling evidence that the administration of inhaled salbutamol is both safe and effective in expediting recovery in neonates with TTN, without any reported adverse effects. These findings advocate for the consideration of salbutamol as an adjunct to supportive therapy in neonates diagnosed with TTN.

DECLARATIONS

Data Availability Statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department Concerned.

Consent for publication
Approved

Funding
Not applicable

CONFLICT OF INTEREST

The authors declared an absence of conflict of interest.

AUTHOR CONTRIBUTION

SUNDAS JAVED (Resident)
Conception of the study, development of research methodology, study design, critical revision of the manuscript, and final approval of the manuscript.
Final approval of the manuscript and provided significant intellectual input was provided.
EMRAN ROSHAN (Head of Department)
Assisted in manuscript drafting and reference management.
Contributed to statistical analysis and interpretation of data.
MUHAMMAD KHIZAR HAYYAT (Senior Registrar)
Conception of the study, development of research methodology, and study design.
Study design and review of literature.
MARIA AFTAB (Resident)
Conception of the study and final approval of the manuscript.
Manuscript revisions and critical intellectual input.
NIMRA JAVED (Medical Officer)
Data entry, data analysis, and initial drafting of the article.
Manuscript revisions and critical review for important intellectual content.
MARYAM MATEEN (Resident)
Manuscript drafting.
Conception of Study, Final approval of manuscript.

REFERENCES

1. Iramain R, Castro-Rodriguez JA, Jara A, Cardozo L, Bogado N, Morinigo R, De Jesús R. Salbutamol and ipratropium by inhaler is superior to nebuliser in children with severe acute asthma exacerbation: randomised clinical trial. Pediatr Pulmonol. 2019;54(4):372–7.
2. Selewski DT, Gist KM, Nathan AT, Goldstein SL, Boohaker LJ, Akcan-Arikan A, et al. The impact of fluid balance on outcomes in premature neonates: a report from the AWAKEN study group. Pediatr Res. 2020;87(3):550–7.
3. Gupta N, Bruschettini M, Chawla D. Fluid restriction in the management of transient tachypnea of the newborn. Cochrane Database Syst Rev. 2021;1(2): CD013844.
4. Moresco L, Calevo MG, Bruschettini M. Antibiotics for the management of suspected transient tachypnea of the newborn. Cochrane Database Syst Rev. 2018;1(9): CD011595.
5. Ali S, Razzaq A, Shah SA, Ahmad Z. Intravenous furosemide in the management of transient tachypnea of newborn. Pak Armed Forces Med J. 2023;73(3):666–9.

[Citation: Javed, S., Roshan, E., Hayyat, M.K., Aftab, M., Javed, N., Mateen, M. (2025). Salbutamol nebulization for the treatment of transient tachypnea of the newborn. *Pak. J. Inten. Care Med.* ***2025****: 43*. doi: https://doi.org/10.54112/pjicm.v5i01.43]

6. Kim MJ, Yoo J, Jung JA, Byun SY. The effects of inhaled albuterol in transient tachypnea of the newborn. Allergy Asthma Immunol Res. 2014;6(2):126–30.
7. Armangil D, Yurdakok M, Korkmaz A, Yigit S, Tekinalp G. Inhaled beta-2 agonist salbutamol for the treatment of transient tachypnea of the newborn. J Pediatr. 2011;159(3):398–403.
8. Sabry AM, Azeem MA, Ismail MM, El Khatib DH, AbdelAziz IA. Comparison of inhaled salbutamol and intravenous furosemide in the treatment of transient tachypnea of the newborn regarding their safety and efficacy. Alexandria J Pediatr. 2022;35(2):92.
9. Kiliçbay F, Gaffari TU, Ünsal G. Assessment of risk factors to predict the duration of tachypnea in the management of infants hospitalised with transient tachypnea of newborns. Turk J Sci Health. 2022;3(2):114–22.
10. Shi Y, Muniraman H, Biniwale M, Ramanathan R. A review on non-invasive respiratory support for management of respiratory distress in extremely preterm infants. Front Pediatr. 2020;8:270.
11. Beretta E, Romanò F, Sancini G, Grotberg JB, Nieman GF, Miserocchi G. Pulmonary interstitial matrix and lung fluid balance from normal to the acutely injured lung. Front Physiol. 2021;12:781874.
12. Al Lahony DM, Elsayed HM, Mohammed IS. The effects of inhaled β-adrenergic agonists in transient tachypnea of the newborn. Menoufia Med J. 2020;33(3):847.
13. Wang Q, Yan SF, Hao Y, Jin SW. Specialised pro-resolving mediators regulate alveolar fluid clearance during acute respiratory distress syndrome. Chin Med J (Engl). 2018;131(8):982–9.
14. Arif E, Nihalani D. Beta2-adrenergic receptor in kidney biology: a current perspective. Nephrology (Carlton). 2019;24(5):497–503.
15. Bruschettini M, Hassan KO, Romantsik O, Banzi R, Calevo MG, Moresco L. Interventions for the management of transient tachypnoea of the newborn: an overview of systematic reviews. Cochrane Database Syst Rev. 2022;2(2): CD013563.
16. Alexiou S, Panitch HB. Physiology of non-invasive respiratory support. Semin Fetal Neonatal Med. 2016;21(3):174–80.
17. Gunes AO, Bozkaya A. Endotracheal surfactant and budesonide combination therapy in neonatal acute respiratory distress syndrome due to late-onset sepsis. Arch Iran Med. 2024;27(10):573–9.
18. De Luca D, van Kaam AH, Tingay DG, Courtney SE, Danhaive O, Carnielli VP, et al. The Montreux definition of neonatal ARDS: biological and clinical background behind the description of a new entity. Lancet Respir Med. 2017;5(8):657–66.
19. De Luca D, Tingay DG, van Kaam AH, Courtney SE, Kneyber MC, Tissieres P, et al. Epidemiology of neonatal acute respiratory distress syndrome: prospective, multicenter, international cohort study. Pediatr Crit Care Med. 2022;23(7):524–34.
20. Amigoni A, Pettenazzo A, Stritoni V, Circelli M. Surfactants in acute respiratory distress syndrome in infants and children: past, present and future. Clin Drug Investig. 2017;37(8):729–36.

[Citation: Javed, S., Roshan, E., Hayyat, M.K., Aftab, M., Javed, N., Mateen, M. (2025). Salbutamol nebulization for the treatment of transient tachypnea of the newborn. *Pak. J. Inten. Care Med.* ***2025****: 43*. doi: https://doi.org/10.54112/pjicm.v5i01.43]